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Note that following the cancellation of the 2020 congress due to the COVID-19 pandemic many of the abstracts submitted in 2020 were presented at the 2021 congress. To prevent duplication of numbers, the numbering of the 2021 abstracts continued the sequence of the 2020 abstracts.

293. Effectiveness of endoscopic application of human collagen type 1 in the treatment of esophageal chemical burns

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Objective: Evaluation of the effectiveness of endoscopic therapy of human collagen type 1 gel (HCG) in the complex treatment of esophageal chemical burns of patients with poisoning with corrosive substances.
Methods: After institutional review board (IRB) approval and written consent, a prospective, open-label, randomized clinical trial was conducted in the Toxicological Department, N. V. Sklifosovsky Research Institute for Emergency Medicine in 2017-2019. Patients with 3rd degree esophageal chemical burns were randomized 1:1 to the study group (administration of 12.5 mL of 0.7% HCG solution) and the comparison group (standard care). The groups were comparable in age, gender, and severity of the lesion. The HCG solution was injected through the endoscope channel. HCG application was started in 5 patients on days 1-4 and in 26 patients on days 6-11, and then repeated every 2-3 days. The number of applications was determined individually depending on the rate of epithelialization. Data were expressed as median [interquartile range] or number (percentages). The Mann-Whitney test was used. The threshold for statistical significance was set at $p < 0.05$.
Results: Overall, 61 patients were included. There were no local irritating or allergic reactions to ulcerative defects after HCG endoscopic application. Epithelialization began on the 6th [5, 8] day after the start of application versus the 7th [5, 10] ($p < 0.05$) day in the comparison group. Complete epithelialization occured on the 12th [10, 14] day ($p < 0.05$) in the treatment group, and on day 14 [10, 16] in the comparison group. Time spent in intensive care was 5.0 [3, 7] versus 6.0 [3, 10] days, and the total hospitalization period was 17.0 [13, 23] versus 21.0 [13, 30.5] days, respectively. With early HCG therapy complete epithelialization was observed after 10 [7, 12] days, the total period of hospitalization was 11 [6, 18] days ($P < 0.05$). With late collagen application, the epithelialization period did not change, but the period of inpatient treatment was 1.6 times higher (18 [15.0, 23.5] days).
Conclusion: The application of HCG in the complex treatment of 3rd degree esophageal chemical burns can reduce the time to complete epithelialization, the duration of treatment in intensive care, as well as the length of hospital stay. Early use of HCG leads to a 1.6-fold reduction in inpatient treatment time.

294. Characteristics and clinical features of patients attending UK emergency departments with analytically-confirmed exposure to the synthetic cannabinoid MDMB-4en PINACA

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Objective: MDMB-4en PINACA (MDMB-PINACA N1-pentyl-4-en isomer) is a potent indazole synthetic cannabinoid receptor agonist (SCRA) first identified in Europe in 2017. Although previously detected in drug seizures and post-mortem blood samples, there is limited information available on epidemiology or clinical features associated with toxicity. Here we describe the characteristics and clinical features of 17 patients presenting to UK emergency departments with analytically-confirmed MDMB-4en PINACA exposure.
Methods: Patients (≥16 years) presenting to participating hospitals with toxicity after suspected drug misuse have been included in the Identification Of Novel psychoActive substances (IONA) study after informed consent (or agreement of a relative/representative if lacking capacity) since March 2015. Demographic and clinical features are recorded using a structured data collection

sheet. Blood and/or urine samples are analysed using liquid chromatography-tandem mass spectrometry.
Results: MDMB-4en PINACA was detected in at least one sample from 17 (12%) of the 141 patients included in the IONA study in the year October 2019 to September 2020, including 11 recruited between July and September 2020, having not been detected in any samples from 727 patients recruited prior to this. The 17 patients had an age range of 19-60 years (median 34) and 14 were male; a high proportion presented in south west (8/11 IONA recruits) and north east England (2/4) and less commonly in London (3/54), Scotland (3/33) and the east of England (1/4). Common clinical features included Glasgow Coma Score (GCS) < 9 ($n = 8$), pH < 7.35 ($n = 6$), $pCO_2 > 6.5$ kPa ($n = 6$), confusion ($n = 5$), tachycardia >110/min ($n = 5$), agitation ($n = 4$), seizures ($n = 4$) and creatinine >150 μmol/L ($n = 3$). Three patients were intubated and ventilated. Eight patients reported use of "spice" or "mamba" but co-use of other drugs was also commonly reported and at least one additional substance (or a metabolite) was detected in all 17 patients, most commonly diazepam (12), methadone (12), heroin (10), cocaine (8), pregabalin (8), tetrahydrocannabinol (7) and other SCRA (7).
Conclusion: MDMB-4en PINACA has increasingly contributed to UK emergency presentations involving drug misuse over the last year, having not previously been detected in this study. The clinical features described here have been reported after use of other SCRA, but all patients co-used other substances and these are likely to have made an important contribution.

295. Changing patterns of synthetic cannabinoid receptor agonists encountered in UK Emergency Departments

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Objective: Synthetic cannabinoid receptor agonists (SCRA) are commonly encountered new psychoactive substances that are often synthesised in China. Here we report the SCRA commonly detected in patients attending UK emergency departments since 2015 and relate these to changes in legal controls in the UK and China (Table 1).
Methods: Patients (≥16 years) presenting to participating hospitals with toxicity after suspected drug misuse have been included in the Identification Of Novel psychoActive substances (IONA) study after informed consent (or agreement of a relative/representative if lacking capacity) since its launch in March 2015. Demographic and clinical features are recorded and blood and/or urine samples analysed using liquid chromatography-tandem mass spectrometry.
Results: By October 2020 analytical data were available for 866 IONA participants; at least one SCRA was identified in samples from 229 (26%) of these (median age 33 years, range 16-70, 81% males). Commonly identified SCRA (Table 1) have been controlled in the UK since 2016 and the proportion of participants with a SCRA identified declined between 2016 (46%) and 2019 (12%), increasing again slightly in 2020 (19%). MDMB-CHMICA and 5F-AKB 48 (controlled in China in 2015), were most common in 2015-16, while 5F-MDMB-PINACA and AMB-FUBINACA (controlled in China in 2018) were common between 2016 and 2018. The SCRA most commonly identified since 2019, MDMB-4en PINACA, 5F-MDMB-PICA and 4F-MDMB BINACA, have been controlled in the UK since 2016 but remain uncontrolled in China.
Conclusion: Legal controls enacted in the UK (2016) and China (2015, 2018) have influenced the SCRA encountered in patients attending UK emergency departments. The SCRA detected most often since 2019 are illegal in the UK but remain uncontrolled in China. These findings illustrate the relevance of Chinese legislation to the SCRA encountered in the UK and emphasise the importance of international approaches to drug control measures.

Table 1. Frequency of detection of common SCRA (detected in 10 or more patients) in the IONA study.

	Date of control (China)	2015	**2016***	2017	2018	2019	**2020****
Patients recruited		56	171	213	157	156	113
Any SCRA	n/a	24 (43%)	78 (46%)	54 (25%)	33(21%)	18 (12%)	22 (19%)
MDMB-CHMICA	October 2015	16 (29%)	21 (12%)	13 (6.1%)	9 (5.7%)	1 (0.6%)	–
5F-PB 22	October 2015	3 (5.4%)	21 (12%)	1 (0.5)	–	–	–
5F-AKB 48	October 2015	4 (7%)	6 (4%)				
5F-AMB	October 2015	–	–	3 (1.4%)	6 (3.8%)	1 (0.6%)	
5F-MDMB PINACA	August 2018	–	43 (25%)	31 (15%)	17 (11%)	2 (0.9%)	1 (1.2%)
AMB-FUBINACA	August 2018	3 (5.4%)	21 (12%)	34 (16%)	5 (3.2%)	3 (1.9)	–
FUB-NPB 22	Not controlled	1 (1.8%)	22 (13%)	3 (1.4%)	1 (0.6%)	–	–
MDMB-4en PINACA	Not controlled	–	–	–	–	1 (0.6%)	16 (14%)
5F-MDMB-PICA	Not controlled	–	–	–	1 (0.6%)	9 (5.8%)	4 (3.5%)
4F-MDMB BINACA	Not controlled	–	–	–	–	4 (2.6%)	6 (5.3%)

*Supply (and possession in prisons) has been illegal in the UK for all SCRA since May 2016 via the Psychoactive Substances Act. Since December 2016 all SCRA listed in the table have also been controlled as Class B compounds via the Misuse of Drugs Act.
**To 22 October 2020

296. Patterns of teenage heroin exposures reported to the US Poison Centers

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Objective: Heroin use in the US has increased significantly with over 15,000 deaths in the year 2018. We sought to characterize heroin exposures among the teenage population reported to the US National Poison Data System (NPDS).
Methods: The NPDS was queried for all teenage exposures (13-19 years) to heroin reported to the US Poison Centers (PCs) between 2008 and 2018. Cases that resulted in fatalities or major medical outcomes were classified as serious adverse events (SAEs). We descriptively assessed the demographic and clinical characteristics. Trends were analyzed using Poisson regression. Independent predictors of SAEs were studied using multivariable logistic regression with adjusted odds ratios (AOR) reported.
Results: There were 4,619 teenage heroin exposure calls made to the PCs from 2008 to 2018, with the proportion of annual exposures with SAEs increasing from 17.5% to 28.1% during the study (total SAEs 768). Single substance exposures accounted for 57.8% of heroin exposures with SAEs. Of the patients reporting heroin exposures with SAEs, 49.9% were admitted to a critical care unit (CCU). The residence was the most common site of exposure (76.1%), and 86.2% of these cases were en route to the hospital via emergency medical services (EMS) when the PC was notified. Among the SAE exposures, 62% were male, with intentional abuse (82.1%) and suspected suicide (7.8%) commonly observed exposure reasons. During the study period, the proportion of heroin abuse exposure cases (63.1% to 70.2%) and suspected suicides (14.8% to 15.1%) both increased. The most frequently co-occurring substance was benzodiazepines (12.9%). During the study period, the rate of heroin exposures with SAEs increased from 28.5 to 53.8 (per 100,000 teenage exposures) ($p < 0.001$). Males (Ref: females) (AOR: 1.18, 95% CI: 1.01 – 1.41) were at a significantly higher risk of SAE. Other factors that increased the odds of SAEs were multi-substance exposures (Ref: single substance exposures) (AOR: 1.26, 95% CI: 1.01 – 1.57), parenteral routes of exposure (Ref: ingestion) (AOR: 2.43, 95% CI: 1.85 – 3.20), and intentional abuse (Ref: unintentional exposures) (AOR: 1.60, 95% CI: 1.19 – 2.16).
Conclusion: There was a significant increase in reports of teenage heroin exposures with SAEs during the study which may be a result of multiple factors including the cheaper cost of heroin and the adulteration of heroin with fentanyl and analogs. Several key characteristics, including reasons for exposure and the presence of multiple substances in exposure, significantly increased the risk of SAE. Greater intervention and awareness initiatives are needed considering the severity of such overdoses.

297. Fomepizole dosing during continuous renal replacement therapy, an observational study

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Objective: Fomepizole inhibits the formation of toxic metabolites in methanol and ethylene glycol poisoning. The old dosing regimen for fomepizole during dialysis recommends dosing every 4 hours, whereas new recommendations for dosing during continuous renal replacement therapy (CRRT) recommend this interval be increased to every 8 hours. However, the latter is based on a theoretical assumption that less fomepizole is removed during CRRT compared to intermittent hemodialysis, and this has only been demonstrated in one case report [1]. The main objective of the current study was to evaluate whether the new regimen during CRRT provides an adequate plasma concentration of fomepizole (> 10 μmol/L) to inhibit formation of toxic metabolites. We also wanted to study fomepizole kinetics during CRRT.
Methods: We conducted a prospective observational study in patients treated with fomepizole and CRRT. Samples were collected from arterial line, post-filter blood and dialysate up to every hour during the observation period. Fomepizole was measured using high-pressure liquid chromatography with a reverse phase column (sensitivity 5 μM; coefficient of variation 4.5% at 25 μM).
Results: Five patients with suspected or confirmed toxic alcohol poisoning were included in this study. They all received continuous venovenous hemodialysis and fomepizole. All plasma fomepizole concentrations were above the minimum value of 10 μmol/L. The median minimum plasma concentration (the lowest concentration observed before new dosing) was 106 μmol/L, range 58-168 μmol/L. Fomepizole was removed during CRRT treatment with a median saturation coefficient of 0.8 (range 0.5-0.9) and median dialysis clearance of 29 mL/min (range 4-35 mL/min).
Conclusion: This study shows that fomepizole is removed during CRRT and that the new dosage recommendations for fomepizole during CRRT maintains a plasma concentration above the minimum value of 10 μmol/L.

Reference

[1] McMartin K, Jacobsen D, Hovda KE. Antidotes for poisoning by alcohols that form toxic metabolites. Br J Clin Pharmacol. 2016; 81:505–15.

298. Unintentional exposure to immediate-release tramadol in ≤6-year-old children: a nationwide French Poison Control Center study

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Objective: To estimate a clinically relevant toxic dose in children ≤6 years old unintentionally exposed to immediate release (IR) tramadol.
Methods: Retrospective analysis of single unintentional IR tramadol exposures in ≤6-year-old children, collected by the French

Table 1. Moderate-severe neurological complications (PSS2-PSS3) observed in 144 children with accidental tramadol ingestion.

Poison severity score	Symptoms	n (%)
2	Brief apnea/bradypnea not associated with oxygen desaturation and/or not requiring naloxone administration and/or intubation	4 (2.8)
	Agitation	5 (3.5)
	Confusion	4 (2.8)
	Unconsciousness with appropriate response to pain (Glasgow Coma Score 8-13)	6 (4.2)
3	Bradypnea associated with oxygen desaturation and/or requiring naloxone administration and/or intubation	11 (7.6)
	Coma (Glasgow Coma Score ≤7)	2 (1.4)

Poison Control Centers in 2003–2019. The Poison Severity Score (PSS) was used to grade severity.

Results: We found 563 single unintentional IR tramadol exposures in ≤6-year-old children. We analyzed 144 cases involving tramadol alone (age, 3 years [1.9–3.0] (median [25th–75th percentiles]); median ingested dose 5.3 mg/Kg [3.3–11.3]). Eighty-two intoxications (57%) were related to therapeutic errors involving IR tramadol drops. No child presented an underlying neurological/cardiac disease and/or ingested concomitant psychotropic drugs. Half of the children remained asymptomatic (PSS0) while 31%, 11% and 8% developed minor (PSS1), moderate (PSS2), and severe symptoms (PSS3), respectively (Table 1). We found a positive correlation between the ingested IR tramadol dose and the PSS ($p < 0.0001$). We did not observe seizures or death. Using a receiver operating characteristic (ROC) curve approach (area under the curve, 0.93; $p < 0.001$), ingestion of ≥7.4 mg/Kg IR tramadol was appropriate to predict the onset of severe neurological symptoms (PSS2-PSS3; sensitivity, 100% [95% confidence interval (95% CI), 85-100], specificity, 74% [95% CI, 66–81], predictive positive value, 48% [95% CI, 44–65], and negative predictive value, 100% [95% CI, 95–100]). Symptomatic children who ingested <7.4 mg/Kg IR tramadol developed minor symptoms.

Conclusion: In children without underlying neurological/cardiac disease and concomitant psychotropic medications, ingestion of >7.4 mg/Kg IR tramadol alone predicts the onset of severe neurological symptoms.

299. Enquiries to the National Poisons Information Centre, Ireland concerning patients who required tracheal intubation

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Objective: To examine the epidemiology of severe poisoning cases that required intubation including demographics, circumstances, agents and patient outcomes.

Methods: Data was collected prospectively on poisoned patients who required tracheal intubation from January 2009 to December 2019. Information recorded included patient age, sex, number and type of agents ingested and clinical outcome. The agents involved were classified according to the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) Index 2020 [1]. The data were then analysed to determine the most common agent class involved in single and multiple ingestions and the clinical outcome for the patient.

Results: A total of 703 cases were identified where tracheal intubation was required secondary to poisoning during the study period. Of these 373 patients (53%) were male and 26 (3.7%) were 14 years of age or less. In 76 cases (10.8%) there was a fatal outcome and sequelae were documented in 126 cases (17.9%). A single agent was ingested/inhaled in 297 (43.2%) of the cases. Pharmacological agent poisonings accounted for the majority of cases 425 (60.4%), followed by drugs of abuse in 90 (12.8%) cases, industrial agents in 78 (11%) cases and agricultural agents in 23 (3.3%) cases. In 570 (81%) of the cases, poisoning circumstance was classified as intentional, followed by unknown reasons (67 cases, 9.5%) and unintentional poisoning (40 cases, 5.7%). In single agent poisonings, the most common agent classes were antidepressants (37/297, 12.5%), stimulant drugs of abuse (31/297, 10.4%), industrial agents (30/297, 10.1%), unknown agent(s) (27/297, 9%) and antipsychotic medications (22/297, 7.4%). Overall the leading agent classes implicated were antidepressants (264 exposures, 37.5%), sedatives (226 exposures, 32.1%), antipsychotics (179 exposures, 25.5%), anti-epileptics (154 exposures, 21.9%) and stimulant drugs of abuse (93 exposures, 13.2%).

Conclusion: Our analysis of all cases of poisoning reported to the NPIC that required tracheal intubation showed that the majority of cases involved pharmacological agents, and multiple agents, and most patients recovered without sequelae. Interestingly, stimulant drugs of abuse were among the commonest agents reported which is at variance with those reported from the US [2].

References

[1] Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) Index 2020 [cited 15 November 2020]. Available from https://www.whocc.no/atc_ddd_index/

[2] Beauchamp GA, Giffin SL, Horowitz BZ, et al. Poisonings associated with intubation: US National Poison Data System Exposures 2000-2013. J Med Toxicol. 2016;12:157–64.

300. A 2-bag intravenous acetylcysteine regimen results in fewer treatment delays in the management of paracetamol overdose

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Objective: Multiple studies have shown that a 3 bag IV acetylcysteine regimen is associated with frequent and long delays during treatment. A newer two-bag regimen (200 mg/Kg over 4 hours

then 100 mg/Kg over 16 hours) is equally effective at preventing hepatotoxicity and has replaced the three-bag regimen as recommended practice in Australia and other countries. While there is some evidence to suggest that the two-bag regimen is associated with fewer interruptions and delays to treatment, the extent of this difference is still unclear.
Methods: We performed a retrospective cohort study of patients who received IV acetylcysteine for the treatment of paracetamol overdose at Monash Health. We compared a cohort of patients who were treated with the three-bag regimen from October 2009 to October 2013 to a cohort of patients who were treated with the two-bag regimen from February 2014 to May 2020. Medical records were used to source the start time of each infusion and delays were calculated by comparing actual infusion time against prescribed time. Our primary aim was to compare the cumulative length of delays during IV acetylcysteine infusion between patients receiving the three-bag regimen and two-bag regimen for the treatment of paracetamol overdose. Secondary aims were to compare the frequency of delays and to identify causes of delay.
Results: Of 974 patients who received IV acetylcysteine for paracetamol overdose, 313 cases were included in the three-bag cohort and 661 cases in the two-bag cohort. The median (interquartile range) cumulative length of delay during acetylcysteine infusion was significantly longer in the three-bag cohort, compared to the two-bag cohort: 65 (40, 105) minutes versus 35 (15, 70) minutes ($p < 0.01$). Additionally, delays longer than one hour were more common in the three-bag cohort: 51% versus 31% ($p < 0.01$). The occurrence of cutaneous anaphylactoid reactions was associated with significantly longer delays (median 135 minutes versus 60 minutes) and were more frequent in the three-bag cohort (10% of patients).
Conclusion: The two-bag IV acetylcysteine regimen was associated with significantly fewer and shorter delays during acetylcysteine infusion, compared to the three-bag regimen. Cutaneous anaphylactoid reactions were associated with significantly longer delays and occurred more frequently with the three bag regimen.

301. Decision support for toxin prediction using artificial intelligence

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Objective: Every day, poison control centers (PCC) are called for immediate classification and treatment recommendations of acutely intoxicated patients. Usually, the toxin is known, and recommendations can be made accordingly; however, in challenging cases, only symptoms are mentioned, and physicians must rely on clinical experience to predict the correct toxin. Our aim was to establish a machine-learning based computer-aided diagnosis (CADx) system, optimize its performance, and compare its poison prediction performance with physicians experienced in clinical toxicology (CTs).
Methods: The CADx system was trained using 10 different toxins from 8995 patients extracted from the PCC database from 2001-2019. Technical specifications are previously published [1]. All cases were mono-intoxications. Patient symptoms and meta-information (e.g., age group, sex, etiology, toxin point of entry, weekday, etc.) were provided. Prediction was optimized using graph convolutional networks and compared to naïve literature-based approaches and different machine learning baselines. The results were validated against 10 CTs with different experience who each classified 50 cases.
Results: Our CADx system was able to predict the correct toxin with a performance of 0.661 ± 0.013 (F1 micro score) and was significantly superior to naïve literature matching and the machine learning baselines ($p < 0.005$). It also outperformed the CTs. The CADx system was then built into an app which can be used by the CTs in the PCC.
Conclusion: A machine-learning based CADx system trained on a large PCC database may be a valuable tool to support a correct diagnosis in complicated intoxication cases since it optimizes the use of meta-data. Nevertheless, an experienced CT will still be required to critically evaluate the results.

Reference

[1] Burwinkel H, Keicher M, Bani-Harouni D, et al. Decision support for intoxication prediction using graph convolutional networks. In: Martel AL, Abolmaesumi P, Stoyanov D, et al (eds). Medical Image Computing and Computer Assisted Intervention – MICCAI 2020. MICCAI 2020. Lecture Notes in Computer Science, vol 12262. Springer, Cham.

302. "Flu" the Looking-Glass: observational poison center study evaluating adverse events secondary to flumazenil administration over time

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Objective: Benzodiazepine (BZD) overdoses can cause central nervous system depression, decreased ventilatory response, and decreased respiratory rate. Flumazenil is a short-acting competitive antagonist of BZDs. Observational studies demonstrate infrequent but consistent and occasionally severe adverse outcomes following flumazenil administration, including seizures, cardiac dysrhythmias, and even death [1]. Our objective was to evaluate the frequency of adverse events following flumazenil administration in cases reported to the Michigan Poison Center (MiPC) between 2012 and 2019.
Methods: Retrospective chart review, approved by our Institutional Review Board, of MiPC cases involving flumazenil between 2012 and 2019. Poison center database queried for "flumazenil" along with study inclusion criteria, including: age, sex, adverse effects, changes in mental status, history of chronic BZD use or seizure disorder, exposure to proconvulsant agents, and co-administration of naloxone. Cases were excluded if miscoded and/or patient did not receive flumazenil.
Results: There were 299 cases coded for flumazenil from 2012-2019; 46 were excluded due to incorrect coding, resulting in 253 cases for analysis. Demographics included 60.5% female (153/253), mean age of 33 years. There were 33 pediatric patients (<18 years). Response to flumazenil was recorded in 212 (84%) patients. The majority (152/212) had some effect [awake (79),

improved consciousness (50), minimal response (18), agitated (5)], while 60 had no response. Nearly 40% (101/253) had no symptom recurrence, while re-sedation occurred in 24% (60/253); 89 cases reported no initial response to flumazenil or had insufficient documentation. The overall frequency of adverse events was 11% (28/253); frequency of serious adverse events was lower. The most common adverse event was agitation (23/28). Five patients had serious outcomes, including dysrhythmia (1/28), neurological deficits (1/28), and seizures (3/28), one of whom died. Greater than half (53.57%) who developed adverse events were chronic BZD users. A total of 118 (46.6%) patients received naloxone during treatment. Proconvulsant substances were present in 26.9% (68/253) of cases. Two patients developed seizures; one was a chronic BZD user. The other patient developed seizures, but had no known exposure to proconvulsant substances and no history of seizures or chronic BZD use. The most common proconvulsant substance was baclofen (9 cases).

Conclusion: Flumazenil administration resulted in a low frequency in overall adverse events, including serious adverse events, in cases reported to the MiPC from 2012 to 2019.

Reference

[1] Kreshak AA, Cantrell FL, Clark RF, et al. A poison center's ten-year experience with flumazenil administration to acutely poisoned adults. J Emerg Med. 2012;43:677–82.

303. The impact of the first wave of COVID-19 on Poison Centre (PC) activities in 4 European countries: a pilot study

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Objective: In February 2020, coronavirus disease (COVID-19) reached Europe and from March, national restrictions and lockdowns were ordered [1]. Also, cleaning and disinfectant protocols were recommended. While US poison control centers reported increased exposures to cleaners and disinfectants during the pandemic [2], the impact of COVID-19 on European PCs activities are unknown. This pilot study evaluated changes in PCs activities in 4 European countries during the first lockdown.

Methods: The major lockdown dates were March 4 (Pavia, Italy (IT)), 13 (Denmark (DK) and Switzerland (CH)), and 16 (The Netherlands (NL)) [1]. We compared the number of calls reported to PCs in March-April 2020 with March-April in 2018 and 2019 (average). We collected: type of caller, age group, reason for exposure and specific exposure (antidepressant, benzodiazepine, antiviral, disinfectant (ECHA-PP-BIO-1/2), cleaning product (ECHA-PC-CLN-2/3) and recreational drugs). Data were normalized to the total number of calls and compared between years. Increases or decreases of 10% in parameters with $N > 5$ were considered a change.

Results: The average number of monthly calls was around 3000 in all centres. No common COVID-19 effect was observed on the total number of calls; a decrease was observed in the Netherlands and Italy, with an increase in Denmark. Calls from the public increased (March 32%, April 22%, CH/DK/IT), while medical professional calls decreased (March 19%, April 24%, CH/IT/NL). More calls concerning small children (0-4 years) occurred (March 15%, April 10%, DK/IT). No common effect was seen for reason of exposure (accidental or intentional), and exposures to cleaning products, antidepressants and benzodiazepines. Very few calls involved antivirals (<5/month) were registered in all countries. Calls about hand disinfectants (March 250%, April 247%, CH/DK/IT/NL) and surface disinfectants markedly increased (March 209%, April 116%, CH/DK/IT/NL). Also, a decrease in alcoholic beverage exposures was observed (March 25%, CH/DK/IT/NL), whereas cannabis exposures increased (April 31%, CH/DK/NL).

Conclusion: The COVID-19 pandemic impacted PCs activity differently in the 4 countries, although several common trends could be identified. PC data can aid in toxicovigilance and expanding data collection with additional countries could strengthen these observations. Although harmonization of data collection proved challenging, this pilot study has paved the way for further collaboration.

References

[1] European Centre for Disease Prevention and Control. Data on country response measures to COVID-19 [cited 16 November 2020]. Available from https://www.ecdc.europa.eu/

[2] Chang A, Schnall AH, Law R, et al. Cleaning and disinfectant chemical exposures and temporal associations with COVID-19 – National Poison Data System, United States, January 1, 2020-March 31, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:496–498.

304. A networked approach to a SARS-CoV-2 information hotline in the state of Florida – design, implementation, and lessons learned

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Objective: Dissemination of accurate health information from a single source during public health emergencies historically has presented challenges to state and local authorities. The public health response to SARS-CoV-2 in the state of Florida, the third most populous state (est. over 21 million citizens) in the US, has presented unique challenges that were addressed through the three poison control centers in Florida that comprise the Florida Poison Information Center Network (FPICN). The FPICN had previous experience with pandemic responses including the Deepwater Horizon Gulf Oil Spill, the H1N1 Influenza event, and the Zika Virus outbreak. Additionally, Florida's geography has required FPICN to prepare and mitigate when natural disasters, such as hurricanes, impact operations.

Methods: FPICN was asked to assist in the response to the SARS-CoV-2 outbreak for the State of Florida on March 13, 2020. After the governor of Florida's declaration of a State of Emergency, the Florida Department of Health (FDOH), recognizing the impending health crisis, established an information hotline to provide accurate information that could be updated as

our understanding of SARS-CoV-2 evolved. As news of the viral outbreak spread, FDOH call-center staff were swiftly overwhelmed and the hotline was transitioned to the FPICN. Infrastructure, staff, guidelines, and processes were implemented, building on experience from previous public health scenarios, but on a scale and timeline unique to this event.
Results: Peak call volume for the hotline was on March 16, where 4,036 calls were made to the hotline. Unlike average poison center calls, these calls took considerably more time. Frequently asked questions (FAQs) were developed and expanded from 100 to more than 150. Each center hired an average of 13 full-time staff for the hotline to minimize the impact on normal poison center operations. Resources were developed for the hotline staff, just-in-time training on call center operations, and prospective data collection tools and reports were developed. Since implementation, the FPICN has answered more than 70,700 hotline calls.
Conclusion: We will describe the process of implementing an efficient medical information hotline through a network of poison control centers using ancillary staff on short notice, lessons learned, data collection procedures and reporting, and how previous experiences allowed scaling up to address a protracted public health event.

305. Intentional poisoning cases reported to the National Poisons Information Centre, Ireland during the initial lockdown phase of COVID-19 public health restrictions

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Objective: The first case of COVID-19 in the Republic of Ireland was confirmed on 29 February 2020. Emergency public health restrictions were introduced on 12 March with school closures and a further "Stay at home" order ("lockdown") on 27 March 2020. COVID-19 has been a cause of anxiety for many and there was a reluctance to attend healthcare facilities. Emergency department (ED) attendances declined by approximately 50% in March 2020 [1]. We aimed to characterise the epidemiology of intentional self-poisoning cases reported to the NPIC during the initial 2-months of a national COVID-19 lockdown compared to the same period in 2019 and 2018.
Methods: A retrospective review of enquiries to the NPIC from 1 March to 30 April inclusive for 2020, 2019 and 2018 was conducted. Data on poisoning circumstances, patient demographics, source of enquiry, agent(s), and the Poisoning Severity Score (PSS) were collated, and chi-squared statistics used to analyse results.
Results: During the initial 8-weeks of the lockdown, the NPIC received 166 enquiries concerning intentional poisoning representing 7.9% of total enquiries, compared to 233 (12.5%) and 207 (11.2%) deliberate poisoning enquiries in 2019 and 2018, respectively [$p < 0.0001$]. Patient demographics showed that approximately two thirds of cases were female for each of the 3 years and the mean age was 32.8 years in 2020 compared to 30.4 years and 35.3 years for 2019 and 2018, respectively. The majority of enquiries originated from hospitals; 72.30% in 2020, 82.83% in 2019 and 78.32% in 2018. During the lockdown, there was a significant increase in enquiries to NPIC from General Practitioners (16.3%) compared to 9.9% and 10.4% in 2019 and 2018, respectively [$p = 0.0071$]. For the 3 time periods, the majority of cases were either asymptomatic or had a mild to moderate PSS when the NPIC was contacted. A severe PSS was assigned to 7.2% of cases in 2020 compared to 4.8% and 3.9% of cases in 2019 and 2018. Paracetamol, alcohol, and pregabalin were among the top 5 agents involved in intentional poisoning for each year.
Conclusion: During the COVID-19 lockdown, there was a significant reduction in the incidence of intentional poisonings reported to the NPIC. Enquiries from hospitals decreased, reflecting the decrease in national ED presentations [1]. There was a significant increase in enquiries to NPIC from General Practitioners during COVID-19 lockdown.

Reference

[1] Brick A, Walsh B, Keegan C, et al. COVID-19 and emergency department attendances in Irish public hospitals [cited 9 November 2020]. Economic and Social Research Institute (ESRI) Special Article. Available from https://www.esri.ie/system/files/publications/QEC2020SUM_SA_lyons.pdf

306. Recreational drug toxicity Emergency Department presentations during the initial months of the COVID-19 pandemic

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Objective: The COVID-19 pandemic has changed the number and type of Emergency Department (ED) presentations around the world. Poisonings and specifically recreational drug toxicity presentations have also been affected. Our aim was to understand the pandemic-influenced differences in characteristics of patients presenting with recreational drug toxicity to our ED since the declaration of national lockdown compared to the same period of the previous year.
Methods: Descriptive cross-sectional observational review of patients presenting with recreational drug toxicity to a tertiary ED through a query of the Clinical Toxicology Unit registry. Clinical variables collected were age and sex, type of drug, single or multiple use and disposition between 15 March and 15 October 2020, compared to the same period in 2019. Chi-square was used for categorical variables and t student test for independent data.
Results: During the study period, there were 39.5% less ED presentations as compared to the previous year. Recreational drug toxicity presentations also fell, but only 17.7% (Table 1). Median and mean age were increased in 2020 with similar distribution by sex. A non-significant increase in multiple drug use presentations was seen in 2020 compared to 2019. In 2020 two drugs were used by 65 patients (28%), three drugs in 18 (7.8%) and four drugs in 2 patients (0.8%). The most commonly used substances are shown in Table 1 with significant decreases in the use of amphetamines and coingestion of alcohol. There was a significant increase in admissions among these patients, with no deaths seen in either year.
Conclusion: Recreational drug presentations decreased in a lesser proportion as compared to overall ED presentations during the first months of the COVID-19 pandemic. The age of patients

Table 1. Comparison of recreational drug toxicity presentations during the 2020 COVID-19 pandemic and the same period of the previous year (abstract 306).

	Year		
15 March–15 October	2019	2020	p*
Total presentations	129,656	78,466	
Recreational drug toxicity presentations (%, as related to total ED visits)	282 (0.22%)	232 (0.31%)	<0.00001
Age (years)			
mean	31.7	36.9	0.301
median	29.5	37	
range	13–74	4–68	
Sex, male (N, %)	200 (70.9%)	164 (70.7%)	0.954021
Substance			
Single substance (N, %)	190 (67.3%)	147 (63.3%)	0.340575
Multiple substances (N, %)	92 (22.7%)	85 (36.7%)	
Substance involved			
Cannabis (N, %)	146 (51.8%)	132 (56.9%)	0.24607
Cocaine (N, %)	131 (46.5%)	126 (54.3%)	0.076273
Amphetamines (N, %)	60 (21.3%)	10 (4.3%)	<0.00001
Heroin (N, %)	21 (7.4%)	21 (9.1%)	0.508607
Spice (N, %)	2 (0.7%)	0	0.680328
LSD (N, %)	2 (0.7%)	1 (0.4%)	0.375208
Ketamine (N, %)	5 (1.8%)	2 (0.9%)	0.248699
Unknown (N, %)	6 (2.1%)	2 (0.9%)	<0.00001
Alcohol coingested (N, %)	196 (69.5%)	114 (49.1%)	0.004621
Benzodiazepines coingested (N, %)	26 (9.2%)	41 (17.7%)	0.416532
Other medication (N, %)	3 (1.1%)	1 (0.4%)	
Arrived by ambulance (N, %)	167 (59.2%)	139 (59.9%)	0.87327
Disposition			
Discharged from ED (N, %)	256 (90.8%)	195 (84%)	0.020626
Self-discharged (N, %)	4 (1.4%)	6 (2.6%)	0.340147
Admitted (N, %)	22 (7.8%)	31 (13.4%)	0.039118
Psychiatry	11	15	0.186699
Intensive care	2	5	0.159277
Other wards	9	11	0.365881
Death (N, %)	0	0	

presenting has increased, as well as the need for admission. The most common drugs used continue to be cannabis and cocaine with alcohol and/or benzodiazepine being frequent coingestants.

307. Foodborne botulism: a large outbreak in Sicily

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Objective: In September-October 2020 our Poison Centre (PC) managed a cluster of 44 workmen who consumed food contaminated by botulinum neurotoxins (BoNT) at a workplace canteen in Sicily.

Case series: Of the 100 workers using the canteen, 44 presented over a 7-day period to 6 Emergency Departments (ED) in Southern Italy complaining of neurological and gastrointestinal symptoms (Table 1). Our PC, consulted first by physicians in Cefalù, made the diagnostic suspicion of foodborne botulism. Heptavalent-botulism-antitoxin (HBAT) was mobilized from different National Stockpiles (Catania, Pavia, Rome, Trieste, Naples) after approval from the Ministry of Health (MoH). The early admitted patients (7/44, 17%, 2-days after meal) worsened rapidly and 5/7 required mechanical ventilation (MV) within 24 hours. Patients with minor symptoms were discharged and managed with telephone follow-up by PC toxicologists.

Conclusion: Botulism diagnosis is based on clinical suspicion; laboratory testing has a crucial role in confirmation, but analyses do not always demonstrate BoNT (15/36 tested positive in our cluster). Therefore, the positivity of at least 1 patient of a cluster confirms the diagnosis. The antitoxin should be administered as soon as clinical suspicion is made. In our outbreak, HBAT was administered due to rapid worsening of neurological symptoms, in order to prevent MV. The rapid deterioration of the first 7 patients is attributable to the ingestion of higher titre of toxin. In Italy, HBAT in the National Stockpile can be mobilized only after MoH approval. The management of the outbreak was challenging because of difficulties in the capacity of the hospitals and the urgent need for antitoxin. An efficient collaboration between local physicians, clinical toxicologists, MoH and the National Stockpile system ensured optimal management with prompt HBAT mobilization in sufficient number. This was also possible because it occured before the second COVID-19 wave in which it would have been difficult to manage 44 patients potentially requiring ICU monitoring.

Table 1. Characteristics of 44 patients in a large foodborne botulism outbreak in Sicily.

Patients characteristics (n = 44)	Median [25th-75th percentile] %
Median age (years)	48 [43-54]
Gender	100% male
Median time between contaminated meal and ED admission (days)	4 [3.5-4.5]
Main clinical manifestations	
Dysphagia	67%
Dysphonia	44%
Blurred vision	44%
Diplopia	25%
Diarrhea	25%
Constipation	18%
Respiratory distress	18%
Vomiting	16%
Ptosis	11%
Mydriasis	9%
Clinical departments involved in the hospitalization of the 44 patients admitted to 6 EDs (38-Cefalù, 2-Caserta, 1-Palermo, 1-Enna, 1-Isernia, 1-Teramo)	
Emergency departments	20/44 (45%)
Internal Medicine	13/44 (30%)
Intensive Care Units	7/44 (16%)
Neurology	4/44 (9%)
Main management	
Activated charcoal	44/44 (100%)
Mechanical ventilation	5/42 (11%)
Antidotal treatment (HBAT)	22/44 (50%)
Adverse reactions after HBAT	0/22
Median length of hospitalization (days)	11.5 [6.75-15.5]
Outcome	100% fully recovered
Specific diagnostic tests	
Presence of BoNTs in fecal samples	15/36 performed (42%)
Electromyography (EMG)/electrical neurography (ENG) compatible with botulism	2/2 performed (100%)

HBAT, heptavalent bolulism antitoxin.

308. Shiitake dermatitis: a French nationwide study 2014–2019

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Objective: Shiitake mushroom (*Lentinus edodes*) is an edible fungus, initially grown in Japan and China, which is becoming more commonly marketed in Europe. We previously reported a systematic retrospective study on shiitake dermatitis (n = 15) [1], and the aim of this study is to describe the evolution of the number of shiitake dermatitis cases since 2014, the clinical characteristics and risk factors.

Case series: This observational study was a prospective review of French Poison Control Centers database cases between 1 January 2014 and 31 December 2019. Of 125 shiitake exposures, we identified 59 cases of dermatitis: male:female sex ratio of 1.8:1; ages ranged from 19 to 69 (median 39) years. Each case was assessed for causality. Dermatitis occurred after raw or undercooked shiitake consumption (e.g., wok, soup, pizza). The rash appeared 1 to 168 hours (median 48 hours) after shiitake ingestion. Linear, erythematous, urticarial papules and plaques (flagella dermatitis), scattered on the trunk, arms and legs within a few hours and persisted for 1 to 40 days (median 10 days). The amount of shiitake (<60 g versus 60-150 g versus >150 g) eaten significantly increased the duration of dermatitis (median days 4 versus 7 versus 15) (p = 0.007). Thirty-eight patients received corticosteroids, antihistaminic drugs, or both without demonstrated benefit. All cases made a complete recovery.

Conclusion: The mechanism of shiitake dermatitis is thought to be caused by lentinan, a heat-labile polysaccharide component [2]. Inadequate cooking clearly seems a determinant of the occurrence of shiitake dermatitis. Some authors postulate an unpredictable, immune-mediated response, occurring in genetically predisposed individuals, independently of dose, representing a hypersensitivity mechanism [3]. Our study demonstrates that there is a dose-dependent response, representing a toxic mechanism. Treatment is focused on symptom management. Health professionals and the general population should be aware of both the risk associated with consumption of inadequately cooked shiitake and of the good prognosis of this still poorly known toxic dermatitis.

References

[1] Boels D, Landreau A, Bruneau C, et al. Shiitake dermatitis recorded by French Poison Control Centers – new case series with clinical observations. Clin Toxicol (Phila). 2014;52:625–8.

[2] Nguyen AH, Gonzaga MI, Lim VM, et al. Clinical features of shiitake dermatitis: a systematic review. Int J Dermatol. 2017;56:610–6.

[3] Corazza M, Zauli S, Ricci M, et al. Shiitake dermatitis: toxic or allergic reaction? J Eur Acad Dermatol Venereol. 2015;29:1449–51.

309. Severe cardiac and neurological toxic effects due to synthetic cannabinoid cumyl-pegaclone (SGT-151) alone: a case report

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Objective: Over the last decades, the recreational use of novel psychoactive substances (NPS) has dramatically increased and represents a growing public health concern. Synthetic cannabinoid receptor agonists (SCRAs) are the largest group of NPS and are usually incorporated into fragrances/pot pourri and incense with a warning label "not for human consumption". Their popularity is due to intense psychoactive effects, lack of detectability in standard drug tests and their legal status in most jurisdictions. Cumyl-pegaclone (SGT-151) was the first cumyl-carrying SCRA with a gamma-carboline-1-one core structure and appeared for the first time on the German drug market in 2016. Cumyl-derivatives are the most potent SCRAs currently available on the NPS market. We report severe neurological and cardiac toxic effects in a patient with analytical confirmation of cumyl-pegaclone exposure not associated with any other substances.
Case report: A 28-year-old male was admitted to the emergency department (ED) with spatial-temporal disorientation, vomiting and sweating. His friends reported tonic-clonic muscle contractions in his upper limbs. His past medical history was positive for bilateral congenital deafness and negative for medications or drug abuse. He reported that he had ingested an alcoholic beverage (about 750 mL of wine) during a graduation dinner the previous night. He denied substance of abuse exposure. The patient presented hypertension, metabolic acidosis (base excess -22 mEq/mL) and atrial fibrillation with rapid ventricular response (190 bpm). As tests for the usual drugs of abuse and ethanol were negative, neurovascular and cardiovascular disorders were initially suspected. Sodium bicarbonate and flecainide were infused with complete cardioversion after 20 minutes and rapid resolution of acidosis. The echocardiogram and computerised tomography (CT) total body scans were normal. On the hypothesis of an acute poisoning, our Poison Center was consulted and indicated second level toxicological analysis which detected cumyl-pegaclone. No other new psychoactive substances were detected. He had clinical improvement in the following days; an electroencephalogram (EEG) revealed subclinical temporal lobe anomalies and he was discharged on day 6 in good clinical condition with levetiracetam 500 mg BID.
Conclusion: SCRA intoxication can lead to life-threatening conditions and diagnosis of SCRA acute poisoning may be a challenge. Particularly, clinical data concerning human toxic effects of cumyl-pegaclone are limited and, to date, all reported cases were associated with ethanol or other drugs of abuse. Our patient developed neurological and cardiac symptoms reasonably related to cumyl-pegaclone solely. Acute neurological and cardiovascular overstimulation in patients suspected of drug abuse could be investigated for SCRAs poisoning and cumyl-derivative intoxication.

310. Beta-hydroxybutyrate closed the gap in a sober patient with high anion gap metabolic acidosis: a case report

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Objective: Alcoholic ketoacidosis (AKA) is a common reason for admission of alcohol dependent patients in emergency departments. We report a case of high anion gap metabolic acidosis (HAGMA) due to increased concentrations of beta-hydroxybutyrate (BHB). Only a few cases with comparable concentrations of BHB, have been reported [1]. With this case report we want to raise awareness of underdiagnosed, but clinically important AKA.
Case report: A 68-year-old male was admitted at the emergency department in a stuporous state. Initial laboratory work-up showed HAGMA (pH 6.85, anion gap 49 mmol/L) with a high osmolal gap (39 mOsm/Kg). Laboratory results revealed acute kidney failure and ketonuria. Anamnesis was vague and incoherent, but the patient claimed that he did not abuse alcohol or drugs. This was initially supported by a negative ethanol concentration in serum. Causes of HAGMA were investigated with normal lactate, negative urine drug screening and normal concentrations of acetaminophen, salicylates, methanol and ethylene glycol. However, the toxicology report showed an elevated concentration of acetone (52 mg/dL) and propylene glycol, which contributed respectively 10 mOsm/Kg and 6 mOsm/Kg of the osmolal gap. Since the patient was known to have a history of alcohol abuse and had an incoherent anamnesis, BHB concentrations were analyzed as a possible cause of HAGMA. An extreme value of 2040 mg/L was measured, closing the osmolal gap with 23 mOsm/Kg. Further analysis of carbohydrate-deficient transferrin (2.2%), together with elevated liver enzymes, confirmed the recent alcohol abuse. He was transferred to the intensive care unit where he received hemodialysis and a sodium bicarbonate infusion leading to clinical improvement.
Conclusion: AKA is a cause of severe metabolic acidosis associated with severely elevated concentrations of BHB, which typically occurs in malnourished patients with a history of a recent alcoholic binge. A BHB above 260 mg/L is potentially fatal without treatment [2]. Therefore, rapid diagnosis is essential. In conclusion, we want to emphasize the importance of considering AKA as a life-threatening cause of HAGMA. Analysis of BHB can close the HAGMA gap in patients with AKA.

References

[1] Noor NM, Basavaraju K, Sharpstone D. Alcoholic ketoacidosis: a case report and review of the literature. Oxf Med Case Reports. 2016;2016:31–3.
[2] Iten PX, Meier M. Beta-hydroxybutyric acid-an indicator for an alcoholic ketoacidosis as cause of death in deceased alcohol abusers. J Forensic Sci. 2000;45:624–32.

313. Poisoning by central stimulant drugs in Oslo, Norway

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Objective: The use of central stimulant drugs causes significant morbidity. The life-time prevalence of use in Norway is 5.0% for cocaine, 4.1% for amphetamine, and 2.3% for 3,4-methylenedioxymethamphetamine (MDMA). We describe poisonings with central stimulant drugs and compare amphetamine, cocaine, MDMA, and other/unspecified central stimulants concerning clinical features, treatment, and co-intoxicants.
Methods: Patients presenting at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) with poisoning related to the recreational use of central stimulant drugs from 1 October 2013 to 31 March 2016 were retrospectively included. Most poisonings related to recreational drug use in Oslo are treated at the OAEOC, a primary care emergency outpatient clinic with limited diagnostic and therapeutic resources available. Diagnosis of toxic agents was based on the clinical assessment of the doctor treating the patient. No toxicological laboratory analyses were done. Amphetamine and methamphetamine were co-categorised as amphetamine.
Results: There were 1131 cases of acute poisoning with central stimulant drugs during two and a half years. Median age was 30 years, 862 (76%) were male. Amphetamine was taken in 808 cases (71%), cocaine in 252 (22%), MDMA in 104 (9%), methylphenidate in 13 (1%). Tachycardia occurred in 44% of cases, agitation in 28%, tachypnoea in 18%, anxiety in 14%, psychosis in 13%, hallucinations in 8%, chest pain in 7%, and palpitations in 6%. Hyperthermia was only seen in 1% of cases, all involving amphetamine. Among cocaine cases, anxiety (23%), chest pain (20%), and palpitations (16%) were particularly common, as were agitation (78%), psychosis (52%), and hallucinations (17%) among unknown stimulant cases. Ethanol was involved in 32% of total cases, but as many as 70% of MDMA cases and 65% of cocaine cases. Opioids were involved in 41% of amphetamine cases, and benzodiazepines in 29%. Naloxone was given in 9% of all cases, and sedation in 5%. Median observation time at the OAEOC was 3 h 1 min (IQR 1 h 38 min – 5 h 12 min). In total 17% were sent on to a somatic hospital and 8% to a psychiatric hospital, while among unknown stimulant cases 26% and 48% were sent on to a somatic or psychiatric hospital, respectively.
Conclusion: Amphetamine was the most common central stimulant drug involved in acute poisoning in Oslo, often combined with opioids and benzodiazepines. Cardiac symptoms were frequent when cocaine was involved, while cases involving unknown stimulants had more severe psychiatric symptoms.

314. Acute poisoning from concurrent use of opioids and amphetamine

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Objective: Concurrent use of opioids and amphetamine is frequent. We describe demographics, additional drugs taken, clinical features, treatment, and clinical course for patients treated for acute poisoning involving a combination of opioids and amphetamine, compared with separate poisonings of the two.
Methods: Patients treated for acute poisoning involving opioids and/or amphetamine were retrospectively included at a primary care emergency outpatient clinic and at a hospital emergency department in Oslo, Norway from October 2013 to September 2016. Diagnosis of toxic agents was based on the clinical assessment of the doctor treating the patient. Toxicological laboratory analyses were not routinely performed, and hence not reported here. Both amphetamine and methamphetamine were categorised as amphetamine. Results were analysed separately for the two centres.
Results: In total, 3038 cases were included at the outpatient clinic and 254 at the hospital. Demographics, clinical features, treatment, and clinical course are presented in Table 1. Among the cases involving opioids and amphetamine, the most frequent additional drugs were benzodiazepines in 36% (148/407) of cases at the outpatient clinic, and gamma-hydroxybutyrate (GHB) in 32% (17/53), benzodiazepines in 26% (14/53), and cocaine in 21% (11/53) at the hospital.
Conclusion: Patients with poisoning involving both opioids and amphetamine presented with symptoms attributable to both drug groups. Patients with combined poisoning were not more

Table 1. Demographics, clinical features, treatment, and clinical course for patients with acute poisoning involving a combination of opioids and amphetamine compared to opioids and amphetamine alone.

	Opioids and amphetamine combined n (%)	Opioids, no amphetamine n (%)	Amphetamine, no opioids n (%)
Outpatient clinic	407 (100)	2047 (100)	584 (100)
Males	317 (77.9)	1650 (80.6)	431 (73.8)
Age (years)[a]	32 (26–39)	38 (30–46)	33 (27–42)
Bradypnoea (< 10/min)	40 (9.8)	334 (16.3)	7 (1.2)
Tachycardia (≥ 100/min)	133 (32.7)	346 (16.9)	262 (44.9)
Hyperthermia (≥ 39.0 °C)	6 (1.5)	11 (0.5)	7 (1.2)
Hallucinations	20 (4.9)	19 (0.9)	71 (12.2)
Agitation	61 (15.0)	240 (11.7)	184 (31.5)
Psychosis	17 (4.2)	17 (0.8)	102 (17.5)
Arrhythmias	1 (0.2)	5 (0.2)	1 (0.2)
Glasgow Coma Score			
15	175 (43.1)	610 (29.9)	375 (64.8)
8–14	221 (54.4)	1380 (67.6)	198 (34.2)
3–7	10 (2.5)	51 (2.5)	6 (1.0)
Sedation	8 (2.0)	7 (0.3)	29 (5.0)

(*continued*)

Table 1. Continued.

	Opioids and amphetamine combined n (%)	Opioids, no amphetamine n (%)	Amphetamine, no opioids n (%)
Naloxone	108 (26.5)	625 (30.5)	16 (2.7)
Length of stay (hours:minutes)[a]	4:42 (2:32–6:16)	4:36 (2:35–6:11)	2:42 (1:28–4:40)
Transferred somatic hospital	71 (17.4)	327 (16.0)	89 (15.2)
Transferred psychiatric hospital	9 (2.2)	14 (0.7)	72 (12.3)
Hospital	53 (100)	109 (100)	92 (100)
Males	39 (73.6)	79 (72.5)	69 (75.0)
Age (years)[a]	31 (22–39)	35 (27–41)	34 (28–39)
Cardiac arrest	4 (7.5)	10 (9.2)	2 (2.2)
Bradypnoea (< 10/min)	7 (13.2)	25 (22.9)	6 (6.5)
Tachycardia (≥ 100/min)	15 (28.3)	18 (16.5)	24 (26.1)
Hyperthermia (≥ 39.0 °C)	6 (11.3)	7 (6.4)	4 (4.3)
Hallucinations	4 (7.5)	6 (5.5)	18 (19.6)
Agitation	21 (39.6)	37 (33.9)	41 (44.6)
Psychosis	2 (3.8)	2 (1.8)	13 (14.1)
Arrhythmias	7 (13.2)	10 (9.2)	3 (3.3)
Glasgow Coma Score			
15	13 (26.5)	24 (22.4)	24 (26.4)
8–14	20 (40.8)	39 (36.4)	34 (37.4)
3–7	16 (32.7)	44 (41.1)	33 (36.3)
Sedation	12 (22.6)	15 (13.8)	34 (37.0)
Naloxone	31 (58.5)	77 (70.6)	26 (28.3)
Length of stay (hours:minutes)[a]	23:35 (8:05–50:20)	17:48 (8:45–33:45)	12:49 (6:50–21:58)
Admitted intensive care	51 (96.2)	100 (91.7)	83 (90.2)
Died in hospital	1 (1.9)	2 (1.8)	–

[a]Median (interquartile range).

likely to be admitted to hospital or intensive care, but stayed longer in hospital.

315. Acute recreational drug toxicity among young patients

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Objective: Recreational drug use is frequent among adolescents and young adults. We describe toxic agents taken, clinical features, clinical course, and treatment among young patients presenting with acute recreational drug toxicity.

Methods: We included patients presenting with acute recreational drug toxicity to a primary care emergency outpatient clinic in Oslo, Norway from October 2013 through March 2017, and excluded patients with sole alcohol intoxications. Data were collected from the local electronic patient records and observational charts. Cases were divided into age groups; ≤17 years, 18-20 years, 21-25 years and ≥26 years.

Results: There were 5045 cases with age recorded; 49 (1.0%) ≤ 17 years, 228 (4.5%) 18–20 years, 806 (16.0%) 21–25 years, and 3962 (78.5%) ≥ 26 years; 1164 (23.1%) were females. Clinical

Table 1. Clinical course, treatment, and toxic agents in young people with acute recreational drug use.

	≤ 17 years n (%)	18–20 years n (%)	21–25 years n (%)	≥ 26 years n (%)
Females	25 (49.0)	69 (30.3)	263 (32.6)	808 (20.4)
Brought by ambulance	21 (42.9)	123 (53.9)	422 (52.4)	2330 (58.8)
Length of stay	2:16 (1:29–3:31)	2:57 (1:39–5:13)	3:01 (1:36–5:13)	4:00 (1:57–5:47)
Treatment beyond observation	5 (10.2)	43 (18.9)	165 (20.5)	961 (24.3)
Treatment – naloxone	3 (6.1)	25 (11.0)	105 (13.0)	742 (18.7)
Treatment – sedation	–	5 (2.2)	28 (3.5)	62 (1.6)
Transferred somatic hospital	11 (22.4)	41 (18.0)	138 (17.1)	716 (18.1)
Transferred psychiatric hospital	2 (4.1)	12 (5.3)	47 (5.8)	155 (3.9)
Toxic agents				
Cannabis	26 (53.1)	75 (32.9)	171 (21.2)	359 (9.1)
Amphetamine	4 (8.2)	49 (21.5)	191 (23.7)	891 (22.5)
Heroin	4 (8.2)	47 (20.6)	297 (36.8)	1919 (48.4)
Benzodiazepines	9 (18.4)	43 (18.9)	231 (28.7)	1292 (32.6)
Cocaine	1 (2.0)	20 (8.8)	95 (11.8)	217 (5.5)
Gamma-hydroxybutyrate (GHB)	1 (2.0)	19 (8.3)	100 (12.4)	400 (10.1)
3,4-Methylenedioxymethamphetamine (MDMA)	2 (4.1)	14 (6.1)	57 (7.1)	94 (2.4)
Lysergic acid diethylamide (LSD)	–	11 (4.8)	21 (2.6)	24 (0.6)
Buprenorphine	1 (2.0)	3 (1.3)	13 (1.6)	71 (1.8)
Novel psychoactive substances (NPS)	1 (2.0)	3 (1.3)	5 (0.6)	5 (0.1)
Methylphenidate	1 (2.0)	1 (0.4)	3 (0.4)	9 (0.2)
Methadone	2 (4.1)	–	10 (1.2)	149 (3.8)
Other opioids	1 (2.0)	9 (3.9)	27 (3.3)	265 (6.7)
Other stimulants	1 (2.0)	3 (1.3)	20 (2.5)	47 (1.2)
Other	8 (16.3)	18 (7.9)	52 (6.5)	220 (5.6)
Ethanol	15 (30.6)	90 (39.5)	258 (32.0)	1007 (25.4)
Total	49 (100)	228 (100)	806 (100)	3962 (100)

course, treatment, and toxic agents taken are presented in Table 1. Clinical features varied across age groups according to toxic agents taken.
Conclusion: There were few cases of acute recreational drug toxicity in patients 17 years and younger, but a larger proportion were females. Cannabis was a more frequent toxic agent in the younger age groups. There were no differences across age groups in the proportion of patients transferred to hospital.

316. Acute poisonings involving cannabis in Oslo, Norway

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Objective: Cannabis is the most widely used illegal drug in Norway. We describe the clinical features and course of acute poisoning involving cannabis, and compare the poisonings involving only cannabis to those involving cannabis combined with other drugs.
Methods: We retrospectively included all patients presenting with poisoning involving recreational use of cannabis at the main primary care emergency outpatient clinic in Oslo, Norway, from October 2013 through September 2017. Eligible patients were identified from patient registration lists. Data were collected from the electronic patient records. Diagnosis of toxic agents was based on the clinical assessment of the doctor treating the patient, as noted in the patient records.
Results: Among 753 included cases, 152 (20.2%) involved only cannabis, 178 (23.6%) cannabis and ethanol only, and 423 (56.2%) cannabis and any other combination of drugs or ethanol. In cases involving cannabis only, patients were younger (median age 23.5 years), more often presented with tachycardia (47.4%), anxiety (36.2%), psychosis (21.1%), palpitations (18.4%), and hallucinations (17.1%) than when combined with ethanol or other drugs (Table 1). Agitation was also frequent (23.7%), as in the polydrug group (22.5%). When only cannabis was involved, the patient stay was shorter (median 2 hours 22 minutes) and they were more frequently transferred to a psychiatric hospital (14.5%). Ethanol was involved in 46.7% of total cases, benzodiazepines in 22.3%, amphetamine in 17.7%, heroin in 15.8%, and cocaine in 8.1%.
Conclusion: Poisoning involving only cannabis more typically presented with features of panic attacks and psychosis, whilst poisoning with cannabis combined with other drugs were characterized by the other drugs taken.

317. Psychosis associated with acute recreational drug toxicity

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Objective: The association between psychosis and acute toxicity with recreational drugs such as amphetamine and cannabis is well known, but there is limited data on how common this is in Norway and which drugs are most frequently implicated. We describe patients with psychosis among patients presenting with acute recreational drug toxicity in Oslo, the capital city of Norway, and estimate the association with psychosis for different recreational drugs.
Methods: Data was collected at the main primary care emergency outpatient clinic in Oslo from October 2013 through May 2018. Most patients with acute recreational drug toxicity in Oslo are treated at this site. Electronic patient records were retrospectively searched. Cases with acute recreational drug toxicity were included, except lone alcohol intoxication. The diagnosis of psychosis and of drugs taken was based on the clinical assessment of the doctor treating the patient as noted in the electronic patient records. We used multiple logistic regression analysis to

Table 1. Cannabis poisoning in Oslo, Norway, comparing clinical features and course of acute poisoning with and without other drugs.

	Cannabis only n (%)	Cannabis combined with ethanol only n (%)	Cannabis and any other drug combination n (%)
Males	108 (71.1)	131 (73.6)	348 (82.3)**
Age (years)[a]	23.5 (20–30)	27 (21–43)	29 (24–39)***
Clinical features			
Tachycardia (≥100/min)	72 (47.4)	68 (38.2)	121 (28.6)***
Anxiety	55 (36.2)	25 (14.0)	49 (11.6)***
Agitation	36 (23.7)	24 (13.5)	95 (22.5)*
Psychosis	32 (21.1)	7 (3.9)	32 (7.6)***
Reduced consciousness (GCS <15)	29 (19.1)	89 (50.3)	184 (43.5)***
Palpitations	28 (18.4)	14 (7.9)	18 (4.3)***
Hallucinations	26 (17.1)	10 (5.6)	36 (8.5)**
Vomiting	25 (16.4)	44 (24.7)	30 (7.1)***
Bradypnoea (<12/min)	3 (2.0)	2 (1.1)	39 (9.2)***
Seizures	3 (2.0)	4 (2.2)	8 (1.9)
Arrhythmia	2 (1.3)	1 (0.6)	–
Treatment			
Sedation	5 (3.3)	2 (1.1)	15 (3.5)
Naloxone	–	1 (0.6)	37 (8.7)***
Length of stay (hours:minutes)[a]	2:22 (1:34–3:46)	3:07 (1:52–4:34)	3:24 (1:45–5:14)***
Disposition			
Transferred somatic hospital	14 (9.2)	12 (6.7)	55 (13.0)
Transferred psychiatric hospital	22 (14.5)	6 (3.4)	26 (6.1)
Medically discharged	85 (55.9)	129 (72.5)	276 (65.2)
Self-discharge	31 (20.4)	31 (17.4)	66 (15.6)
Total	152 (100)	178 (100)	423 (100)

Comparisons across toxic agent groups: *p < 0.05, **p < 0.01, ***p < 0.001.
[a]Median (interquartile range).

estimate associations between psychosis and drugs taken. The patients who had not taken the specified drug were used as the reference group.
Results: Psychosis was present in 367 (5.4%) of 6829 cases. Among the 367 cases with psychosis, median age was 31 years (interquartile range 25–39), 282 (76.8%) were male, 167 (45.5%) had taken amphetamine, and 90 (24.5%) had taken cannabis. In 192 (52.3%) cases, the patient was admitted to a psychiatric ward. The drugs with the strongest associations with psychosis were methylphenidate (psychosis in 26.3% (5/19) of cases, adjusted odds ratio (aOR) 3.9 (95% confidence interval 1.3–12.1)), amphetamine (10.8% (167/1543), aOR 2.5 (2.0–3.0)), cannabis (10.1% (90/890), aOR 1.6 (1.2–2.1)), other/unspecified hallucinogens (42.1% (8/19), aOR 8.0 (3.0–21.4)), and other/unspecified central stimulants (32.3% (21/65), aOR 6.5 (3.6–11.7)). Patients with psychosis more frequently were agitated (52.3% versus 17.1%) hallucinating (42.8% versus 2.8%), tachycardic (38.4% versus 23.4%), and had anxiety (24.3% versus 7.2%), than those without psychosis ($p < 0.001$ for all comparisons). Among the 257 cases with acute recreational drug toxicity admitted to a psychiatric ward, psychosis was present in 192 (74.7%), agitation in 145 (56.4%), hallucinations in 97 (37.7%), and anxiety in 68 (26.5%).
Conclusion: Psychosis is a substantial problem associated with acute recreational drug toxicity, occurring in 5.4% of cases, and in 3 out of 4 of the cases admitted to psychiatric care. Amphetamine and cannabis were the most frequently taken drugs associated with psychosis.

318. E-liquid sold as CBD e-liquid containing XRL-11: 4 cases reported. A warning signal to health authorities and e-cigarettes users

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Objective: XLR-11 ([1-(5-fluoropentyl)-1H-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone; 5-fluoro-UR-144) is a synthetic cannabinoid. It is a full agonist of cannabinoid receptor type 1 (CB1) and type 2 (CB2) receptors. First described in 2012, XRL-11 was scheduled in 2016 in France. We report four cases of XRL-11 found in e-cigarette users, seen in our Emergency Department in 2019. The e-liquid was sold as cannabidiol (CBD) e-liquid.
Cases series: Case 1. A 17-year-old male developed hallucinations, gastrointestinal signs, and sweating, after smoking an e-liquid. He was admitted 48 hours later for withdrawal syndrome. Cyamemazine was administered with psychiatric follow-up. XRL-11 was identified in e-liquid with gas chromatography-tandem mass spectrometry (GC-MS-MS). Case 2. A 13-year-old male was admitted for unsociable behaviour, after smoking two e-cigarettes a week. XRL-11 was found in the e-liquid. Case 3. A 20-year-old male was admitted after seizures (first event) with mild hypothermia (35.8 °C). His only clinical sign was amnesia. XRL-11 and nicotine were found in the e-liquid. Case 4. A 15-year-old male was admitted with withdrawal syndrome, 48 hours after he stopped using e-cigarettes. Cyamemazine was administered with psychiatric follow-up. XRL-11 and AICAR (acadesine) were found in urine.
Conclusion: Many e-cigarette users are consuming CBD (known as Cannabis Light) in e-liquid for its relaxing effects, sold without quality control and bought in 80% of cases on the Internet. CBD in e-liquid is actually not illegal in our country if the tetrahydrocannabinol (THC) concentration is under 0.2%. Harmful CBD effects on humans are known, but unusual psychiatric or withdrawal symptoms lead to a biological study on 4 e-cigarette users and on the e-liquid used. XRL-11 was found in urine and e-liquid. Clinical signs were psychiatric (delirium) 36%, neurological (seizures, coma) 20%, gastrointestinal (nausea, vomiting) 18%, cardiovascular (hypertension, tachycardia) 16% and withdrawal 10%. Due to related risk for e-cigarettes, we are collecting data from e-smokers (Vapotox© inquiry), particularly young people, after use of e-liquid sold as CBD e-liquid. These liquids could theoretically contain CBD (100 mg/10 mL up to 1 g/10 mL) and where possible we ask about clinical symptoms, and collect biological samples and expertise on e-liquid use. With our Vapotox© inquiry, regarding the Law, we are documenting e-liquid enquiries for identification of New Substances Products and reporting to the French Addictovigilance Network System or European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). E-liquid sold as CBD may contain components such as XRL-11 or contaminants which is a public health issue.

319. Significant cannabidiol (CBD) urine concentration in a young male admitted after using an e-cigarette obtained from a street market

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Objective: Cannabidiol (CBD) is a component of some e-liquid for e-cigarettes, sold widely for recreational vaping use. E-cigarettes are prohibited in minors. We report a CBD urine concentration in a young male using an e-cigarette liquid containing CBD.
Case report: A 16-year-old male developed hallucinations (seeing people taller) and loss of bearings, after using an e-cigarette containing an unknown amount of CBD. He was admitted two hours later and was alert, without gastrointestinal signs, presenting moderate headache with normal pupils. Blood pressure was 117/65 mmHg, heart rate 67/min and temperature 36.6 °C. An electrocardiogram (ECG) and biochemical tests were unremarkable. Urine screening with liquid chromatography-tandem mass spectrometry (LC-MS/MS) was tetrahydrocannabinol (THC) positive and the CBD concentration was 4.17 µg/L. He remembered puffing 6 times on an e-cigarette for a first experimentation. His past history was 5 cigarettes daily, with infrequent alcohol consumption and no declared illicit drugs use. He was discharged on day 2.
Conclusion: Due to increasing cases of young people admitted after vaping we have been monitoring cases since 2019 in a study called Vapotox©, collecting data on toxidromes, screening of urine for drugs [1], number of puffs, and mode of vaping. The CBD concentration in e-liquid results in variable absorption in the body. In e-liquids on the market, CBD dosage ranges from 100 mg/10 mL up to 1 g/10 mL, with less than 0.2% THC. In experimental studies on humans and animals, following inhalation, the peak plasma CBD concentration occurs after 0.5-

1 hours with a short blood half-life (1.5 hours). The half-life in urine is 31 ± 4 hours and the volume of distribution is 3.4 L/Kg (calculated) [2,3]. Symptoms in our cases have not been reported yet but this case is of interest, even though the e-liquid was not available for testing. Increased use of e-cigarettes is recognised with a warning for illicit drugs in e-liquids. Experimentation of CBD with THC for medical use will start in France in 2021 under a pharmacovigilance survey by the Health Ministry. This case demonstrates that inhalation of high dose CBD e-liquid may induce pronounced symptoms in naïve young people.

References

[1] Huestis MA, Solimini R, Pichini S, et al. Cannabidiol adverse effects and toxicity. Curr Neuropharmacol. 2019;17:974–989.

[2] Lucas CJ, Galettis P, Schneider J. The pharmacokinetics and the pharmacodynamics of cannabinoids. Br J Clin Pharmacol. 2018;84: 2477–2482.

[3] Meier U, Dussy F, Scheurer E, et al. Cannabinoid concentrations in blood and urine after smoking cannabidiol joints. Forensic Sci Int. 2018;291:62–67.

320. Swedes like their O-juice from Florida and their E-juice from California

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Objective: During the second half of 2019 an outbreak of e-cigarette, or vaping, product use-associated lung injury (EVALI) was detected in the USA. It is thought to have been caused by vitamin E acetate (VEA), an oily substance surreptitiously used to dilute tetrahydrocannabinol (THC)-containing vaping liquids without altering their physical appearance. Since February 2020 the number of new cases has been negligible, making the total toll 2807 hospital cases and 68 deaths from all over the US. In Sweden the outbreak was initially perceived as an exclusively North American affair, but in the late fall of 2019 two cases of severe lung injury in patients with a history of heavy use of THC-containing vaping fluids occurred in Sweden calling this assumption into question. The cases, which were never conclusively linked to VEA, prompted an inquiry into the workings of the THC-vaping markets in Sweden.

Methods: The Intelligence Division of the National Operations Department of the Swedish Police provided data on the evolving number of vendors of THC vaping-products on the most important Swedish darknet market for recreational drugs ("Flugsvamp 2.0 and 3.0") during 2018-2020. Swedish National Forensic Centre (NFC) provided data on the number of seized THC-containing vaping products during the same period and analyzed a convenience sample of products seized during October-December 2019 for VEA.

Results: There was a marked increase in the number of sellers of THC vaping products on the Swedish darknet site "Flugsvamp", with products typically advertised as "made in the USA". NFC seizures paralleled this increase and the presence of VEA was confirmed in several products (Table 1).

Conclusion: The US appears to be an important exporter of THC-containing vaping products and future outbreaks of lung injury or other harms connected to these products cannot be assumed to be locally constrained.

321. Hydroxyphencyclidines (OH-PCPs), fluoroamphetamine (FA) and fluoromethamphetamine (FMA): an explosive NPS mixture and a challenge for appropriate sedation in a severely intoxicated patient

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Objective: Hydroxyphencyclidines (OH-PCPs), including isomers (e.g., 3-HO-PCP), seem to be common novel psychoactive substances (NPS) with dissociative effects, frequently used in association with other illegal substances. OH-PCPs act primary as N-methyl-D-aspartate (NMDA) receptor antagonists, with affinity also for μ-opioid receptors. Little is known about OH-PCP toxicity in humans, except for user reports on web-forums. They may cause hyperthermia, euphoria, hallucinations, anesthesia, tachycardia, hypertension, and (rarely) respiratory depression. We describe an analytically confirmed case of severe acute toxicity related to a NPS mixture including OH-PCPs.

Case report: A 24-year-old male (75 Kg) was admitted to ED with severe psychomotor agitation, excitatory behavior, aggressiveness, confusion, hallucinations, horizontal spontaneous nystagmus, hypertonia, with generalized hyperkinetic movements (rapid and unpredictable contractions as well as chorea), xerostomia, flushing, hypertension (185/90 mmHg), and tachycardia (120 beats/min); body temperature, oxygen saturations and arterial blood gases were normal. He reported recent abuse of cannabis,

Table 1. Swedish National Forensic Centre seizures and analysis of THC-containing vaping products (2018-2020).

	2018		2019		2020	
THC-containing vaping products	first half	last half	first half	last half	first half	last half
Sellers at "Flugsvamp"	0	7	10	40	20	53
Seizures by police/customs	2	3	18	50	69	n.a.

Analysis of notorious vitamin E acetate (VEA)-containing brands seized Oct-Dec 2019	"Dank Vapes"	"Smart Cart"	"TKO"
Number of items	3	3	1
With confirmed VEA	2	3	0

dimethyltryptamine (nebulized) and other unspecified substances. For the safety both of the patient and healthcare personnel, physical restraint was necessary and sedation treatment was started with diazepam (10 mg IV) followed by midazolam (20 mg IV), clothiapine (80 mg IV), delorazepam (5 mg), ketamine, and propofol 1% (3 mL). Due to the poor clinical response, ketamine (100 mg IV) and haloperidol (4 mg IM) were then administered. Nevertheless, a more profound sedation (propofol 2% at 12 mL/hour + midazolam 10 mg/hour) and oro-tracheal intubation were needed one hour later for persistent severe agitation. Dexmedetomidine (0.3 μg/Kg/hour) associated with continuous infusion of haloperidol, tiapride and clonidine were then used during the 3 days of intensive care unit (ICU) stay. Electrocardiogram (ECG), chest X-ray and cranial computerised tomography (CT) scan showed no abnormalities. He was transferred to a psychiatric ward on day 6. The first urine immunoassay tested positive for cannabinoids/cocaine/amphetamines/ecstasy. Second level (gas chromatography-mass spectrometry (GC-MS) plus liquid chromatography-tandem mass spectrometry (LC-MS/MS)) toxicological analysis confirmed Δ9-tetrahydrocannabinol (THC) and 11-Nor-9-carboxy-THC (THCCOOH) in serum (0.8 ng/mL and 44 ng/mL, respectively), and revealed the presence of OH-PCP in serum (480 ng/mL) and OH-PCP, fluoromethamphetamine (FMA) and fluoroamphetamine (FA) in urine. Dimethyltryptamine was negative in urine.
Conclusion: Appropriate sedation in intoxicated and agitated patients is a challenge, particularly after unspecified NPS consumption. Due to the lack of a suitable history and the large number of different NPS, analytical support for correct diagnosis is essential for a proper treatment.

322. Recreational, inhalational misuse of hyoscine butylbromide (Buscopan®) tablets as reported to the UK National Poisons Information Service

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Objective: Hyoscine butylbromide is an antispasmodic drug. When heated, it liberates hyoscine (scopolamine), whose psychotropic effects include delirium and hallucinations. This has led to recreational misuse, particularly in prison [1]. Public Health England (PHE) and NHS England issued advice against prescribing hyoscine butylbromide in prisons in 2015 [2]. Our objective was to establish the incidence of exposures relating to the inhalation of hyoscine butylbromide for recreational misuse in the UK as reported to the UK National Poisons Information Service (NPIS) between 1 January 2010 and 31 August 2020.
Methods: A retrospective analysis was undertaken of enquiries relating to inhalation of hyoscine butylbromide.
Results: Eight cases were identified, two of which occurred before dissemination of the 2015 PHE/NHS England advice. Five patients were female, three male. The median age was 31.5 years (range 24–40 years). Five exposures occurred in prison and three in the home. All exposures were due to recreational misuse. Five patients had smoked crushed tablets in a cigarette form. In two enquiries the tablets were heated on foil and the liberated fumes inhaled. In the remaining case, the route of exposure was recorded as "being vaped in an e-cigarette". The Maximum Poisoning Severity Score (MAXPSS) [3] at the time of the enquiry was moderate in 6 cases and severe in two. Features reported were agitation (n = 5), somnolence/stupor (n = 4), confusion (n = 3) , mydriasis (n = 2), slurred speech (n = 1), tachycardia (n = 1), hallucination (n = 1), hypoxia (n = 1), lactic acidosis (n = 1), ataxia (n = 1), hypotension (n = 1) and tetany (n = 1). Both patients whose MAXPSS was severe had suffered transient loss of consciousness after exposure. No long-term follow up of these enquiries was undertaken.
Conclusion: Despite advice against prescribing hyoscine in prisons, exposures continue to occur. Clinicians and Specialists in Poisons Information need to be aware of the hazards of hyoscine butylbromide misuse.

References

[1] Jalali F, Afshari R, Babaei A. Smoking crushed hyoscine/scopolamine tablets as drug abuse. Substance Use & Misuse. 2014;49:793–797.
[2] Farmer D, Ryan G. Misuse of hyoscine butylbromide (Buscopan). 2015 [cited 1 Oct 2020]. Available from https://medicines.necsu.nhs.uk/wp-content/uploads/2015/07/MisuseXofXhyoscineXbutylbromideXletterXV5XFinal.pdf
[3] Persson HE, Sjöberg GK, Haines JA, De Garbino JP. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol. 1998;36:205–213.

323. A case of crack-lung-like syndrome due to new synthetic opioid consumption with analytical confirmation

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Objective: Crack-lung is an acute pulmonary syndrome occurring within 48 hours after crack (cocaine free-base) smoking. It is characterized by acute dyspnea and diffuse ground-glass opacities. We describe a crack-lung-like syndrome in a case of analytically confirmed new synthetic opioid (NSO) consumption.
Case report: A 20-year-old male was admitted to the intensive care unit (ICU) with worsening dyspnea that appeared 48 hours after snorting a drug of abuse, reported as a synthetic opioid. On admission, arterial blood gases (ABG) showed hypoxia (PaO_2 56 mmHg, oxygen saturations 89% on room air). Blood biochemistry was normal, except for white blood cell count of 12,710/μL and PCR 48 mg/L. Chest X-ray and computerised tomography (CT) scan showed a mediastinal widening and bilateral parenchymal ground-glass opacity, mostly with bilateral near-hilum distribution. The clinical picture raised the diagnostic suspicion of crack-lung syndrome (denied by the patient). He was afebrile, and blood cultures for bacterial/viral infection were negative. He was treated symptomatically for 72 hours, with nasal high-flow-oxygen and steroids. After a progressive improvement, he recovered and was discharged after 10 days with normal biochemistry

and CT scan. Toxicological urinary screening performed in the ICU was negative for cocaine and other drugs (cannabis, opioids, methadone, methamphetamines). A blood sample (from admission) and residue of the abused substance (powder labelled as "Research Chemical Powder 2-methyl-AP-237, not for human consumption") were analysed, confirming the presence of methyl-AP-237. No other substances were detected. Blood was tested for conventional drugs of abuse and new psychoactive substances (NPS), was positive only for methyl-AP-237 (25 ng/mL).
Conclusion: 2-Methyl-AP-237 (AP-237) is an opioid classified by the United Nations Office on Drugs and Crime (UNODC) as a non-fentanyl opioid. It was first identified in a seizure (March 2019) in Slovenia. The only available information on the effects of 2-methyl-AP-237 is found on user forums, reporting euphoria, muscle relaxation and severe respiratory depression. This case was characterized by a clinical and radiological crack-lung-like syndrome without crack smoking. The absence of opioid neurological clinical manifestations is probably due to the delayed hospital admission. The patient was not tested for COVID-19 because he was hospitalized before the COVID-19 pandemic. Moreover, he was afebrile and CT images differed from those of COVID-19 patients. The availability of NSOs on the drug market is increasing and the related clinical picture can be different from the typical opioid toxidrome. This case underlines the importance of specialized laboratory analysis to identify NPS exposure early, which can explain unusual clinical presentations.

324. A comparative analysis between acute ethanol poisoning and acute ethanol combined with drugs of abuse poisoning in adolescents

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Objective: To compare clinical features between acute ethanol poisoning and acute ethanol combined with drugs of abuse poisoning in adolescents.
Methods: We analyzed cases of adolescents with acute poisoning with ethanol alone or in combination with drugs of abuse, during a 5-year period, using the medical records and taking into consideration age, gender, environment, severity of clinical picture evaluated by the presence of coma and length of hospitalization. The patients were divided in to two samples. Sample 1 included adolescents with acute ethanol poisoning and sample 2 adolescents with acute ethanol combined with drugs of abuse poisoning. Statistical analysis was performed using Mann-Whitney, chi-squared and binomial tests.
Results: A total of 229 patients with acute ethanol poisoning (sample 1) and 28 patients with acute ethanol combined with drugs of abuse (sample 2) were admitted in our centre between 2014-2018.
The characteristics of the two samples are presented in Table 1. Regarding the age, gender and environment the analysis showed that there were no significant differences between the two samples. There was no significant difference between the two samples regarding the severity of the clinical picture quantified by the presence of coma (41.7% versus 46.4%, $p = 0.864$). The length of hospitalization, however, was significantly longer in patients from sample 2 compared to sample 1 (1.09 days versus 2 days, $p = 0.0005$).
Conclusion: Consuming drugs of abuse with ethanol does not significantly influence the development of severe symptoms but the length of hospitalization is significantly longer in acute poisoning with ethanol plus drugs of abuse compared to acute ethanol poisoning alone.

325. Predicting hypertension using subjective symptoms in recreational drug users at first-aid stations at dance events

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Objective Large dance events have become very popular. Notably, adverse health incidents associated with drug abuse occur at many events. Previously, we found a correlation between headache and hypertension in recreational drug-exposed patients presenting to first-aid stations at dance events, whose blood pressure was logged (20% of all patients, ~75% hypertension). To corroborate this finding in the whole population of drug-exposed patients presenting to first-aid stations, we conducted a prospective study.
Methods: We included drug-exposed patients presenting to a first-aid station at two dance events in the Netherlands. Data on drug use and symptoms were collected with a questionnaire and blood pressure was measured. Outcome parameters were the presence of several subjective symptoms and the severity of hypertension discriminating moderate hypertension (systolic blood pressure (SBP) > 140 mmHg or diastolic blood pressure (DBP) > 90 mmHg) and severe hypertension (SBP >160 or DBP >100). The correlation was assessed using univariate logistic analyses.

Table 1. Characteristics of adolescents with acute ethanol poisoning, with and without drugs of abuse, treated over a 5-year period (2014-2018).

Criteria	Sample 1: Ethanol acute poisoning (n = 229)	Sample 2: Ethanol and drugs of abuse poisoning (n = 28)
Gender	Male 141 patients (61.6%) Female 88 patients (38.5%)	Male 15 patients (53.5%) Female 13 patients (46.5%)
Age	11-14 years 59 patients (25.8%) 15-18 years 170 patients (74.2%)	11-14 years 8 patients (25%) 15-18 years 20 patients (75%)
Environment	Urban 172 patients (75.1%) Rural 57 patients (24.9%)	Urban 26 patients (92.8%) Rural 2 patients (7.2%)
Coma	94 patients (41.7%)	13 patients (46.4%)
Length of hospitalization	1.09 day	2 days
Drugs of abuse	Not applicable	Cannabis 22 patients LSD 3 patients New psychoactive substances 3 patients

Table 1. The number of drug-exposed patients presenting to a first-aid station at dance events with headache and moderate (SBP >140 mmHg) or severe (SBP >160 mmHg) hypertension.

	Hypertension >140 / >160 mmHg	No hypertension >140 / >160 mmHg	Total
Headache	28 / >15	5 / >18	33/33
	True positive	*False positive*	
No headache	43 / >20	23 / >46	66/66
	False negative	*True negative*	
Total	71 / 35	28 / 64	99/99

Results: We included 99 patients, median age of 23 years [IQR: 20-28] and 58% male. Most patients reported the use of only one drug (N = 72, 73%), most commonly 3,4-methylenedioxymethamphetamine (MDMA, N = 71, 72%). The mean SBP and DBP were 144 mmHg (SD =18) and 94 mmHg (SD =13), respectively. Moderate hypertension was observed in 72% (N = 71/99) of patients. Amongst patients with headache, 85% had moderate hypertension (N = 28/33) (Table 1). Moderate hypertension was associated with headache (OR =3.0, 95% CI: 1.02-8.8), with a specificity of 82% and, sensitivity of 39%. No significant correlation was found between additional subjective symptoms and severe hypertension.

Conclusion: The presence of headache was correlated with moderate hypertension, however, due to a low sensitivity, neither the presence or absence of headache can be applied in triaging which patients should be further assessed for hypertension. The number of patients with severe hypertension was low and a larger population is necessary to confirm a correlation.

326. Acute recreational drug toxicity in Ghent, Belgium. Comparison of self-reports and analytical detection by immunoassay (IA) and mass spectrometry (MS) testing

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Objective: To compare self-reported and analytically confirmed substance use in cases of acute recreational drug toxicity at Ghent University Hospital (UZGent), which participates in the European Drug Emergencies Network Plus Project (EuroDEN Plus).

Methods: Between January 2018 and December 2019, 250 patients who presented at the Emergency Department of UZGent with symptoms of acute recreational drug intoxication were screened by laboratory analysis and were included. In 2018, 83 patients underwent immunoassay (IA) tests and, when new psychoactive substance (NPS) or specific drug use was clinically suspected, we also used additional analytical tests (e.g., gas chromatography-mass spectrometry (GC-MS)). In 2019, 167 patients were systematically subjected to both IA and MS tests [1].

Results: Analytical confirmation of self-reported methadone, cannabis, cocaine and 3,4-methylenedioxymethamphetamine (MDMA) in 2018 and 2019 and of gamma-hydroxybutyrate/gamma-butyrolactone (GBH/GBL), amphetamines, ketamine and NPS in 2019 only, was high (>70%). It was low for heroin and lysergic acid diethylamide (LSD) (<25%) in 2018 and 2019. In 2018 and 2019, self-reporting was low for analytically detected

Table 1. Comparative table of self-reported and analytically detected substance use in 2018 and 2019.

	2018					2019				
Substance (group)	Only reported	Reported and detected	Only detected	% Reported among total detected	% Detected among total reported	Only reported	Reported and detected	Only detected	% Reported among total detected	% Detected among total reported
Classic drugs										
Cannabis	1	16	17	49%	94%	15	37	39	49%	71%
Cocaine	4	23	7	77%	85%	7	35	11	76%	83%
Amphetamines	10	10	6	63%	50%	8	28	21	57%	78%
Methamphetamines	2	1	5	17%	33%	3	2	4	33%	40%
MDMA/MDA/MDEA	1	3	3	50%	75%	5	16	15	52%	76%
Benzodiazepines/ Z-drugs	11	8	17	32%	42%	7	10	67	13%	59%
Heroin	10	1	0	100%	9%	11	0	0	/	0%
Methadone	0	1	0	100%	100%	0	5	8	39%	100%
Opiates (excluding methadone and heroin)	1	1	1	50%	50%	0	1	27	4%	100%
GHB/GBL	4	4	3	57%	50%	3	8	3	73%	73%
Ketamine	4	2	0	100%	33%	4	12	4	75%	75%
LSD	4	0	0	/	0%	3	1	0	100%	25%
NPS										
All NPS	5	0	1	0%	0%	3	8	18	31%	73%

cannabis, benzodiazepines/Z-drugs, methamphetamines, other opiates and NPS (<50%) (Table 1).
Conclusion: When additional analytical methods are systematically applied, detection of methadone, cannabis, cocaine, MDMA, GHB/GBL, amphetamines, ketamine and NPS appears to be accurate compared to self-reporting. When they are not, this reporting accuracy appears to be less for GHB/GBL, amphetamines, ketamine and NPS. When cocaine and ketamine are detected by laboratory analysis, the self-reporting of these drugs appears to be accurate. This accuracy seems to be low for cannabis, benzodiazepines/Z-drugs, methamphetamines, other opiates and NPS.

Reference

[1] Liakoni E, Yates C, Dines AM, et al. Acute recreational drug toxicity: comparison of self-reports and results of immunoassay and additional analytical methods in a multicenter European case series. Medicine. 2018;97:e9784.

327. In vino veritas: accidental MDMA poisoning by illicit drug trafficking

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Objective: Trafficking and transportation of illicit drugs in wine bottles is reported in the media [1] and precursors of metamphetamine derivatives have been found in confiscated liquids [2]. We present a patient with a sympathomimetic toxidrome after consumption of presumed wine.
Case report: A 25-year-old previously healthy Caucasian male was admitted to the emergency department (ED) with sympathomimetic symptoms. The symptoms developed 15 minutes after drinking a glass of prosecco and a sip of red wine, which had a strange and acidic taste. The wine bottle had been bought at an auction of unclaimed parcels at a post office near the border. The patient denied any medication, illegal drug use or allergies. On arrival to the ED he was severely agitated with arterial hypertension (systolic blood pressure 160 mmHg), tachycardia (180 bpm) and tachypnea (40/minute). He presented with mydriatic pupils, dry mucous membranes, diaphoresis, tympanic temperature of 38.3 °C, shaking chills and a symmetric tremor of the lower extremities. An electrocardiogram (ECG) and chest X-ray were unremarkable as well as laboratory values (including hepatic, renal, hematologic and inflammatory parameters, D-dimers (0.22 mg/L; < 0.5), arterial blood gas parameters (pH 7.41, pCO_2 4.98 kPa), thyroid stimulating hormone (1.95 mU/L; range 0.29-4.2)). An infectious etiology, pulmonary embolism and thyrotoxic crisis were excluded. Blood alcohol concentration was 0.3 g/L. Immunological urine toxicology screen was positive for methamphetamine, amphetamine and 3,4-methylendioxy-N-methylamphetamine (MDMA). Initial treatment comprised intravenous morphine (2.5 mg), pethidine (25 mg) and metoprolol (2 mg). Agitation improved after IV diazepam (10 mg); blood pressure and respiratory rate normalized. Tachycardia, discreet diaphoresis and temperature improved a few hours later. Except for occasional symmetrical tremors of the lower limbs neurological status was normal. The subsequent clinical course was uneventful and he was discharged the following day. Due to the credible history of the patient, who denied being a drug user, further chromatographic analysis were performed. MDMA was found in a concentration of 40%, and acetone (5.6%) and isopropyl alcohol (2.7%) in all samples of the purple liquid in the confiscated wine bottles.
Conclusion: Manipulated bottles may be used for the transport of dissolved illegal drugs. Highly concentrated MDMA, as analysed in the camouflaged liquid in our case, may cause life-threatening poisoning.

References

[1] Boffey D. Belgian woman dies after taking sip of MDMA-laced wine. The Guardian, 27 February 2020 [cited 26 October 2020]. Available from http://www.theguardian.com/world/2020/feb/27/belgian-woman-dies-after-taking-sip-of-mdma-laced-wine
[2] Collins M, Donnelly C, Cameron S, et al. Identification and characterization of N-tert-butoxycarbonyl-MDMA: a new MDMA precursor. Drug Test Anal. 2017;9:399–404.

328. Frequent hospitalization for synthetic cathinone poisonings: a case series reported to the Dutch Poisons Information Center

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Objective: In Europe, synthetic cathinones (SCs) are among the most commonly detected new psychoactive substances (NPS) in consumer drug samples and forensic seizures. Although the prevalence of use of NPS is low, health incidents are reported. From 2013 onwards, the annual number of SC poisonings reported to the Dutch Poisons Information Center (DPIC) has increased from 8 cases in 2013 to 42 cases in 2019, and currently SCs represent the largest group of NPS poisonings. Therefore, we investigated the circumstances and clinical course of SC poisonings.
Case series: Between January 2016 and July 2019 61 SC poisonings were reported to the DPIC, and were followed-up by telephone using standardized questionnaires with the patient and/or physician. Male patients were overrepresented (N = 49, 86%) and the median age was 25 years (IQR 19-39 years, range 15-61 years). Two patients were repeatedly exposed, with a total of 6 poisonings. Use of 3-methylmethcathinone (3-MMC) was reported most often (N = 18, 30%), followed by alpha-pyrrolidinopentiophenone (alpha-PVP) (N = 15, 25%) and mephedrone (4-MMC) (N = 14, 23%). Other reported SCs were 4-methylethcathinone (4-MEC), 3-chloromethcathinone (3-CMC), methylone, N-ethylhexedrone (Hex-en), alpha-pyrrolidinohexiophenone (alpha-PHP), 4-chloro-alpha-PVP, and ethylone. The most common routes of exposure were ingestion (N = 22, 36%), snorting (N = 14, 23%), and injection (N = 13, 21%). In about one third of the poisonings (N = 23, 38%) multiple doses were used in one session. Common reasons for using SCs were recreational (N = 15), to reduce stress (N = 6), because of addiction (N = 6), and as an aphrodisiac (N = 5). Co-exposure to other illicit substances and/or alcohol (> 2 standard drinks) was frequently reported (70%), including cannabis, amphetamine, cocaine, 3,4-methylenedioxymethamphetamine (MDMA), alkyl nitrites ("poppers"), and gamma-hydroxybutyrate/gamma-butyrolactone (GBH/GBL). Symptoms in cases of poisonings with SCs only (N = 16) included agitation/

aggression, anxiety, confusion, insomnia, tachycardia, mydriasis, perspiration, muscular effects (muscle twitching/spasms or tremor), and hallucinations. One 3-MMC-related fatality was reported. This male patient (60-65 years) suddenly developed coma and asystole after rectal exposure to 3-MMC, alkyl nitrites ("poppers") and sildenafil. Resuscitation was unsuccessful. The majority of poisonings presented to an Emergency Department (N = 46, 75%) and 51% were admitted to hospital (N = 31). Twelve patients (20%) were admitted to an intensive care unit. The median duration of admission was 13 hours (IQR 6-38 hours, range 3 hours-11 days).
Conclusion: The majority of SC poisonings result in sympathomimetic toxicity requiring hospital admission. Most patients reported co-exposure to other illicit substances and/or alcohol, which may have aggravated the clinical course. Toxicological analysis of biological samples is needed to relate clinical characteristics to SC exposure.

329. Exposures involving opioids and alcohol reported to the US Poison Centers

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Objective: In 2018, opioids accounted for 69.5% of all overdose deaths. In 2019, 25.8% of people aged 18 or older reported binge drinking in the past month. The aim of the current study was to evaluate the epidemiology of exposures reporting both opioid and alcohol use to the US Poison Centers (PCs).
Methods: The National Poison Data System (NPDS) was queried for all exposures reporting both opioids and alcohol from 2011 to 2018. Cases resulting in major medical outcomes or deaths were categorized as serious medical outcomes (SMO). We descriptively assessed the demographic and clinical characteristics of exposures. Temporal trends were evaluated using generalized linear mixed models. Independent predictors of opioid mortality were studied using logistic regression.
Results: There were 48,127 exposure calls involving opioids and alcohol during the study period. The frequency of such exposures decreased by 29.5% ($p < 0.001$), and the rate of exposures decreased by 21.2% ($p < 0.001$). There were 1,112 deaths in our study sample (2.3%), with 9.1% of cases demonstrating major effects. Among cases with SMO, there was a greater proportion of cases demonstrating the presence of additional substances (72.8% versus 64.1%), including multiple opioids (13.9% versus 8.4%) as compared to non-SMO exposures. Cases over 50 years of age (28.8% versus 21.6%) and males (56.1% versus 49.2%) were more common in the exposures that resulted in SMO. Suspected suicides accounted for approximately half of the exposures with SMO. Hydrocodone exposures were most frequently observed and naloxone was a commonly used therapy. The risk of SMO was the highest in patients over 60 years of age (Ref: 20 – 29 years) (AOR: 1.99, 95% CI: 1.75 – 2.26). Males were 15% more likely than females to have serious exposures to opioids and alcohol (AOR: 1.15, 95% CI: 1.08 – 1.22). In cases involving substances in addition to opioids and alcohol, the risk of SMO increased 2-fold. Other important predictors of an SMO were suspected suicide (Ref: Unintentional exposure) (AOR: 1.74, 95% CI: 1.57 – 1.92), parenteral route of administration (Ref: Ingestion) (AOR: 3.85, 95% CI: 3.01 – 4.94) and exposure to benzodiazepines (Ref: no benzodiazepines) (AOR: 1.10, 95% CI: 1.02 – 1.18).
Conclusion: Analysis of calls to US PCs indicated a decreasing trend of exposures involving both alcohol and opioids. Exposures resulting in SMO demonstrated a high risk among intentional reasons for exposures and occurred in older age groups. Continued surveillance is key to ensuring the implementation of timely and tailored responses.

330. The Color Purple: death associated with brorphine, an emerging novel synthetic opioid

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Objective: Novel synthetic opioids continue to fuel and exacerbate the US opioid epidemic. While previous reports demonstrate increases in synthetic opioid-related deaths as largely driven by fentanyl and fentanyl analogs, recent toxicosurveillance has identified emerging trends in other synthetic opioids [1]. Reports in our state reveal an increasing presence of a product known only as "purple heroin". It is unknown at this time whether the color carries any significance. In our state, purple heroin has so far been associated with three documented acute overdoses, including one fatality. Seized samples tested by the State Police Laboratory revealed several components of this product including fentanyl and a novel compound, brorphine. Brorphine (chemical name 1-(1-(1-(4-bromopheny)ethyl)piperidin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one) is a synthetic opioid with a piperidine benzimidazolone structure. It was first reported in scientific literature in 2018 and *in vitro* pharmacological studies demonstrate a similar structure, mechanism, and potency with fentanyl. Reports indicate brorphine has been found in combination with heroin and fentanyl [2]. As of July, 2020, brorphine has been confirmed in seven blood samples from US fatalities. We present the first documented fatality associated with brorphine in our state.
Case report: A 61-year-old female with history of obesity, hypertension, chronic obstructive pulmonary disease (COPD), schizophrenia, hyperlipidemia, and without documented history of substance use, died due to fatal overdose associated with brorphine. She was found in her home five days after last being seen alive. The only reported paraphernalia found at the scene were several cut straws and unopened vials of her antipsychotic medication. Postmortem toxicology results were positive for: Heart blood – ethanol 27 mg/dL, 4-anilino-N-phenethylpiperidine (ANPP) screen positive, brorphine 2.0 ng/mL, gabapentin 6.8 μg/mL, chlorpromazine 82 ng/mL, fentanyl 0.32 ng/mL and urine drug screen presumptively positive for benzodiazepines and amphetamines. The Medical Examiner postmortem examination report ruled cause of death due to toxic effects from brorphine and fentanyl and the manner as accidental.
Conclusion: This is the first documented fatality with postmortem blood concentrations of the novel synthetic opioid brorphine within our state.

References

[1] Wilson N, Kariisa M, Seth P, et al. Drug and opioid-involved overdose deaths – United States, 2017–2018. MMWR Morb Mortal Wkly Rep. 2020;69:290–297.

[2] Verougstraete N, Vandeputte MM, Lyphout C, et al. First report on brorphine: the next opioid on the deadly new psychoactive substances' horizon? J Anal Toxicol. 2021;44:937–946.

331. A 1-year prospective analysis of propranolol exposures reported to the UK National Poisons Information Service (NPIS)

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Objective: To clarify the circumstances surrounding overdose in patients prescribed propranolol.
Methods: Prospective analysis of twelve months' enquiries involving propranolol to the Birmingham and Edinburgh Units, from 1 June 2019 to 31 May 2020.
Results: We received 171 enquiries regarding 164 patients. Most exposures (140) occurred at home; 17 were in prison. Further analysis will concentrate on the 82 (50%) patients who took a deliberate overdose of prescribed propranolol, 22 of whom (27%) had taken overdoses previously. The tablet size was documented in 65 cases (79%); 10 mg (n = 14), 40 mg (n = 38), 80 mg (n = 12) and 160 mg (n = 1). Only 2/65 were sustained release preparations. The median dose of propranolol taken (n = 71) was 600 (IQR 260–1240) mg. The median dispensed dose (n = 21) was 980 (IQR 560–2240) mg. Twenty-eight patients took an overdose of propranolol alone, with alcohol (n = 2), other drugs (n = 44), or alcohol and other drugs (n = 8). Propranolol was prescribed for anxiety (n = 46), migraine (n = 8), mood stabilisation (n = 2), hypertension (n = 2), and essential tremor (n = 1). Of the 46 patients prescribed propranolol for anxiety, 14 (30%) had taken overdoses prior to this exposure, and 16 (35%) suffered severe or fatal poisoning as a consequence of this most recent overdose. Seventeen patients took a deliberate overdose of both prescribed propranolol and one or more selective serotonin reuptake inhibitors (SSRIs); sertraline (n = 8), citalopram (n = 6) and fluoxetine (n = 5). SSRIs had been prescribed to at least 12 of these patients. Nine of the 17 patients developed severe poisoning and at least one died. In 82 patients taking an overdose of prescribed propranolol, the maximum Poisoning Severity Score [1] was unknown (n = 4), none (n = 22), minor (n = 28), moderate (n = 3), severe (n = 20), and fatal (n = 5). In those who developed severe or fatal propranolol toxicity, the median recorded dose (n = 17) was 1600 (IQR 1120–3000) mg. The indications in the five patients who died after taking prescribed propranolol were: anxiety (n = 3), migraine (n = 1), and unknown (n = 1). All had intentionally ingested propranolol with other drugs and the doses, documented in four cases, were 240, 840, 1600, and 2240 mg.
Conclusion: Propranolol had been prescribed for anxiety to more than half of the patients who took a deliberate overdose; 30% had taken overdoses previously and 35% developed severe or fatal poisoning. Co-ingestion with an SSRI may increase the risk of severe toxicity in those taking propranolol overdoses.

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.

332. Intravenous pentobarbital overdose treated with supportive care and multidose activated charcoal

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Objective: Pentobarbitone (pentobarbital) is a short-acting barbiturate used for animal euthanasia in Australia; 10-15 g of intravenous pentobarbitone causes human death after a median time of 16 minutes [1]. Multidose activated charcoal (MDAC) is used for phenobarbitone overdoses [2], however it is not described for pentobarbitone. In animal studies, pentobarbitone and its metabolites were excreted in bile [3] and in large overdose, there may be benefit of MDAC in enhanced elimination. We describe the use of MDAC in a severe pentobarbitone overdose case.
Case report: A 25-year-old female veterinary nurse student was found unconscious after injecting an estimated 8.125 g of pentobarbitone. On initial examination, she had a Glasgow Coma Score (GCS) 3, oxygen saturations 74%, respiratory rate 10-12/min, blood pressure (BP) 77/50 mmHg, heart rate 106 beats min, temperature 36.1 °C and 4 mm pupils with sluggish pupillary responses. She was rapidly intubated in the emergency department (ED). After intravenous fluid boluses, her BP needed further inotropic support in the intensive care unit (ICU). She received 50 g of activated charcoal in ED and two more doses of 25 g each at 2 and 4 hours after initial dose. She became hypothermic to 33.5 °C requiring re-warming and developed a lactic acidaemia peaking at 10.6 mmol/L. Extravasated pentobarbitone had caused necrosis in the bilateral cubital fossae, complicated by occlusive thrombus in bilateral cephalic and left basilic veins. Her initial serum showed a pentobarbitone concentration of 33.6 mg/L. She remained unresponsive with a GCS of 3 for 2 days in ICU whilst receiving supportive care. She had three further 25 g doses of activated charcoal on day 2 of admission. On day 3 she developed a cough reflex and by day 4 began to withdraw to painful stimuli. On day 5, she was moving all limbs spontaneously and subsequently required sedation for agitation. She had gradual improvement in neurological state and was extubated on day 10 of admission. Her bilateral cubital fossa wounds required skin grafting. She has made good functional neurological recovery.
Conclusion: In severe pentobarbitone poisoning, supportive care and MDAC resulted in good neurological outcome.

References

[1] Bosshard G, Ulrich E, Bär W. 748 cases of suicide assisted by a Swiss right-to-die organisation. Swiss Medical Weekly. 2003;133:310–317.

[2] Roberts DM, Buckley NA. Enhanced elimination in acute barbiturate poisoning – a systematic review. Clin Toxicol. 2011;49:2–12.
[3] Klaassen CD. Biliary excretion of barbiturates. Br J Pharmacol. 1971;43:161–6.

333. The impact of codeine upscheduling on prescriptions, overdoses, Emergency Department presentations and mortality in Victoria, Australia

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Objective: Prior to February 2018, codeine was available over-the-counter (OTC) in Australia as a pharmacist-only medicine (Schedule 3) in low-strength formulations with 15 mg or less per tablet. In February 2018, The National Drugs and Poisons Schedule Committee (NDPSC) upscheduled codeine-containing medicines (CCM) to Schedule 4 (prescription-only medicine). This study aimed to determine the impact of upscheduling on prescriptions, overdoses and deaths.
Methods: This study used interrupted time series analysis, a quasi-experimental design, to retrospectively evaluate the impact of upscheduling on codeine-related prescriptions, overdose poisoning calls to the Victorian Poisons Information Centre (VPIC), Emergency Department (ED) presentations to Austin Health, and deaths reported to the Victorian Coroner from 1 January 2013 to 31 December 2019.
Results: The rate of some high-strength codeine formulation prescriptions (codeine 30 mg) dropped in February 2018 ($P = 0.047$), but plateaued thereafter. Prescriptions of low-strength codeine products increased post-upscheduling in February 2018 ($P = 0.001$) and from February 2018 to December 2019 ($P < 0.0001$), a change from their steady decrease between 2013 and 2018 ($P < 0.0001$). There was a significant reduction in the trend of high-strength codeine poisoning calls ($P = 0.03$). Low-strength codeine poisoning calls to the VPIC were already reducing pre-upscheduling, but upscheduling in February 2018 coincided with a greater reduction ($P < 0.0001$), and was followed by continued reduction. High-strength codeine overdose ED presentations reduced in February 2018 ($P = 0.02$), then plateaued. Low-strength codeine overdose ED presentations reduced in February 2018 ($P = 0.02$) with a downward trend thereafter, a significant deviation from their previously increasing trend ($P = 0.03$). Codeine-related deaths also dropped in February 2018 ($P < 0.001$).
Conclusion: Codeine upscheduling to prescription-only medicine has increased codeine prescriptions and reduced codeine-related overdose and unnatural death in Victoria.

334. Intravenous iron overdose: don't trust the blood levels

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Objective: Colorimetric plasma iron assays involve *in vitro* acidification that unbinds iron from transferrin in the sample to enable analysis of total iron. Acidification will also dislodge a portion of the iron bound to the carbohydrate shell of any intravenous iron preparations present, creating elevated iron concentrations *in vitro* that do not correspond to increases in free iron *in vivo* [1]. Furthermore, the uptake of some intravenous iron preparations to the reticuloendothelial system (RES) is saturable, resulting in prolonged elevations of the parent compound in the plasma compartment [2]. The present case illustrates how these little-known properties may lead to unnecessary and potentially harmful interventions in overdoses of intravenous iron.
Case report: An 82-year-old man with moderate renal insufficiency and warfarin-treatment for atrial fibrillation was admitted for anemia and dehydration caused by gastrointestinal bleeding. After initial resuscitation, he was ordered intravenous iron-isomaltoside (Monofer) 1 g as a single injection to correct his iron deficiency. The dose was erroneously repeated on the two following days, making the total dose 3 g. The mistake was realized on day 5 when plasma-iron (by colorimetric assay) was 90 μmol/L (500 μg/dL). The patient was without gastrointestinal or hemodynamic symptoms, had no acidosis and no elevated transaminases. He was started on desferoxamine due to fears that he might be in the "latent period" of iron toxicity. Plasma-iron concentrations remained at 90-95 μmol/L (500-530 μg/dL) for another five days. During this time the patient intermittently received a total of 80 ampoules (40 g) of deferoxamine and two 4 hour sessions of hemodialysis on the assumption that the persistently elevated plasma-iron was due to inadequate renal elimination of the iron-deferoxamine complex. None of these interventions affected the plasma-iron and the patient remained asymptomatic. All treatments for iron poisoning were stopped on day 9 and the plasma-iron concentration had normalized by day 12.
Conclusion: In intravenous iron preparations a carbohydrate shell shelters the bloodstream from the toxic effects of iron in a manner functionally similar to ferritin. Highly stable, large diameter preparations can have a saturable RES-clearance and can persist in plasma for >1 week after large doses [2]. Elevated plasma-iron concentrations are to be expected after the administration of intravenous iron, may be prolonged and are useless as indicators of iron toxicity.

References

[1] Seligman PA, Scleicher RB. Comparison of methods used to measure serum iron in the presence of iron gluconate and iron dextran. Clin Chem. 1999;45:898–901.
[2] Henderson PA, Hillman RS. Characteristics of iron dextran utilization in man. Blood. 1969;34:357–75.

335. Favorable acute toxicity profile of the "hiking" stimulant nikethamide

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Objective: Nikethamide is a CNS stimulant with main effects on cardiovascular and respiratory function. Formerly, it was used as an antidote against long-lasting narcotics, such as tribromethyl alcohol or barbiturates. In Switzerland chewable tablets, containing 125 mg nikethamide and 200 mg glucose (Gly-Coramin®), are still available as a non-prescription drug for fatigue, mainly

Table 1. Severity of exposure in children and adults after oral nikethamide (n = 99).

Severity	Number	Dose in mg N/total range average; median	Dose in mg/Kg N/total range average; median	Symptoms
Children				
No effects	69	N = 55/69 62.5-2500 449.4; 437.5	N = 17/69 7.8-67.3 35.3; 31.3	None
Minor	19	N = 18/19 125-2400 687; 750	N = 10/19 11.4-83.3 36.5; 26.0	Vomiting, tachycardia, mild agitation
Moderate	1	3750 (= 30 chewable tablets)	192.3	Vomiting, tachypnoea, agitation, hallucinations
Adults				
No effects	5	N = 2/5 3750 both	Not known	None
Minor	5	N = 4/5 2500-25000 19375; 5000	Not known	Vomiting, tachycardia, mild agitation

advertised as a booster for hiking in the Swiss mountains. The tablets resemble a popular candy and are often accidentally ingested by children. Oral doses ≤7500 mg nikethamide in adults result in only minor symptoms such as nausea and vomiting [1], however, modern drug approval trials or data in children are lacking. The aim of this retrospective study was to determine the acute toxicity profile of nikethamide after oral exposure.

Methods: Retrospective review of acute oral nikethamide exposures reported to the Swiss Poisons Information Centre between 1966 and 2019. All cases with single substance ingestion, sufficient evidence of exposure and causality, and medical follow up were included. Severity was graded according to the Poisoning Severity Score.

Results: Overall 99 patients (32 males, 28 females, 39 unknown) were included, 89 children (90%) and 10 adults (≥ 17 years). The exact age was reported in 87/89 children (average 3.7 years, range 0.8-12 years). No symptoms occurred in 69 children and 5 adults. Minor symptoms were observed in 19 children and 5 adults. There was one moderate course in a 5-year-old girl, who developed agitation and hallucinations. No severe courses or deaths were reported (Table 1).

Conclusion: Overdose with nikethamide is well tolerated, even in young children and observation at home seems reasonable. Only one child developed CNS excitation with 192 mg/Kg, corresponding to 30 ingested tablets.

Reference

[1] Macarthur JG. The effect of nikethamide by mouth in man. Br Med J. 1953;1:547.

336. Successful 40-hour delayed acetylcysteine treatment in a severe acetaminophen acute hepatitis

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Objective: Acetaminophen (APAP) overdose is a common cause of hepatotoxicity. We report a case of APAP-related hepatotoxicity that resolved despite delayed antidotal treatment.

Case report: A 55-year-old female was found unconscious about 4 hours after she was last seen. No medicines or drugs of abuse were recovered nearby and her husband denied any psychiatric disorder. She was comatose (Glasgow Coma Score (GCS) 3), with bilateral mydriasis, severe hypothermia (25 °C), bradypnea, hypotension, atrial fibrillation with ventricular bradycardia and hypokalemia (2.5 mmol/L). Her medical history included a meningioma resection three years before, that left disabling frontal-temporal pain. APAP, tramadol, APAP/codeine, carbamazepine, pregabalin, oxycodone/naloxone had been prescribed without benefit. Due to the intractable pain, a peripheral nerve stimulation was started. In the ICU, she was unresponsive to adrenaline (0.2 μg/Kg/min) and noradrenaline (0.2 μg/Kg/min), and developed lactic acidosis. Urinary tests were positive for benzodiazepines, opiates, and 3,4-methylenedioxymethamphetamine (MDMA). After normalization of body temperature, hemodynamic instability and atrial fibrillation resolved. Two days later, AST 3182 U/L (normal 13-40), ALT 2612 U/L (normal 7-40), LDH 2900 U/L (normal 120-246), total bilirubin 2 mg/dL (normal 0.2-1.2) and PT-INR 2.23 (normal 0.8-1.25) were detected. On the hypothesis of MDMA acute hepatitis and following advice from the Poison Center, a second level toxicological test was performed on samples from arrival. About 5 hours after ingestion, the serum APAP was 199.8 μg/mL, carbamazepine 11.7 μg/mL (normal 8-12), trazodone 3158 ng/mL (normal 700-1600) and bromazepam 590 ng/mL (normal 700-1600); urine drug results were positive for codeine, oxycodone, and morphine and negative for MDMA. The MDMA positivity was a trazodone-associated false-positive. At 13 hours, APAP was 125.7 μg/mL and at 40 hours, APAP 102 μg/mL and carbamazepine 30.2 μg/mL. Given these findings, intravenous N-acetylcysteine (NAC) infusion and administration of repeated oral doses of charcoal were started 40 hours after ingestion. The day after, ALT increased to 5206 U/L, AST 4605 U/L, PT-INR 4.4 and, according to King's College criteria, the patient was listed for liver transplantation. Surprisingly, hepatic function normalized during the following 96 hours of NAC infusion.

Conclusion: NAC has the highest efficacy if started within 8 hours after an APAP overdose. In our case, persistently elevated APAP concentrations and decreased N-acetyl-p-benzoquinonimine formation could be related to CYP2E1 inhibition by bromazepam and competition for CYP3A4 by codeine, tramadol and

naloxone. Although delayed, NAC infusion was probably effective and improved the hepatic function until the resolution of the acute hepatitis after 96 hours of treatment.

337. "Reversal" of dabigatran-induced anticoagulation with idarucizumab: experience of an Italian hospital

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Objective: Idarucizumab is a monoclonal antibody to reverse anticoagulation induced by the oral direct thrombin inhibitor dabigatran. Despite international recommendations on usage, stakeholders involved in management of anticoagulation vary in each hospital. Local anticoagulant reversal protocols must therefore be developed, involving all relevant disciplines, to ensure the best cost-benefit results. The aim of this study is to evaluate appropriateness of indication, haemostatic effectiveness and clinical outcomes of idarucizumab through practice-based data.
Methods: A retrospective study enrolled all patients treated with idarucizumab at Bergamo ASST Papa Giovanni XXIII Hospital, from January 2016 to July 2020. Efficacy and appropriateness of idarucizumab use were assessed by two independent operators according to the International Society on Thrombosis and Haemostasis (ISTH) recommendations. In addition, coagulation parameters (PT-INR, aPTT ratio) and plasma concentrations of dabigatran before and after administration were evaluated. Patients were followed for up to 90 days for occurrence of thromboembolism, re-bleeding or death.
Results: Idarucizumab was used in 29 patients: 22 (76%) presented with life-threatening bleeding (12 intracranial, 10 gastrointestinal) and 7 (24%) required urgent surgical intervention. Effective haemostasis was achieved for all patients, including those with severe renal impairment and a high plasma dabigatran concentration (>500 ng/mL). A good correlation was observed between dabigatran plasma concentrations and coagulation parameters, suggesting their predictive role to rapidly identify patients with an over-therapeutic concentration of dabigatran, that could benefit from reversal of anticoagulation according to their clinical setting. Five patients died within 15 days after administration (mortality rate of 17%), none of these deaths could be attributable to lack of efficacy or side effects of idarucizumab. Complications within 60 days after treatment were recorded for two patients (6.9%). One patient with amyloid angiopathy experienced a recurrence of thromboembolism and one patient had anemia due to a hematoma of the thigh 10 days after idarucizumab. Use of idarucizumab was judged appropriate for 28 patients (96%).
Conclusion: In this cohort, idarucizumab use was safe, effective and appropriate, with rate of re-bleeding, thromboembolism and mortality lower than those observed in the RE-VERSE-AD trial [1]. This suggests that the presence of shared protocols and a multidisciplinary team (emergency physician, hemostasis and thrombosis experts, clinical toxicologists) may play a key role to guarantee the correct use of idarucizumab, the safety of the patient and reasonable use of economic resources.

Reference

[1] Pollack CV Jr, Reilly PA, Bernstein R, et al. Design and rationale for RE-VERSE AD: A phase 3 study of idarucizumab, a specific reversal agent for dabigatran. Thromb Haemost. 2015;114: 198–205.

338. Metformin-related enquiries from hospitals to the National Poisons Information Service (NPIS) between 2010–2019: a comparison of metformin only and polypharmacy exposures

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Objective: We present an overview of metformin exposures involving hospitalised patients reported to the NPIS, and describe the ingested doses that corresponded to the severity of symptoms.
Methods: A retrospective study of hospital enquiries. Data was extracted from the UK Poisons Information Database, which included metformin-related enquiries to the NPIS from 1 January 2010 to 31 December 2019. The incidence and epidemiology characteristics were described. Metformin doses were examined for both metformin only exposures and polypharmacy exposures involving metformin. The Mann-Whitney test was used to analyse differences in median doses for each poisoning severity score [1]. A $p < 0.05$ was considered significant.
Results: The NPIS received 3134 metformin enquiries over the 10 year period, of which 693 were from hospitals. Hospital enquiries fell by 3.6% from 2010 to 2019. The median age of patients involved was 48 years (range 0-89 years). Overall, 73.7% (474) of exposures were intentional, mainly involving 40-69-year-olds and 14.6% (94) were accidental and most common in children aged <5-years-old. Therapeutic errors were involved in 11% (71) of enquiries, most commonly in adults aged >50-years-old. Overall 23.2% (161) of patients involved were asymptomatic, compared to 67.8% (470) symptomatic patients. Only metformin was involved in 17.5% (121) of enquiries, while 82.4% (571) of enquiries were polypharmacy exposures. For enquiries involving metformin only, one death was recorded following ingestion of 48 g (551.7 mg/Kg). Higher doses of metformin corresponded to more

Table 1. Median ingested dose of metformin and Poisoning Severity Score (PSS) in metformin only exposures and polypharmacy exposures.

Poisoning severity score (PSS)	Median dose (g) in metformin only exposures (IQR)	Median metformin dose (g) in polypharmacy exposures (IQR)
Minor	9.4 (18.3)	7 (10.8)
Moderate	34.5 (26)	10.5 (14.4)
Severe	44.1 (36.7)*	14 (20.5)*

* $p < 0.05$; IQR Interquartile range

severe symptoms for both "metformin only" and "polypharmacy exposures" (Table 1).
Conclusion: Over 67% of hospital enquiries involved symptomatic patients. In patients with a severe PSS, the median metformin doses were higher in patients with single metformin exposures compared to polypharmacy exposures, suggesting that other agents may influence poisoning severity scores in polypharmacy overdoses.

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.

339. Characteristics of emergency department presentations following a drug suicide attempt

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Objective: A relatively high proportion of suicide attempts accounts for self-poisoning with medication [1]. Data from emergency department presentations can contribute to the identification of risk drug classes, which can vary among countries and over time, and provide a basis for future preventive measures.
Methods: Retrospective analysis of cases presenting at the emergency department of the University Hospital of Bern, Switzerland, from May 2012 to August 2016 after a drug suicide attempt. Exclusion criteria were suicide attempts with only alcohol or other non-medical substances and chemicals.
Results: During the study period, there were 1876 cases related to suicide attempts including 494 cases (471 patients) with medical substances. The median age of these patients was 33 years (range 16-93) and 73% were female. The most commonly involved substances/drug classes were benzodiazepines (34%), neuroleptics (23%), paracetamol (23%), and selective serotonin or serotonin-norepinephrine reuptake inhibitors (19%), followed by nonsteroidal anti-inflammatory drugs (16%), Z-drugs (15%), opioids (9%) and tri-/tetracyclic antidepressants (8%). Use of only one substance was reported in 47% of the cases. Co-consumption of alcohol or other psychoactive substances was reported in 29% and 6% of the cases, respectively. Common symptoms included somnolence (50%), tachycardia (23%) and nausea/vomiting (16%). In most cases the poisoning was of minor severity (48%) or asymptomatic (14%) and there were no fatalities. Most patients (54%) were admitted to a psychiatric ward, 20% to the intensive care unit, 12% to another hospital ward, and 13% were discharged home.
Conclusion: Apart from paracetamol, the most commonly involved substances were prescription drugs used in the treatment of psychiatric disorders. Careful monitoring of the patients for suicidality when prescribing psychotropic drugs, and pack size restrictions as well as raising awareness among healthcare professionals qualified to prescribe or supply paracetamol could be important preventive measures in the future.

Reference

[1] Muheim F, Eichhorn M, Berger P, et al. Suicide attempts in the county of Basel: results from the WHO/EURO Multicentre Study on Suicidal Behaviour. Swiss Med Wkly. 2013;143:w13759.

340. Propylthiouracil administration in 5 cases of thyroid hormone intoxication

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Table 1. Characteristics of 5 patients with thyroid hormone overdose treated with propythiouracil (PTU).

Sex, age and body weight	Product	Type of exposure and dose assumed	Symptoms at ED admission	Thyroid function	Treatment
F, 47 y, 31 Kg	Levothyroxine	Chronic, 1 mg/day for 8 days	Atrial fibrillation, insomnia, agitation, gastrointestinal symptoms.	TSH <0.01 [0.15-3.5 mUI/L] FT3 > 25 [2-3.5 pg/mL] FT4 > 9 [0.7-1.7 ng/dL]	Propranolol, PTU 300 mg/day for 6 days.
F, 43 y, 55 Kg	Levothyroxine	Chronic, 45 mg/day for 6 months	Tachycardia (140 bpm), hyperpyrexia (39.5 °C), agitation, insomnia.	TSH 0.01 [0.15-3.5 mUI/L] FT3 32 [3-8.5 pg/mL] FT4 77.7 [9-17 pg/mL]	Propranolol, hydrocortisone 300 mg bolus +100 mg x 3/day, PTU 300 mg/day.
F, 38 y, 65 Kg	Galenic preparation	Chronic, unknown dose for 6 months	Supraventricular tachycardia (180 bpm), confusion, agitation, respiratory distress.	TSH 0.01 [0.15-3.5 mUI/L] FT3 32 [2-4.4 pg/mL] FT4 7.77 [0.93-1.7 ng/dL]	Adenosine, metoprolol, diazepam, promazine, PTU 350 mg/day for 10 days.
M, 62 y, 70 Kg	Levothyroxine	Acute, 6.25 mg	None.	TSH 2.373 [0.15-3.5 mUI/L] FT3 6.28 [2.3-4.2 pg/mL] FT4 42.50 [0.89-1.76 ng/dL]	PTU 700 mg/day for 4 days.
M, 34 y, nk	Levothyroxine	Acute, 20 mg	None.	TSH 0,03, FT3 32.55 FT4 7.77	PTU 150 mg/day for 3 days.

Thyroid stimulating hormone TSH, Thyroxine T4, Triiodothyronine T3, Free triiodothyronine FT3, Free thyroxine FT4

Objective: Thyroid hormone intoxication can occur following acute overdose or chronic abuse of drugs including galenic preparations used to lose weight. In chronic poisoning, patients present to hospital with symptoms, but in acute overdose clinical manifestations are typically delayed 2-5 days after ingestion, because peripheral conversion of thyroxine (T4) to the metabolically active form triiodothyronine (T3) is required. Propylthiouracil (PTU) is an antithyroid drug that decreases endogenous hormone synthesis, mainly inhibiting the activity of thyroid peroxidase and, in a less extent, the peripheral conversion of free thyroxine (FT4) to free triiodothyronine (FT3), mediated by 5′-deiodinase. We present a case series of acute and chronic thyroid hormone intoxication treated with propylthiouracil.
Cases series: Patient 1: History of anorexia, she took a variable daily dose of thyroid hormone and furosemide to lose weight. After PTU administration she developed septic shock and cardiac arrest, unrelated to the intoxication. She was discharged 1 month later with a complete recovery. Patient 2: Chronic therapy with levothyroxine for thyroidectomy. She ingested a chronic higher dose to lose weight and improved after PTU administration. Patient 3: She chronically took a galenic slimming product (thyroid hormone concentration unknown). Her severe clinical picture (she required mechanical ventilation) made it difficult to evaluate PTU efficacy. Thyroid hormone values were still altered a month after admission. Myopathy was a complication in this case. Patients 4 and 5: Suicide attempts with thyroid hormone. PTU was promptly administered, on the basis of the anamnestic data. Patients remained asymptomatic.
Conclusion: Chronic high-dose thyroid hormone intake causes symptoms that are often severe, while acute overdoses are often clinically silent for at least 48 hours. PTU can be used in chronic poisonings to limit the toxic effects, and in severe acute overdose to prevent the onset of symptoms, in association with symptomatic treatment.

341. Evaluation of the overdosage section in Summaries of the Product Characteristics for medicines responsible for exposure calls to the Belgian Poison Centre

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Objective: To evaluate the overdosage sections (OS) in the summaries of the product characteristics (SmPC) from all medicines containing one of the 25 active pharmaceutical ingredients (API) most responsible for medication exposure calls to the Belgian Poison Centre (BPC) in 2019.
Methods: SmPC were retrieved from the national competent authority's website. Then the information in its OS about decontamination, antidotes, enhanced elimination, symptoms to expect, toxic dose, poison centres contact data or other relevant issues was evaluated for presence and consistency with up-to-date clinical toxicology practice guidelines.
Results: The BPC received 9,764 medication exposure calls for the 25 API in a total of 21,077 calls in 2019. These API were present in 144 officially authorised medicines. In the 144 corresponding SmPC, 86.1% (N = 124) of the OS had no or misguiding information about decontamination techniques such as induce vomiting, gastric lavage or activated charcoal. Additionally, 65.3% (N = 94) lacked or had incomplete information about antidotes such as the use of insulin/glucose and L-carnitine or the contraindications of flumazenil. Similarly 52.1% (N = 75) had absent information about enhanced elimination techniques or suggested them despite their ineffectiveness. Although 66.7% (N = 96) cited the correct symptoms to expect, 33.3% (N = 48) did not mention toxidromes such as serotoninergic syndrome or neuroleptic malignant syndrome or lacked important symptoms like hyperthermia, hepatitis or hyperammonaemia. Furthermore 12.5% (N = 18) had misguiding information about blood analyses, half-life or treatment options. Correct information about the toxic dose was cited by 41.7% (N = 60) of the OS. Finally 94.4% (N = 136) did not suggest contacting the BPC in case of overdosage. Complete contact data for the BPC were given in 2.8% (N = 4) of all the OS.
Conclusion: Important information was found to be lacking, incomplete or misguiding in the OS of the SmPC from medicines containing one of the 25 API most responsible for medication exposure calls to the BPC in 2019. Lacking or misguiding information can influence the management of overdosages by healthcare professionals. The marketing authorisation holders should thus revise their OS accordingly. Poison centres or clinical toxicologists can thereby have an advisory role and ensure correct and current advice in SmPC.

342. Is haem arginate safer in overdose than previously thought? An uneventful four-fold accidental overdose

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Objective: Haem arginate (Normosang®) is used in the treatment of acute intermittent porphyria (AIP) attacks. It is formulated from human hemin, propylene glycol, ethanol and water [1]. Acute renal failure, liver failure and liver transplantation have previously been reported following overdose [1,2]. We report an accidental overdose of haem arginate with uneventful clinical course and recovery.
Case report: A 22-year-old female, with known AIP, was admitted with worsening abdominal pain, knee pain and vomiting. Her clinical observations were stable. Other than a chronically elevated bilirubin concentration (36 μmol/L) and mildly elevated amylase activity (134 U/L), her blood tests were normal. Following advice from the National Acute Porphyria Service, she was prescribed 210 mg (3 mg/Kg) intravenous haem arginate once daily for 4 days. She accidentally received 1 g of haem arginate at 18:45 h, nearly 5 times higher than the recommended dose. This was discovered following a medication stock check around 10:00 h the next day. The UK National Poisons Information Service (NPIS) and the manufacturing company Recordati, were consulted. At this time, the patient was still vomiting. Blood tests demonstrated normal renal function and stable liver function including bilirubin 38 μmol/L and ALT 27 U/L. The patient had an anion gap of 21 mmol/L and an osmolar gap of 10 mOsm/L with no metabolic acidosis. There were no signs suggestive of propylene glycol toxicity. Based on advice from NPIS and Recordati utilising published literature, the patient received 25 g oral activated charcoal, 1 unit of intravenous 20% albumin and 7 L intravenous 0.9% saline over 48 hours. Her vomiting settled and she was discharged with normal renal and liver function

Table 1. Case reports of antidotal use of carbapenems use in valproic acid toxicosis.

Study	Age/ gender	Coingestants	Initial [VPA] (μg/mL)	Peak [VPA] (μg/mL)	Carbapenem	Other therapies	Outcome	Comment
Zosel et al (2015)	31/M	Lorazepam	>300	>300	Ertapenem 1 g × 1 dose	Levocarnitine	Gradual clinical improvement, discharged to psychiatric facility on day 4	Significant decrease in apparent half-life in period 18-29 hours after ertapenem administration, then gradual increase back to pre-carbapenem half-life by 40 hours post-dose; patient improved clinically after ertapenem despite increasing ammonia concentrations
Doad et al (2017)	29/M	none	>450	>450	Ertapenem 1 g IV × 1 dose	AC, levocarnitine, lactulose	Mental status improved, extubated on day 2, transferred out of ICU on day 3	Apparent VPA half-life of 5.7 hours after ertapenem administration
Khobrani et al (2017)	45/M	None	396.2	415	Meropenem 500 mg IV q6 x 8 doses	AC, levocarnitine	Extubated after 26 hours, transferred to inpatient psychiatry on day 5	Meropenem given for suspected aspiration pneumonia and to decrease VPA concentrations; 56% reduction in apparent half-life (4 versus 9.06 hours) compared to patient's previous VPA overdose admission (did not receive AC or levocarnitine in the first case); also received naloxone
Dreucean et al (2019)	38/F	Quetiapine	82	278	Meropenem 1 g IV q8h × 2 doses	AC, levocarnitine	Transferred to inpatient psychiatry on day 5	VPA concentration dropped into therapeutic range 1 hour after second dose of meropenem
Gazwi et al (2019)	41/M	None	>576 (>4000 μmol/L)	>576 (>4000 μmol/L)	Ertapenem 1 g daily × 2 doses	AC, HD, l evocarnitine	Complete neurologic recovery from coma and extubated on day 2, transferred to inpatient psychiatry on day 5	Also received naloxone due to suspicion of opioid toxicity
Thomas et al (2019)	42/F	Quetiapine	134	224	Ertapenem 1 g IV × 1 dose, then meropenem 2 g q8h	AC	Extubated on day 2; switched to ampicillin/sulbactam on day 4 after sputum and blood cultures grew *A. baumannii*, VPA restarted; transferred out of ICU on day 13; discharged on day 18	VPA concentration decreased after initial dose of ertapenem, then increased to peak, and decreased again after meropenem q8h started; VPA concentration dropped into therapeutic range within 24 hours of initial carbapenem dose; meropenem given for suspected aspiration pneumonia and to decrease VPA concentrations; switched from ertapenem to meropenem due to hospital formulary; also received naloxone
Munoz-Pichuante et al (2020)	30/F	Clonazepam, APAP	335.2	335.2	Meropenem 1 g IV q8h	Gastric lavage	Improvement in mental status and able to be weaned off of pressors within 24 hours of stopping meropenem; transferred to inpatient psychiatry on day 3	VPA concentration dropped into therapeutic range 18 hours after starting meropenem; levocarnitine was not available; decrease in ammonia concentrations after lavage and carbapenem (80.2 to 60.2 in 18 hours); patient was taking VPA for epilepsy; also received NAC for APAP toxicity
Sanivarapu et al (2020)	42/F	None	144	144	Meropenem 1 g q8h × 3 doses	Levocarnitine	Improvement in mental status and extubated after 3 doses of meropenem	VPA concentration dropped from 135.2 to 96 μg/mL after first dose of meropenem, down to 11.5 μg/mL after 3 doses

AC: activated charcoal; APAP: acetaminophen; HD: hemodialysis.

blood tests. Transaminase activities were mildly increased a week after discharge (ALT 51 U/L, AST 93 U/L) but had improved one month later (ALT 30 U/L, AST 57 U/L).
Conclusion: There is currently limited available literature on haem arginate toxicity. Though published case reports suggest severe toxicity at similar doses; this patient did not develop any features of toxicity. Further information and evidence is required to confidently determine the safety of this compound in overdose.

References

[1] Normosang® – Summary of Product Characteristics, Labelling and Package leaflet. Recordati Rare Diseases Ltd, 2019 [cited 18 October 2020]. Available from https://www.recordatirarediseases.com/sites/www.recordatirarediseases.com/files/inline-files/NOR_SmPC.pdf
[2] Frei P, Minder EI, Corti N, et al. Liver transplantation because of acute liver failure due to heme arginate overdose in a patient with acute intermittent porphyria. Case Rep Gastroenterol. 2012; 6:190–6.

343. Literature review of antidotal carbapenem use in valproic acid toxicity

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Objective: Decreases in valproic acid's (VPA) half-life with coadministration of carbapenems have previously been described in therapeutic use. Suggested mechanisms include decreased absorption and enhanced glucuronidation of VPA when given in conjunction with carbapenems. This study aims to explore existing literature on antidotal use of carbapenems in acute valproic acid toxicity.
Methods: A literature review was conducted using PubMed, Google Scholar, and Google and the keywords: "valproic acid," "carbapenem," and "toxicity" to identify reports of carbapenems used in VPA poisoning. Additionally, abstracts from the North American Congress of Clinical Toxicology (NACCT) and European Association of Poison Control Centres and Clinical Toxicology (EAPCCT) between 2011-2020 were searched. Cases were only included if they reported acute valproic toxicity after acute intentional ingestion.
Results: Eight case reports were identified that met criteria (Table 1). Peak VPA concentrations ranged from 144 to >576 μg/mL. All patients exhibited some degree of altered mental status, ranging from mild somnolence to coma. The most frequently used carbapenem was meropenem (5/8, 62.5%), followed by ertapenem (4/8, 50%), with one patient receiving doses of both antibiotics. Dosing strategies varied, with most patients receiving multiple doses of carbapenems until clinical improvement and/or VPA returned to therapeutic range. In two cases, carbapenems were given for the dual purpose of treating aspiration pneumonia and decreasing VPA concentrations. All patients received at least one other therapy for VPA toxicity, including activated charcoal (5/8, 62.5%), L-carnitine (5/8, 62.5%), lactulose (1/8, 12.5%), hemodialysis (1/8, 12.5%), and gastric lavage (1/8, 12.5%). No seizures were reported in any cases. All patients achieved resolution of symptoms with no ongoing sequelae of toxicity noted.
Conclusion: Literature on use of carbapenem usage in acute VPA toxicity remains extremely limited. While case reports have reported a temporal improvement with addition of carbapenems, further research is greatly needed.

344. Comparison of acute kidney injury and renal replacement therapy in patients with rhabdomyolysis acutely intoxicated with psychotropic or chemical substances

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Objective: We determine the risk factors for the development of acute kidney injury and the necessity of renal replacement therapy (RRT) for patients with rhabdomyolysis due to acute intoxication with psychotropic and chemical substances.
Methods: This was a prospective clinical study conducted from 1 January to 31 December 2019 at the University Clinic for Toxicology in Skopje. The study included patients with rhabdomyolysis divided in to two groups in accordance with the substance used for intoxication (psychotropic or chemical). Rhabdomyolysis was defined as a creatine phosphokinase (CPK) > 250 U/L. The diagnosis and the stages of the acute kidney injury were defined using the Kidney Disease: Improving Global Outcomes (KDIGO) classification. Data were statistically analyzed in SPSS software, version 22.0 for Windows (SPSS, Chicago, IL, USA).
Results: Acute kidney injury occurred in 15% of 140 patients with rhabdomyolysis of whom 66.7% (n = 14) had psychotropic intoxication and 33.3% had chemical intoxication (n = 7). Statistical analysis showed significantly increased prevalence in the psychotropic group compared to those with chemical intoxication ($p = 0.0002$). The highest prevalence of acute kidney injury in the psychotropic intoxication group was heroin (60%) and methadone (40%), followed by neuroleptics (25%), anticonvulsants (17.7%) and antidepressants (8.3%). In the chemical intoxication group, acute kidney injury was registered in 15.9% of patients. The highest prevalence of acute kidney injury in this group was due to ethylene glycol (100%) and fungus poisoning (33.3%), followed by pesticides (20%) and corrosives (16.7%). With regards to RRT, there was a significantly higher prevalence in patients with psychotropic intoxication compared to chemical intoxication ($p = 0.0001$). Patients intoxicated by psychotropic or chemical substances, with acute kidney injury and rhabdomyolysis had higher values for aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine phosphokinase (CPK), troponin and myoglobin. In the group with chemical intoxication, patients with acute kidney injury had higher values for AST ($p = 0.3277$), ALT ($p = 0.9616$) and troponin ($p = 0.0051$) compared to those without acute kidney injury. The quantity/value of CPK ($p = 0.8348$) and myoglobin ($p = 0.1127$) was higher in patients with acute kidney injury intoxicated by chemical substances.
Conclusion: The prevalence of acute kidney injury and necessity for RRT was significantly higher in psychotropic intoxication compared to chemical intoxication. Certain toxic agents in acutely intoxicated patients with rhabdomyolysis may have an important role in the development of acute kidney injury. Patients with acute kidney injury and rhabdomyolysis as well as those intoxicated with psychotropic substances have significantly higher

values for CPK, AST, ALT, troponin, and myoglobin compared to those without acute kidney injury.

345. Increasing enquiries to the Norwegian Poison Information Center (NPIC) concerning ozone

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Objective: Ozone (O_3) is an irritant gas with oxidizing properties. Uses include disinfection, bleaching and in removing bad odours. Ozone generators for private use are readily available, both for sale and for rent. Inhalation of ozone can cause severe lung toxicity, depending on the degree and duration of the exposure and individual risk factors. We have looked closer at ozone related enquiries to NPIC during the last decade. The aim has been to examine whether there has been a statistically significant increase in the number of enquiries.
Methods: We conducted a search covering all telephone enquiries from January 2010 until the end of August 2020. Enquiries concerning human exposures with "oson/ozon" were mapped. Non-relevant matches were excluded manually, such as "*fenozon*" and "*nalozon*". Finally, the numbers were adjusted to ensure that each enquiry was registered only once.
Results: There were 176 different ozone related telephone enquiries. Certain trends are obvious with regards to age and gender distribution. The majority of the enquiries involved the age group from 20 to 69 years (84%) and the exposed were mainly men (females 17%, males 70%, both 5% and unknown 8%). The exposures were registered as a private accident (53%) or as occupational accident (39%). The telephone enquiries most often came from the public (54%), doctors/emergency rooms (30%) and the work place (10%). The risk assessment at the time of the enquiry was as follows: "*Risk of minor poisoning*" (41%), "*risk of moderate poisoning*" (21%), "*impossible to assess*" (25%), "*risk of severe poisoning*" (7%), "*poisoning unlikely*" (3%) and "*symptoms, not poisoning*" (3%). In 2010 there were only 7 different enquiries, compared with 31 different enquiries in 2019. The average number of enquiries over the period from 2010 to 2020 equals 17.3. An up- and downward fluctuation of two standard deviations with respect to the mean would correspond to 26 and 9 enquiries, respectively. Thus, the data shows a significant increase in the number of telephone enquiries over the past decade.
Conclusion: Most of the persons exposed to ozone are men aged 20 to 69 years. Overall, 39% of the enquiries were registered as occupational accidents and 53% as private accidents. After the assessment, 29% of the enquiries were categorized as "*risk of moderate or severe toxicity*". Ozone related enquiries have increased substantially during the last decade and this cannot be explained by statistical fluctuations.

346. A 10-year review of ocular exposures reported to the Irish National Poisons Information Centre

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Objective: Ocular chemical exposure is an ophthalmic emergency which can cause permanent visual loss. Severity depends on the substance involved and the contact duration. Alkaline powders and gels are particularly hazardous, some causing irreversible blindness within minutes. Such incidents are particularly challenging in children as examination can be difficult and the lifelong sequelae potentially profound. Regardless of the agent, treatment focuses on removal of xenobiotics and irrigation of the ocular surface [1,2]. We aimed to analyse the epidemiology and trends relating to ocular exposures reported to the Irish National Poisons Information Centre (NPIC) over a 10-year period.
Methods: A retrospective review of all recorded cases involving ocular exposure from 2010 to 2019, inclusive. Data included: agent name, agent type, patient demographics, location of incident, symptoms, severity, treatment advised, and provenance of enquiry.
Results: The NPIC received 3,198 cases involving ocular exposure, a 36% increase from 2010 (n = 281) to 2019 (n = 381). Agent type was identified in 99.6% of cases. The commonest categories were household (39%, n = 1,644) and industrial (36%, n = 1,527), together comprising 75% of all cases. Liquid detergent capsules were the commonest agent (11%, n = 342). Most enquiries (67%) were from healthcare professionals, with 29% from members of the public. Most incidents (82%) occurred at home and 54% of calls concerned males and 44% females, with 2% unknown. Over 50% (n = 1,627) of calls concerned children (0-9 years of age). Overall 62% (n = 1,987) of patients were symptomatic, 98% of these were classified as mild. Eye pain was the main symptom (n = 552). Referral to hospital for treatment was recommended to 12% of callers. Two adult cases were classified as severe and 25 adult (1.6%) and 16 paediatric cases (1%) were moderate. Sodium hydroxide made up 0.8% of exposures but resulted in 16% of adult moderate injuries. Liquid detergent capsules represented 11% of exposures but accounted for 69% of moderate paediatric cases.
Conclusion: Enquiries concerning ocular chemical exposure have increased in Ireland over the past decade. More than 50% of cases involved children. The most serious paediatric cases are disproportionately related to liquid detergent capsules, reflecting international trends [1,2].

References

[1] Heise CW, Agarwal S. Ocular exposures reported to poison control centers from 2011 to 2015. Am J Ophthalmol. 2019;204:46–50.
[2] Haring RS, Sheffield ID, Channa R, et al. Epidemiologic trends of chemical ocular burns in the United States. JAMA Ophthalmol. 2016;134:1119–1124.

347. Fatalities due to acute poisoning: a one year retrospective study

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Objective: To present a retrospective analysis of fatal cases of acute poisoning in our toxicological department during a one year period.
Methods: The records of the Toxicology Clinic, Emergency University Hospital "N.I.Pirogov", Sofia, Bulgaria were reviewed retrospectively for all poisonings in adults during a one year period, from 1 January to 31 December 2019. The fatal cases

were analyzed with regard to gender, age and type of agent. The main reasons for the unfavourable outcome were evaluated.
Results: A total of 2298 patients were hospitalized in the Toxicology Clinic over the study period, and there were a total of 27 fatal poisonings during this period (1.2%). Eleven cases of fatal poisoning (40.8%) involved pharmaceutical agents, 5 cases (18.5%) involved alcohols, including methanol and 11 cases (40.8%) involved other agents such as corrosive products, pesticides, carbon monoxide and detergents. The most commonly implicated drug groups were benzodiazepines, antihypertensives, antidepressants and neuroleptics. The patients with a lethal outcome of poisoning were aged between 30 and 90 years. The highest incidence was found in the patients aged over 70 years (n = 16, 59.6%), followed by patients aged 51-70 years (n = 7, 25.9%) and those, aged 30-50 years (n = 4, 14.8%). Female mortality was higher (n = 17, 63.0%) compared to males (n = 10, 37.0%). Unintentional exposure was the most common cause of fatal poisoning (n = 17, 63.0%). In 10 cases (37.0%) of fatal poisoning the exposures were intentional. In patients with fatal outcome we observed the following most common complications: bronchopneumonia (7 cases, 25.9%), exotoxic shock (5 cases, 18.5%), multiple organ failure (4 cases, 14.8%), and secondary anemia (3 cases, 11.1%).
Conclusion: Pharmaceutical agents were the most common products causing fatal poisoning. The highest incidence was found in patients aged over 70 years. Unintentional exposure was the most common cause of fatal poisoning in this cases series.

348. Veratrum Aqua poisonings resulting from its misuse: a case series from Moscow, Russia

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Objective: Veratrum Aqua (VA) is an over-the-counter drug in Russia, used topically to treat pediculosis. It is a tincture of *Veratrum lobelianum* diluted 50:50 with water. VA is sometimes misused in traditional medicine for treatment of alcoholism. VA peroral administration results in acute and, in rare cases, lethal poisoning. Such poisonings are sometimes challenging to confirm due to concealment by patients and lack of analytical methods. We present a case series of 4 patients admitted to the Toxicological Department (TD), N.V. Sklifosovsky Research Institute for Emergency Medicine from October to November 2020.
Case series: Four patients, 2 male and 2 female, ingested 50-100 mL of VA and were treated with atropine and prednisolone by the ambulance service. They arrived at the TD in critical but stable condition. Descriptive analysis is presented in Table 1. On admission to the TD all patients had clouded consciousness, muscle weakness, pallor, repeated vomiting, and abdominal pain. Three of them exhibited bradycardia and hypotension. Patient 3 showed decreased blood pressure and bradycardia after 4 hours. Two were also under the influence of alcohol. Ethanol concentrations were measured by gas chromatography. The three main veratrum alkaloids (jervine, protoveratrin A and B) were monitored in blood plasma and urine by high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) at hospital admission and during treatment. All patients underwent detoxification, cardioprotective, symptomatic and vitamin therapy. After 24 hours, the symptoms of poisoning subsided in three patients, and the concentrations of alkaloids decreased to the limit of detection. In patient 3 a decrease in alkaloid concentrations and normalization of the condition occurred after 70 hours. She was additionally given an intestinal lavage.
Conclusion: It is critical to determine veratrum alkaloid concentrations in patients with poisoning as it correlates with condition severity and affects treatment duration.

349. Lethal poisoning with *Oenanthe crocata*. Survive or not?

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Objective: Survival courses in the wilderness carry the risk of intoxication linked to the consumption of toxic wild plants. We report the case of lethal intoxication after ingestion of *Oenanthe crocata* rhizome. This plant contains oenanthotoxin, a long chain polyacetylenic alcohol, which is a powerful central nervous system stimulant that blocks gamma-aminobutyric acid A ($GABA_A$) receptors causing neuronal depolarisation resulting in grand mal convulsions.
Case report: Inside a survival camp, 15 minutes after having ingested a piece of saffron-coloured *Oenanthe crocata* root approximately 3 cm^3 a 25-year-old man developed hypersalivation then seizures with coma requiring ventilation. Just before endotracheal intubation, he had a brief cardiac arrest (low flow less than 10 minutes) responding to adrenaline infusion. Blood biochemistry at 2 hours revealed a severe mixed acidosis, renal failure, rhabdomyolysis associated with pronounced

Table 1. Characteristics, ethanol and alkaloid concentrations and hospitalization time in patients with Veratrum Aqua poisoning.

Patient	Blood pressure (mmHg)	Heart rate	Ethanol concentration (g/L)		Alkaloid concentration in admission (ng/mL)				Time in intensive care unit (hours)	Duration of hospitalization (days)
					Jervine		Protoveratrine A			
			Blood	Urine	Blood	Urine	Blood	Urine		
1. Male, 20 years	110/70	50	0	0	0.52	0.58	0.2	37.7	38	3
2. Male, 47 years	125/70	42	1.95	4.11	0.35	0.24	0.11	6.13	48	4
3. Female, 45 years	165/147	52	2.08	3.23	5.01	1.71	0.67	4.87	70	6
4. Female, 74 years	80/60	46	0	0	0.10	0.23	0	0.15	36	3

hyperphosphatemia, probably related to early cell destruction. The patient received a dose of activated charcoal, and the early initiation (at 3 hours) of continuous venovenous hemodialysis. The first urine was orange in color (saffron). Acute circulatory distress with multi-organ failure (muscular, renal, liver, digestive, brain) developed. At 48 hours, a state of clinical brain death was observed in connection with magnetic resonance imaging (MRI) with diffuse cortical anoxo-ischemic lesions and central grey nuclei. Toxicological analysis of the rhizome revealed a concentration of 17 mg/g of oenanthotoxin, 12 mg/g of dihydrooenanthotoxin and 0.39 mg/g of tetrahydrooenanthotoxin. Only the two metabolites were found in blood samples at 3 hours (0.83 and 1.2 μg/mL, respectively) and 36 hours (1.0 and 3.1 μg/mL). Tetrahydrooenanthotoxin was also found in urine (1.2 and 3.1 μg/mL). Autopsy analysis revealed the presence of both metabolites in the brain, liver and kidneys.
Conclusion: This case highlights the high metabolic toxicity of oenanthotoxin with multiorgan damage in the form of refractory ischemic lesions (brain, digestive tract) and biological evidence of muscular, renal and hepatic damage. Oenanthotoxin, dominant in the plant, seems to transform very quickly into dihydrooenanthotoxin and tetrahydrooenanthotoxin derivatives whose clinical evolution suggests a specific toxicity. Even with optimal work between intensivists and toxicologists, the fatal evolution highlights the importance of prevention, including people attending survival camps.

350. The White Panther: rare exposure to *Amanita multisquamosa* causing clinically significant toxicity

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Objective: The mushroom genus *Amanita* includes a number of toxic species. *Amanita multisquamosa* (aka *Amanita cothurnata*) is known as the "white panther" or "small funnel-veil *Amanita*" [1]. Very few poisoning cases have been unequivocally attributed to *Amanita multisquamosa*. Previously reported cases in Canada included a family, who experienced gastrointestinal symptoms 3 hours after eating cooked specimens and developed erratic behavior, resembling *Amanita muscaria* toxicosis [2]. High concentrations of muscimol and ibotenic acid were reported, increasing comparison to *Amanita muscaria* [3]. We present a rare case involving a patient who developed toxicity secondary to confirmed *Amanita multisquamosa* ingestion.
Case report: A 30-year-old female presented with altered mental status 3 hours after cooking and ingesting an unknown mushroom species in upstate New York. She vomited approximately 6 hours after ingestion. Vital signs were blood pressure 126/78 mmHg, heart rate 84 bpm, respiratory rate 27 breaths/min; oxygen saturations 97% (room air), afebrile. Upon physical exam, she was somnolent, only responsive to sternal rub, pupils equal, round, reactive to light, and normal bowel sounds. All labs including liver enzymes were unremarkable. She was admitted to the intensive care unit (ICU) for further monitoring. Photographs and physical mushroom specimens were transported for analysis by mycologists at Cornell University, New York. The mushrooms were identified via macroscopic features including the stature, pale cap with darker disc and striate margin, pale, prominent warts, and truncate lamellulae. Spore measurements supported the identification. A similar species, *Amanita velatipes*, can be differentiated by its larger spores, yellow colors, and typically larger size. She received intravenous acetylcysteine (NAC), nasogastric milk thistle extract 50 mg/Kg/day in 4 divided doses and activated charcoal due to initial suspicion of amatoxin exposure. Repeat vital signs and labs at 6, 8, 17, 26, and 38 hours remained stable and unremarkable. Her mental status improved approximately 14 hours after exposure. Acetylcysteine was completed and she was discharged on hospital day 2.
Conclusion: This was a patient case involving rare exposure to an uncommon *Amanita* species, *A. multisquamosa*, resulting in clinically significant central nervous system toxicity but no hepatotoxicity.

References

[1] Tulloss RE, Rodríguez Caycedo C. *Amanita multisquamosa*. In Tulloss RE, Yang ZL, eds. Amanitaceae studies [cited 8 November 2020]. Available from http://www.amanitaceae.org?Amanita+multisquamosa
[2] Dearness J. Mushroom poisoning due to *Amanita cothurnata*. Mycologia. 1935;27:85–86.
[3] Chilton WS, Ott J. Toxic metabolites of *Amanita pantherina, A. cothurnata, A. muscaria* and other *Amanita* species. Lloydia. 1976; 39:150.

351. Protective effects of hypercalcaemia in the setting of severe hypermagnesaemia

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Objective: Hypermagnesaemia is commonly iatrogenic or self-induced, particularly in the setting of normal renal function, and toxicity is characterised by progressive loss of neuromuscular, respiratory and cardiovascular function. Severe hypermagnesaemia is often fatal as progressive sinoatrial and atrioventricular nodal block precedes cardiorespiratory arrest, with reports of fatalities associated with serum magnesium concentrations of 3.7 mmol/L (9.1 mg/dL) and higher [1]. Serum calcium concentrations are usually low or unchanged, and intravenous calcium has been used to reverse the calcium-channel blocking effects of hypermagnesaemia, in particular to treat cardiac arrhythmias, hypotension and respiratory depression [2].
Case report: A previously well 21-year-old female presented following a mistaken ingestion of six tablespoons of magnesium chloride salts. Her intention had been to take Epsom salts (magnesium sulphate) as a cathartic. One-hour post-ingestion she developed flushing and light-headedness. On hospital arrival 90 minutes post-ingestion her Glasgow Coma Score was 9 with mydriasis, heart rate 85 beats per minute, blood pressure 141/89 mmHg, respiratory rate 16 with oxygen saturation of 96%. She was hypotonic with absent deep tendon reflexes and was in urinary retention. The ECG demonstrated a 1st degree heart block (PR interval 203 ms) and incomplete right bundle branch block (RBBB). Her initial serum magnesium concentration was 9.3 mmol/L (22.6 mg/dL) (reference range 0.7 to 1.1 mmol/L), with serum calcium of 3.1 mmol/L (12.3 mg/dL) (reference range 2.1 to 2.5 mmol/L), creatinine of 52 μmol/L and glomerular filtration rate of $>$90 ml/L/1.73 m^2. She received supportive care without endotracheal intubation and was treated with 2 litres of intravenous Hartmann's solution with resolution of her symptoms

corresponding to serial down-trending magnesium concentrations. By 12 hours post-ingestion she had full clinical recovery with serum magnesium concentration of 1.6 mmol/L (4.06 mg/dL), serum calcium 2.3 (9.2 mg/dL) and an electrocardiogram (ECG) with normal PR interval and resolution of the RBBB. Chemical analysis of the ingested salts are awaited. We postulate that the hypercalcaemia resulting from the unlabelled calcium contained in the ingested salts prevented our patient developing the cardiac or respiratory complications that might be expected with severe hypermagnesaemia.
Conclusion: Coexistent hypercalcaemia may have been protective against the respiratory and cardiovascular effects of severe hypermagnesaemia.

References

[1] Bokhari S, Sirki R, Teran F, et al. Fatal hypermagnesemia due to laxative use. Am J Med Sci. 2018;355:390–5.
[2] Cholst I, Steinberg S, Tropper P, et al. The influence of hypermagnesemia on serum calcium and parathyroid hormone levels in human subjects. N Engl J Med. 1984;310:1221–5.

352. Caustic exposures attending the Emergency Department: results of the Spanish Toxic Surveillance System (STSS) 2010–2019

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Objective: Caustic exposure is not a frequent event in our emergency department (EDs) despite the fact that several potentially dangerous commercial products of this type are authorized for domestic use. They belong to the category of substances submitted to the Spanish ToxicoSurveillance System established by the Health Ministry and held by the Spanish Foundation of Clinical Toxicology (FETOC). We examined the characteristics of these cases obtained by the Program in the last 10 years showing its usefulness to verify the current risk of authorized chemicals.
Methods: Participating hospitals report cases of intoxication due to household, agricultural or industrial chemicals treated in their ED. An online questionnaire is accessible through the FETOC website by means of an encrypted system and files are downloaded on a regular basis to a database (File Maker 9.0®). The evaluated data included demographics, intentionality of poisoning, main agents, severity, and evolution.
Results: From 2010 to 2019 the Program collected 10,174 cases from 22 hospitals covering a population of about 8 million people. There were 2,029 cases (9.6%) involving caustics. The mean age of patients was 40 ± 25 years and 973 (48%) were males (37 ± 24 years) and 1024 (50%) were females (age 40 ± 25 years). There were 379 (18%) young patients under 16 years. Domestic accidents were significantly prevalent (1275, 63%) followed by suicide gestures (496, 24%) and occupational accidents (199, 10%) ($p < 0.05$). The main chemicals involved, either alone or in mixtures were bleach (1074, 53%), ammonia (241, 12%), sodium hydroxide (156, 8%), and hydrochloric acid (142, 7%). The main route of entry was oral (1486, 73%), ocular (399, 20%) and cutaneous (103, 5%). Overall, 83% of the patients were symptomatic at admission presenting with digestive 1091 (53%), ocular 423 (21%) and cutaneous 120 (6%) symptoms. Most patients (1516, 75%) received treatment, mainly symptomatic 1441 (71%) with ocular decontamination (365, 18%), cutaneous decontamination (91, 5%) and gastric decontamination (24, 1%). Only 113 cases (6%) required hospital admission for 24-hour observation and 43 (2%) were admitted to the intensive care unit (ICU). The mortality rate (49 cases) was 2.4%. Bleach was involved in 14 cases, hydrochloric acid in 28 cases (20% of total hydrochloric acid cases). Nearly all lethal cases (45) were suicidal.
Conclusion: Acute poisoning by caustics in Spain are low risk events, caused mainly by domestic accidents. Bleach stands out in terms of frequency of poisoning and hydrochloric acid, commercialized as a domestic cleaning agent, in terms of lethality.

353. Accidental exposures to caustic drain cleaners

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Objective: Accidental exposures to caustic drain cleaners is a public health event. Drain unblocker products are more hazardous and patients with exposure often require more significant medical management than exposure to household and cleaning products.
Methods: Accidental exposures to drain cleaners reported to an Italian Poison Control Center from 1 November 2017 to 31 October 2018 were analyzed. The data collected included: patient identification, call site, route of exposure, dose value and unit, agent name, active ingredients, colour of the product, colour of the packaging, product diluted, circumstances of exposure, symptoms present, therapy, medical assessment, symptoms duration, outcome, degree of severity according to the Poison Severity Score (PSS).
Results: During the study period 229 exposures were reported. The age group distribution was <1 year n = 2 (0.8%), ≥ 1 < 5 years n = 25 (10.9%), ≥ 5 < 18 years n = 7 (3.0%), and ≥18 years n = 195 (85.2%). Of these, 126 patients were taken to the hospital, 96 stayed at home with 7 unknown. The respiratory route was involved in 38.4%, skin in 35.8%, oral route was involved in 12.6%, ocular in 3.5%, and multiple routes in 9.7%. Of the oral caustic exposures 42.9% involved children <6 years old. Adults most often experienced cutaneous and respiratory exposures. Misuse occurred in 30.1% of cases (23.1% mixing, 2.2% transfer from original container, 4.8% other). The most frequently reported clinical effects were pharyngodynia, oral inflammation, first and second degree burns, disepithelization of the lips, dysphonia, cough, vomiting, heartburn, necrosis, corneal lesions, ocular pain and inflammation, and skin burns. No symptoms were present in 24 cases; minor symptoms were present in 158 cases, moderate symptoms in 30 cases, severe symptoms in 5 cases, of these, 2 pediatric oral exposures presented severe oral effects and gastroesophageal lesions and they required endotracheal intubation. There were 2 deaths reported in elderly patients that ingested the drain cleaner in mistake for an alimentary product. PSS was not assignable in 10 cases.

Conclusion: Children are less involved in accidental exposures to caustic drain cleaners because intoxication often happens during the normal use and misuse of these products by adults. Accidental exposures involving children could have been prevented through safer use, disposal and storage. 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 in adults. The primary focus for risk reduction and prevention should be on consumer education.

354. The "lactate gap" as a useful tool to detect ethylene glycol intoxication

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Objective: The fast recognition and early treatment of ethylene glycol (EG) intoxications in comatose patients with high anion gap metabolic acidosis (HAGMA) is essential. As EG is used in different antifreeze formulations, accidental or intentional ingestion is not uncommon. In 2018, the American Association of Poison Control Centers received 7,260 reports of EG intoxications of which over 5000 were unintentional [1]. Metabolism of EG leads to toxic metabolites, causing metabolic acidosis, kidney damage, coma and possible death, making early treatment of utmost importance. We present two cases of EG intoxication in which blood gas analysis showed a falsely elevated lactate concentration.
Case series: Both patients presented with an altered mental state (Glasgow Coma Score 3/15) and HAGMA (anion gap: 40.8 and 41.3 mmol/L, respectively, osmol gap: 64 and 20 mOsm/Kg). Point of Care Testing (POCT) blood gas analysis (Siemens® RAPIDPoint) showed a lactate concentration of 25.5 and 23.3 mmol/L, whereas routine laboratory measurement (Roche® Cobas c502) showed 3.1 and 9.6 mmol/L, resulting in a "lactate gap" between both methods of 22.4 and 13.7 mmol/L. Gas chromatography-mass spectrometry (GC-MS) analysis revealed EG concentrations of 276 and 69 mg/dL. Both patients were treated with fomepizole and hemodialysis and recovered quickly.
Conclusion: In both cases a significant difference in lactate concentration was observed when measured by two different methods. EG is metabolized into more toxic metabolites such as glycolic, glyoxylic and oxalic acid [2] of which the former may cause falsely elevated lactate concentrations. As different manufacturers use various technologies and enzymes to determine the lactate, some of these methods are unable to differentiate glycolate and lactate concentrations. Combining such methods with a more sensitive measurement of lactate alone, results in a lactate gap which indicates the presence of EG metabolites [3,4]. Hence, the lactate gap can be a useful tool in identifying an EG intoxication.

References

[1] Gummin DD, Mowry JB, Spyker DA, et al. 2018 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 36th Annual Report. Clin Toxicol (Phila). 2019;57:1220–1413.

[2] Langman LJ, Bechtel LK, Meier BM, et al. Clinical toxicology. In: Rifai N. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. St. Louis, Missouri: Elsevier. 2017, pp. 843–844.

[3] Shirey T, Sivilotti M. Reaction of lactate electrodes to glycolate. Crit Care Med. 1999;27:2305–7.

[4] Sagar AS, Jimenez CA, Mckelvy BJ. Lactate gap as a tool in identifying ethylene glycol poisoning. BMJ Case Rep. 2018;2018: bcr2018224243.

355. A one-year review of enquiries to the UK National Poisons Information Service involving cosmetic products

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Objective: To review enquiries to the UK National Poisons Information Service (NPIS) involving cosmetic products.
Methods: A retrospective analysis was undertaken between 1 April 2018 and 31 March 2019 for enquiries relating to "cosmetic products" as defined by the coding system on the UK Poisons Information Database (UKPID).
Results: There were 2084 enquiries involving 2046 patients, of whom 2012 had been exposed to one cosmetic product. Thirty-four exposures involved more than one cosmetic product. In 22 enquiries the cosmetic product was co-ingested with one or more pharmaceutical or household products. Exposures in children ($\leq$ 18 years) accounted for 76.6% of exposures (n = 1548), of which 62.5% (n = 1284) involved children under 5 years. Of the 473 exposures in adult patients, 30.6% of patients were 65 years or older. The patient age was not known in 25 enquiries. Exposures typically occurred in the home/domestic setting (n = 1820; 89%), nursing/care homes (n = 83; 4.1%), hospital setting (n = 76; 3.7%) and school (n = 22; 1.1%). The circumstances of exposure were accidental in 89.6% of enquiries, intentional in 6.8% and recreational misuse in 1.3%. Thirteen cases of recreational misuse involved children (age range 9-17 years), 8 of which involved aerosol inhalation. The type of products most frequently involved in all exposures were dental products (15.2%), skin care products (12.8%), hand sanitiser gel (9.8%), bath/shower products (8.1%) and nail care products (7.8%). The Maximum Poisoning Severity Score (MAXPSS) [1] at the time of the enquiry was none (n = 1442; 70.5%), minor (n = 565; 27.6%), moderate in 1% (n = 20) and severe in just 2 enquiries. The 20 exposures with a moderate MAXPSS involved 7 children $\leq$5 years, 2 teenagers, and 10 adults; the age was unknown in 1 enquiry. The circumstances of exposure were accidental (n = 12), intentional (n = 4), recreational misuse (n = 3), and adverse reaction (n = 1). The most common products were skin care products (n = 4), nail care products (n = 3) and shampoo/conditioner (n = 3). Of the two enquiries with severe MAXPSS, both involved males (aged 34 and 41) and the intentional ingestion of alcohol and isopropa-

nol-based hand sanitiser/washes whilst in hospital. A complete recovery was documented in one, the outcome was unknown in the second case.
Conclusion: Enquiries to the NPIS involving cosmetic products most frequently involve accidental exposures in young children and the majority of patients are asymptomatic at the time of the enquiry.

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.

356. Acute ethylene glycol poisoning: a one year epidemiological study

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Objective: Ethylene glycol is a common cause of toxic ingestion. The aim of the study was to examine ethylene glycol poisoning cases and to define the demographic features, clinical characteristics and outcome of poisoning.
Methods: The records of the Toxicology Clinic, Emergency Hospital "N.I.Pirogov", Sofia, Bulgaria were reviewed retrospectively for all ethylene glycol poisonings during a one year period, 1 January 2019 to 31 December 2019. The patient's age, gender, clinical characteristics and outcome of intoxication were recorded. Blood ethylene glycol concentration, acid-base status, and renal function were assessed.
Results: There were 13 patients hospitalized in the Clinic, due to ethylene glycol poisoning in the form of antifreeze during the study period. There were 12 men (92.30%) and 1 woman (7.69%); median age 41.9 (range 19-80) years. Most patients were aged 19 to 50 years old (69.2%). The reason for ingestion was accidental in 11 cases (84.6%) and suicide attempt in 2 cases (15.4%). The blood ethylene glycol concentrations ranged widely from 0.01 to 1.57 g/L. Signs of mild intoxication were nausea and vomiting, headache, confusion, slurred speech and in-coordination. One patient developed severe intoxication. One patient with chronic alcoholism developed aspiration pneumonia as a complication. Conventional treatment of ethylene glycol intoxication was used: emergent stabilisation, treatment with intravenous fluids, correction of metabolic acidosis by parenteral infusions of bicarbonate, oral ethanol such as whisky or vodka or administration of 95% ethanol solution as an antidote, and haemodialysis in severe poisoning. There were no fatal cases during the study period.
Conclusion: Ethylene glycol, a common ingredient of antifreeze, is responsible for many instances of accidental and intentional poisoning annually. Prompt diagnosis, early treatment and administration of ethanol as an antidote are important for a favorable outcome.

357. Button battery ingestion: experience of the UK National Poisons Information Service (NPIS)

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Objective: The numbers of household devices containing button batteries has increased in recent years and this has been accompanied by an increase in the number of button battery ingestions reported worldwide [1]. Severe or fatal injury can occur if the battery becomes lodged in the oesophagus, which can lead to serious complications including perforation, vocal cord paralysis, strictures and/or fistula formation [2]. The aim of this study was to review button battery ingestions in the UK, as reported in enquiries to the National Poisons Information Service (NPIS).
Methods: The NPIS UK Poisons Information Database was interrogated for all cases relating to button battery ingestion or insertion for the 11.5 year period from January 2009 to June 2020.
Results: There were 210 enquiries to NPIS relating to 202 reported cases of button battery ingestion or insertion. Of 198 cases related to ingestion, 172 (86.9%) involved children aged 5 years or under including 101 (58.7%) boys. In 35 cases (17.7% of cases related to ingestion), multiple button batteries were ingested. Four cases involved insertion of a button battery into the ear, nose, mouth, or trachea. Across all age groups, most patients (82%) were asymptomatic following button battery ingestion but commonly reported symptoms included abdominal pain (3.5%), melaena (3.5%), vomiting (2.0%) and diarrhoea (1.5%). Where the position of the battery was known (125 cases), 116 (92.8%) were located in the stomach or at/beyond the pylorus, and of these patients, 11 (9.5%) were symptomatic. The battery was lodged in the oesophagus in 9 (7.2%) cases, of whom 4 (44.4%) were symptomatic; all 9 underwent surgical or endoscopic removal. No long-term complications were recorded in these cases but follow up was incomplete.
Conclusion: This case series demonstrates that most ingested button batteries pass through the gastrointestinal tract uneventfully and most patients remain asymptomatic. Lodging of batteries in the oesophagus is an uncommon but potentially severe event, although some patients are asymptomatic on presentation. Button battery ingestions occur most frequently in the paediatric population, where ingestion may be prevented by implementation of additional safety measures by manufacturers and increased awareness among parents.

References

[1] Litovitz T, Whitaker N, Clark L, et al. Emerging battery-ingestion hazard: clinical implications. Pediatrics. 2010;125:1168–1177.
[2] Litovitz T, Whitaker N, Clark L. Preventing battery ingestions: An analysis of 8648 cases. Pediatrics. 2010;125:1178–1183.

358. Hepatorenal dysfunction following fipronil ingestion

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Objective: Fipronil, a GABA-A gated chloride channel blocker, usually causes mild toxicity to humans with favourable outcome, but neurotoxicity with agitation and seizures are reported after ingestion of a large dose. Hepatotoxicity and renal toxicity are not common in fipronil toxicity. We report a patient with severe fipronil poisoning.
Case report: A 72-year-old male patient with a history of chronic obstructive pulmonary disease (COPD), presented with alleged history of ingestion of approximately 450 mL of pesticide product containing fipronil 5%. He presented with vomiting, loose stools and worsening sensorium. He had 3 to 4 episodes of seizure while in hospital and received antiepileptics. He had no previous history of any seizures. His clinical status worsened the next day, and he developed respiratory distress and hypotension. He was intubated and received inotropic support. He also developed fever spikes and was managed with broad-spectrum antibiotics. Investigations showed worsening renal function (creatinine increased from 79.5 to 565.9 μmol/L) with elevation of transaminases and creatine kinase. Arterial blood gas analysis showed severe metabolic acidosis. The diagnosis was fipronil toxicity, status epilepticus, acute kidney injury and aspiration pneumonia. He was managed with hemodialysis and other supportive measures. He gradually improved and was extubated on day 7. Renal function and urine output improved after 3 cycles of hemodialysis. An ultrasound of the abdomen showed bilateral normal appearing kidneys of 11 cm each with bilateral non-obstructive renal calculi. Liver, gallbladder, pancreas, spleen, urinary bladder and prostate appeared normal.
Conclusion: Direct toxicity of fipronil on the renal and hepatic systems is attributed to free radical formation and oxidative stress. In addition, there is also the risk of rhabdomyolysis following status epilepticus that can cause acute kidney injury and ischemic injury as in our case.

359. Malathion poisoning causing prolonged cholinergic crisis and refractory hypotension requiring high-dose atropine treatment

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Objective: The lipophilic organophosphate malathion undergoes activation in the liver to its toxic metabolite malaoxon, which inhibits acetylcholinesterase (AChE), leading to cholinergic excess. Malathion sequestered in lipid stores can lead to prolonged toxicity. Excess acetylcholine at muscarinic receptors in vascular beds, via release of nitric oxide, can cause vasodilatation [1]. We describe a case of malathion poisoning requiring prolonged atropine treatment to combat cholinergic signs, warranting high dosages of atropine for refractory hypotension.
Case report: A 55-year-old man was found unconscious alongside various chemicals, including a 200 mL bottle containing malathion (500 g/L) and toluene (435 g/L). He was noted to have emesis, diarrhoea, diaphoresis and pinpoint pupils raising the possibility of organophosphate toxicity, and was intubated by paramedics at the scene. On arrival to the emergency department, he was found to have a chemical fetor, heart rate 90 bpm, blood pressure 120/90 mmHg, perspiration, lacrimation, and crepitations in the lung but remained easy to ventilate and oxygenate. He had an initial plasma cholinesterase (pAChE) activity of 0.3 kIU/L (reference range 7-15). At 6 hours post-arrival, in the intensive care unit (ICU) he developed a cholinergic toxidrome together with tachycardia and hypotension. He was commenced on a doubling regimen of atropine reaching 16 mg, followed by an infusion of 2-5 mg/h with stabilisation of secretions and haemodynamics. When atropine was weaned after 24 hours he again became unstable with persistent hypoxia and hypotension, despite inotropic support by way of adrenaline, noradrenaline and vasopressin. Atropine was recommenced on day 3 with rapid resolution of the patient's haemodynamic instability. Subsequent atropine dosing ranged from 3.6-15 mg/h over the next 2-3 days. Following this, intermittent signs of excess secretions were managed with atropine which was ultimately ceased on day 31. The lowest pAChE activity, 0.1 kIU/L, was recorded on day 4 and the lowest red blood cell AChE activity, 0.5 U/mL, on day 9. He required a tracheostomy for prolonged ventilatory support and ventilator-associated pneumonia. His hospital stay was also complicated by sepsis, lower limb deep venous thrombosis, ileus and critical illness polymyopathy.
Conclusion: Malathion can cause severe and protracted poisoning requiring prolonged atropine treatment. High-dose atropine treatment was effective in refractory hypotension due to malathion.

Reference

[1] Buckley NA, Dawson AH, Whyte IM. Organophosphate poisoning: peripheral vascular resistance – a measure of adequate atropinization. J Toxicol Clin Toxicol. 1994;32:61–8.

360. Evaluation of biocidal product enquiries to the Austrian Poisons Information Centre, 2017

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Objective: A biocidal product is any substance or mixture intending to destroy, deter, render harmless, prevent the action of, or exert a controlling effect on any harmful organism by any means other than mere physical or mechanical action. Biocidal products are divided into 4 main groups: disinfectants, preservatives, pest control and other biocidal products. We analysed enquiries to the Austrian Poisons Information Centre involving biocidal products.
Methods: On behalf of and funded by the Austrian Federal Ministry of Climate Action, Environment and Energy, Mobility, Innovation and Technology the local Poison Information Centre

(PIC) retrospectively evaluated enquiries regarding exposures to biocidal products in 2017.
Results: PIC Austria received in total 28,244 telephone enquiries in 2017. Regarding biocidal product exposure the PIC was contacted in 847 cases: 434 (51.2%) involved children under the age of 15, and 413 (48.8%) persons 15 years and older. In 720 cases a poisoning could be excluded due to minor exposure. In 23 cases the risk of intoxication could not be estimated due to lack of sufficient information at the time of consultation. In 87 cases intoxication was suspected and medical observation was recommended. In only 17 patients an intoxication could be verified due to the severity of the symptoms. The causative substances were industrial disinfectants (n = 8), skin disinfectants (n = 3), chlorine gas (n = 4), wasp spray (n = 1) and textile bleaching agents (n = 1).
Conclusion: In relation to the total number of calls, enquiries regarding biocidal products are relatively rare and the number of human intoxications seems to be small. Only 17 cases with severe symptoms, which had to be treated medically, were recorded. No deaths were recorded by the local PIC.

361. Biological sample collection in the emergency department and laboratory substance abuse investigation and confirmation: a methamphetamine case report

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Objective: Considered mainly as a working performance enhancer, Shaboo (methamphetamine) is gaining popularity as a recreational drug due to its effects on self-confidence and loss of inhibition.
Case report: A 37-year-old Filipino man with familiar history of hypertension presented to the emergency room (ER) in 2011 for dyspnea; blood pressure (BP) was 190/140 mmHg, heart rate 120 bpm, laboratory testing was significant for elevated prohormone brain-type natriuretic peptide (NT pro-BNP, 3891 ng/L). Diagnostic procedures showed signs of hypertensive cardiomyopathy and moderate left ventricular hypertrophy. He was diagnosed with familiar hypertension and antihypertensive therapy was prescribed. He was admitted for the same symptoms in 2012 and screened for secondary hypertension. Mild left adrenal hyperplasia was found on abdomen computerised tomography (CT) scan. Substance abuse was not investigated in the first two hospitalizations. In November 2014, while he was being arrested for amphetamine dealing, he reportedly ingested an envelope containing Shaboo and lost consciousness. In the ER samples for substance abuse tests were collected (positive for methamphetamine >5000 ng/mL). He was later discharged after BP normalized. After he interrupted antihypertensive treatment, in June 2015 he was admitted again to ER for dyspnea and high BP (240/160 mmHg). Laboratory testing showed troponin-T 140 ng/L, CK-MB 11.5 g/L, creatinine 3 mg/dL, and proteinuria 3 g/24 h. Echocardiogram showed a significant reduction of ejection fraction (EF) 31%, hypokinesia and reduced global systolic function, with impaired tricuspid annular plane systolic excursion <16 mm and mild mitral regurgitation. Ocular investigations revealed angiosclerosis and retinal haemorrhage. Global peripheral vascular damage was confirmed by brain CT showing bilateral signs of ischemia and by kidney failure due to acute angiosclerosis. Urine and blood tests were positive for methamphetamine 5000 ng/mL and 326 ng/mL, which progressively fell to 9 ng/mL after 5 days. Hair testing (3 cm), showed methamphetamine/amphetamine 124/12 ng/mg. Up to 24 cm was analysed, demonstrating chronic use of methamphetamine. He admitted chronic use of Shaboo and was discharged with an angiotensin converting enzyme (ACE) inhibitor, a beta blocker, loop diuretic, antialdosteronic and a calcium channel blocker.
Conclusion: This case highlights the long-term cardiovascular effects of methamphetamine use. Our work is focused on the need to collect a complete anamnesis, as well as collaboration between healthcare professionals in poison centers, cardiology and psychiatric departments, biochemical/toxicology laboratory, to promptly address methamphetamine abuse and related symptoms and to correctly treat patients and avoiding unnecessary diagnostic procedures.

362. Post-mortem ethanol concentrations

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Objective: Ethanol is important in forensic toxicology. Interpretation of toxicological data is, however, complicated by considerable inter-subject variation in ethanol toxicokinetics and toxicodynamics and by post-mortem changes. We sought to establish ethanol concentrations in deaths referred to Coroners.
Methods: We collected post-mortem toxicology results and brief clinical and demographic details from consecutive cases referred to Clinical Biochemistry, Betsi Cadwaladr University Health Board, Bangor, UK by two HM Coroners covering North Wales, in 2018. Cases of suspected adverse drug reaction or lacking toxicological data were excluded. Data are presented as median and interquartile range (IQR). Proportions are expressed as a percentage with a 95% confidence interval (95% CI) and compared by chi-squared or Fisher's exact test. The Mann-Whitney and the Kruskal-Wallis tests were used to compare non-parametric data. Spearman's coefficient was used to determine correlation. P_α less than 0.05 was considered significant.
Results: The presence of ethanol was confirmed analytically on post-mortem toxicology in 23/40 cases (58%, 95% CI 41–71%), median age at time of death was 45 (IQR 36–62) years. Thirteen cases were female and 12 male (P = 0.84). Three had evidence of trauma. Nineteen had analytical evidence of other xenobiotics at post-mortem, median of 4 additional xenobiotics, IQR 1.5–13.5. Of the 55 additional xenobiotics detected, 41 affect the nervous system. Post-mortem blood was positive for ethanol in 22 cases, median concentration 146 (IQR 25–204) mg/dL. Ethanol was present in urine in 17 cases, median concentration 199 (IQR 42–323) mg/dL. Blood ethanol correlated positively with urine ethanol in the 18 paired samples available, r = 0.97 (95% CI 0.92–0.99) (P < 0.0001). Urine ethanol concentrations were greater than blood ethanol concentrations. Ethanol poisoning was mentioned on the death certificate in five cases whose median blood ethanol concentration was 225 (IQR 201–265) mg/dL, compared with 85 (IQR 6–217) mg/dL in cases where ethanol was not mentioned (P = 0.0005). A blood ethanol concentration exceeding 200 mg/dL was associated with inclusion of ethanol intoxication on the death certificate (odds ratio 30, P = 0.001).

Conclusion: Ethanol was frequently detected in post-mortem blood or urine samples or both. Concentrations in paired samples were closely correlated. Ethanol intoxication was likely to be included on the death certificate if the concentration exceeded 200 mg/dL. Multiple xenobiotic exposure was common and often included central nervous system depressants with the potential for synergistic toxicity.

363. Requests regarding snus to the Poisons Information Centre in Austria

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Objective: Snus, a tobacco for oral use, is used as a nicotine resource instead of cigarettes. It is placed between the upper lip and gum, releasing nicotine slowly. Besides other substances like flavourings and salt snus mainly contains tobacco. The aim of this study was to analyse the severity of symptoms after intake of snus.
Methods: Data from the Poisons Information Centre (PIC) database involving exposures of snus were evaluated for the period from 2016 to September 2020. Acute exposures were analysed for age, time to contact the PIC, symptoms at the time of PIC consultation and Poisoning Severity Score (PSS).
Results: In total, 70 cases of snus intake were documented in the database; three cases were excluded due to intake of other substances. From the remaining 67 cases, there were 33 paediatric cases (aged 6 months to 14 years). The PIC was contacted within 5 minutes to 3.5 hours after the intake. In 22 cases no symptoms (PSS 0) were reported, while in 10 cases mild symptoms (PSS 1) such as vomiting one to three times (in 9 cases), nausea, tremor and drowsiness occurred. A 14-year-old boy used snus for the first time and developed moderate symptoms (PSS2) after 10 minutes of use with collapse, vertigo, nausea, vomiting and sinus tachycardia. In adults (aged 15 to 50 years) there were 34 cases. The PIC was contacted within 10 minutes to 1 day after the intake. In total 15 patients had no symptoms (PSS 0; time to contact PIC: 10 minutes to 1 day), while 19 had mild symptoms (PSS 1; time to contact PIC: 10 minutes to 17 hours) including nausea (in 12 cases), vomiting one to three times (in 5 cases within 10 minutes to 2 hours), gastralgia, abdominal pain, gastrointestinal mucous membrane irritation, tremor, drowsiness, and vertigo (in 5 cases within 10 to 30 minutes). No moderate or severe symptoms were reported in adults.
Conclusion: There is a high incidence of symptoms after the ingestion of snus. In the paediatric group 11 out of 33 (33%) reported symptoms within 3.5 hours. In adults 19 out of 34 (56%) cases developed symptoms within 10 minutes to 17 hours.

364. Multiple treatments of clotrimazole during pregnancy

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Objective: Current literature considers single exposures to clotrimazole safe to treat vulvovaginal candidiasis during pregnancy, but very little information is available on more than two vaginal clotrimazole treatments during pregnancy. Information on exposure to pharmaceuticals during pregnancy is limited and mainly originates from case studies documented in the literature. We report a patient who received multiple clotrimazole treatments during pregnancy.
Case report: A 30-year-old female was treated with a 500 mg vaginal pessary of clotrimazole ten times during pregnancy, twice during the first trimester, four treatments during the second trimester and four treatments during the third trimester for candidiasis confirmed by vaginal swab. Concurrent topical treatment was prescribed for seven days every time a pessary was administered. Clotrimazole cream 1% was prescribed on four occasions, clotrimazole cream 2% on four occasions and on the final two treatments clotrimazole 1% cream with hydrocortisone 1% was prescribed. Other medications taken included folic acid during the first trimester, ferrous fumarate during the third trimester and vitamin D throughout the pregnancy. During the last vaginal swab for vulvovaginal candidiasis at 38 weeks +6 it was retrospectively noted that the patient was positive for group B streptococcus (GBS). The infant was born at 39 weeks +6. The pregnancy was uncomplicated but labour complications included a spontaneous rupture of membranes 33 hours prior to birth, maternal haemorrhage during active labour and delivery of the infant via emergency caesarean section. These complications were attributed to the untreated GBS infection. The newborn check carried out when the infant was 18 hours old and follow ups at 10 days, four, eight and 15 months by a health visitor were all as expected.
Conclusion: Clotrimazole is widely available as an over the counter pharmaceutical in the UK to treat candidiasis. It is generally regarded as a safe and effective treatment for non-pregnant patients. There is an absence of case reports and clinical trials covering multiple doses of clotrimazole during pregnancy. Due to the presence of GBS, it is unclear if clotrimazole contributed to the labour complications seen in this case. There were no adverse outcomes in the infant. It is hoped that this report will contribute to the currently available safety information for clotrimazole use in pregnancy.

365. Challenges facing the UK National Poisons Information Service (NPIS) ahead of EU Exit and commencement of Annex VIII of Article 45 (Classification, Labelling and Packaging)

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Objective: Following "Brexit", a transition period is in place until 31 December 2020, during which EU legislation continues to apply. The NPIS, as the Appointed Body in the UK under Article 45 of Regulation 1272/2008 (Classification, Labelling and Packaging), receives safety data on the hazards of mixtures. Annex VIII will harmonise information notified under this regulation, and come into force on 1 January 2021.
Methods: We reviewed the implications of both "Brexit" and the introduction of Annex VIII on the NPIS.
Results: Three main areas were identified that required preparatory work. **1. Impact of the political arrangement:** The UK will have to operate a dual notification system as a result of the Northern Ireland Protocol. For products marketed in Northern Ireland, safety information will have to be submitted in the harmonised Annex VIII format. There will be no such requirement

on products placed on the market in Great Britain (England, Wales or Scotland). **2. Technical requirements of the Annex VIII format:** As a result of EU exit, it is unlikely the NPIS will be able to access chemical safety dossiers submitted by industry to the European Chemicals Agency (ECHA) Poison Centre Notification Portal (PCN). Annex VIII requires the dossiers to be submitted in a proprietary XML format, which is not legible to poison centre staff. This has necessitated the development of a bespoke system in the UK that can both receive safety data as submitted by industry and automate its conversion to a legible format. **3. Information Sharing:** Compliance with Article 45 and "Brexit" have both led to considerable confusion for all stakeholders. The NPIS has received multiple queries on these matters. Examples include questions around the requirement for Unique Formula Identifiers (UFIs) and access to the ECHA PCN. It has been necessary for the NPIS to collaborate regularly with colleagues in Public Health England, the Health and Safety Executive and the Department for Health and Social Care to provide a coordinated response. The NPIS has also specifically updated its website to act as a repository of reference information for industry.
Conclusion: There are many challenges for Poison Centres in complying with the EU CLP Regulation and Annex VIII. The impact of "Brexit" has added an additional layer of complexity for the UK. It is important that in addition to addressing the technical challenges, there is sufficient communication of the new requirements to industry.

366. When volvulus hides a poisoning: a case of severe foodborne botulism

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Objective: Diagnosis of botulism is still a challenge for physicians, due to the rarity of the clinical condition and non-specific symptoms. We report a severe case of botulism, initially mistaken for intestinal occlusion and managed with surgical intervention.
Case report: A 21-year-old man, a student at the local university, was referred to the emergency department (ED) with abdominal pain, nausea and diplopia. During physical examination, the clinical condition worsened rapidly and severe respiratory failure occurred due to inhalation of copious vomitus, requiring oro-tracheal intubation with respiratory support. A computerised tomography (CT) scan confirmed bronchial inhalation and showed intestinal obstruction. He was taken to the operating room, but exploratory laparotomy was negative for intestinal occlusion. Upon awakening in ICU the patient presented intact consciousness, fixed mydriasis, ophthalmoplegia, no cranial reflexes, no respiratory drive, paralysis of limbs, hypertension and tachycardia. Nevertheless, through a binary code, the patient communicated that he had eaten homemade food. An electromyography demonstrated presynaptic block of neuromuscular cholinergic conduction, and the differential diagnosis included Eaton-Lambert myasthenic syndrome and Miller Fisher (variant of Guillain-Barré) syndrome. Further investigation revealed that, the day before (15 hours before the onset of clinical manifestations), the patient had ingested improperly prepared home-canned red beans in a glass jar prepared months before. Foodborne botulism was suspected. Heptavalent antitoxin was administered without acute or delayed adverse effects 47 hours after ingestion. Serum, leftover food samples, and rectal swabs were immediately sent for analysis. Foodborne poisoning was confirmed (positivity for botulinum neurotoxin type in serum in serum and by means of mouse neutralization assay). Respiratory failure required prolonged ventilation for four months and aspiration pneumonia was treated with antibiotics. The patient had a complete recovery 8 months after the ingestion.
Conclusion: There are several considerations arising from this case. Diagnosis of botulism may be challenging due to the variability of clinical presentation; therefore, a careful assessment to exclude other surgical and neurological diseases must be performed. Recovery may require several months of mechanical ventilation, since botulinum toxin induces irreversible injury to the nerve terminals and new formation of nerve cells is necessary, consequently, early clinical suspicion and prompt antitoxin administration may reduce the length of hospital stay.

367. The importance of free digoxin serum concentrations: case report of an infant treated for digoxin poisoning

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Objective: Digoxin poisoning is a potentially life-threatening problem. We report a case of an infant, following an incorrect administration of digoxin, treated with digoxin-specific antidote, who was been managed with monitoring of serum concentrations of free digoxin.
Case report: A male 54-day-old infant, treated with atrial stimulation, already receiving amiodarone and propranolol for paroxysmal supraventricular tachycardia, started Lanoxin (digoxin) therapy (5 μg/Kg/day). Serum concentrations of total digoxin were measured using an electrochemiluminescence immunoassay (Elecsys Digoxin, Roche Diagnostics) and revealed adequate concentrations. During the maintenance therapy, an incorrect dose of Lanoxin was administered (500 μg) and the appearance of bradycardia, hyperkalaemia (6.65 mEq/L) and hypermagnesemia (2.25 mEq/L) were recorded. Analysis of serum concentrations of total digoxin revealed a concentration of 21.1 ng/mL (therapeutic range 0.6-1.2 ng/mL, laboratory alert >2 ng/mL), and a vial of 40 mg of digoxin-specific antidote (DigiFab®) was administered. Therefore, in order to exclusively measure only the free digoxin fraction, serum samples were subjected to an ultrafiltration procedure using Centrifree® devices (Merck Millipore) following the manufacturer's instructions [1]. These disposables allow separation of free digoxin from the protein-bound drug fraction and in our settings were used to measure the proportion of unbound digoxin that was still pharmacologically active. In fact, a day after the first measurement (Day 1), serum concentrations of total and free digoxin were 14.90 and 0.66 ng/mL, respectively. In the

following days, in order to ensure that digoxin concentrations were within the therapeutic range, both drug fractions were monitored daily.
Conclusion: Digoxin toxicity among children is more likely to cause bradyarrhythmias rather than ventricular arrhythmias [2]. To better perform therapeutic drug monitoring (TDM), since the half-life of the Fab fragment is about 15-20 hours (less than the half-life of digoxin), it could be useful to measure free digoxin concentrations. In fact, following the reduction of free digoxin serum concentrations, the concentration gradient leads to an easier dissociation of digoxin from sodium-potassium ATPase. Free digoxin concentrations should be measured in order to optimize clinical treatment and to establish a more tailored Fab administration regimen.

References

[1] Palma EC, Laureano JV, de Araújo BV, et al. Fast and sensitive HPLC/UV method for cefazolin quantification in plasma and subcutaneous tissue microdialysate of humans and rodents applied to pharmacokinetic studies in obese individuals. Biomed Chromatogr. 2018;32:e4254.
[2] Thacker D, Sharma J. Digoxin toxicity. Clin Pediatr (Phila). 2007; 46:276–9.

368. Fentanyl transdermal patch mistaken for wound patch: two pediatric case reports

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Objective: Transdermal therapeutic systems (TTS) are drug delivery systems that are applied directly to the skin with the purpose of a systemic effect. Accidental pediatric cutaneous exposure to fentanyl TTS can cause respiratory distress that may be lethal. We report two pediatric cases were the fentanyl TTS was applied to the skin in error instead of a wound patch (or plaster).
Case reports: Case 1. A 3-year-old girl (15 Kg), was admitted to the emergency department after her 16-year-old sister had mistakenly applied their grandmother's transdermal patch containing fentanyl (25 μg/h) to a wound on her knee. It had been mistaken for a common wound patch and had been in place for 1 hour before removal. At home the child had vomiting, lipothymia and lethargy. She was observed for 48 hours in the pediatric intensive care unit without the appearance of further symptoms. Naloxone administration was not necessary and she was discharged. Case 2. A 4-year-old girl (18 Kg) was admitted to the emergency department after her father mistakenly applied one of his fentanyl patches (50 μg/h) to a leg wound. The patch was in position for 9 hours. She developed nausea, vomiting and miosis. A dose of 0.2 mg naloxone (0.01 mg/Kg) and intravenous fluids were given. The child was observed for 48 hours and she was discharged with full recovery.
Conclusion: Accidental exposure to fentanyl TTS can lead to symptoms of overdose, respiratory depression being the most severe and potentially lethal. The early symptoms of accidental exposure to fentanyl are difficult to identify in young children. The clinical evolution of these two pediatric cutaneous case reports was not severe but since there are patches with higher drug concentrations it is necessary to prevent the risk of therapeutic errors. As with other medications, to reduce the risk of pediatric accidental exposure it is important to keep fentanyl TTS in a safe place out of sight and reach of children. It is advisable to explain to parents and caregivers that wound patches cannot be replaced with other types of patch. Instructions on the package to keep fentanyl patches in a separate place away from common wound patches and to keep them inside their original packaging, may reduce the risk of therapeutic errors.

369. Bottles and messages revisited: circumstances of poisonings among infants under 1 year old in Estonia

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Objective: After analyzing 10 years' data of caustic exposures and their relation to usage of incorrectly stored chemicals in Estonia [1] we discovered that in children under 1 year old 51% of accidents happened with chemicals in their original package. Children this young depend on their carers. At the same time, in adults aged 19-69 years who are most likely to look after young children the occurrence was only 14%. This left the authors with questions about how much of the 51% is due to children aged >6 months able to move and grab things independently and how much is a result of mistakes by their carers. This study analyzes how and what kind of substances are involved in toxic exposures among children <1 year old.
Methods: Calls to the Estonian Poisons Information Centre (EPIC) from 1 January 2009 to 31 December 2019 were analyzed retrospectively in age groups looking at children aged over and under 6 months. In each group it was evaluated whether the substance was accessed by the child or given to them by someone. In addition, we examined what kind of product it was and how it was packaged.
Results: Overall, 945 calls were analysed; 164 (17%) of them involved children <6 months old and 781 (83%) children >6 months old. Age groups differed strongly in all parameters. In the younger group 83.3% of wrongly administered substances were given by the carer, and in older group only 19%. In the younger group 83% of wrongly administered substances were in their original package and mostly included medications/supplements (59.7%), with household chemicals (28.6%) taking second place; cosmetic products and plants/mushrooms were practically absent. The mix up of medications and supplements usually involved products in similar packaging, most often 10 mL bottles containing vitamin D versus lookalike bottles containing eye drops, essential oils, e-cigarette refill liquids, etc., and similar looking small ointment tubes. In older children, about half of the packages were original, and the product given by the carer (46%) and half taken by the child (50%). The most common agents involved were household chemicals (35.5%) followed by plants/mushrooms (20.4%), medications/supplements (15.3%), and cosmetic products (9%).
Conclusion: Careless handling of medications and chemicals around young children is a serious problem in Estonia and needs to be properly addressed in future prevention campaigns.

Reference

[1] Kastanje R, Kukker A, Oder M. Message on the bottle: how does the wrong package influence occurrence of caustic and corrosive chemical exposures – the Estonian experience. Clin Toxicol (Phila). 2020;58:601.

370. Alcohol abuse among teenagers during the vacation period: description and pattern differences by gender

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Objective: Alcohol is the most commonly consumed legal drug by adolescents, with a relevant impact on recreational activities [1]. This study describes adolescent alcohol acute intoxication (AAI) in a hospital emergency department and analyses differences by gender [2]. The aim is to describe acute alcohol intoxication in adolescents in a hospital emergency department in an area with high tourist influence, during the summer of several years, analyzing gender differences.
Methods: Retrospective medical record review of patients aged up to 19 years with AAI during the summer (2015-2019) in an area with high tourist influence. We analysed sociodemographic factors and characteristics of the episodes by gender. We made a multivariate analysis of the variables according to gender perspective.
Results: A total of 701 cases, aged 8 to 19 years old (42.7% female) were analysed. The majority of patients arrived by conventional ambulance (90.7%). The most common clinical symptoms were coma or decreased level of consciousness (77.5%), traumatic brain injury (12%), other wounds and/or trauma associated (8.2%), psychomotor agitation and need for sedation (7.3%). Overall, 6.3% of patients took alcohol and other substances and 1.4% showed a related suicidal motivation in this AAI. In cases where toxicological analysis was performed (21%) the mean blood alcohol concentration was 1.99 g/L (SD =0.66). No deaths were recorded. Only 0.4% of patients required hospital admission and 98.7% were in the hospital less than 24 hours; the average stay in hospital lasted 5.55 hours (SD =16.1). In the comparative analysis between genders, the presence of traumatic brain injury (15.4% versus 7.4%; $p = 0.001$) and other wounds and/or trauma (1.7% versus 3.7%; $p < 0.001$) was associated with alcohol poisoning and the average of ethanolemia (2.08 versus 1.85) were significantly higher in males.
Conclusion: Adolescent alcohol poisoning in areas of tourist influence is usual in the summer months. Although there is a tendency to equalize between sexes, males showed a higher accident rate and ethanolemia.

References

[1] Kelly TM, Donovan JE, Cornelius JR, et al. Predictors of problem drinking among older adolescent emergency department patients. J Emerg Med. 2004;27(3):209–18.
[2] Trefan L, Gartner A, Alcock A, et al. Epidemiology of alcohol-related emergency hospital admissions in children and adolescents: An e-cohort analysis in Wales in 2006-2011. PLoS One. 2019;14:e0217598.

371. Childhood poisonings: five-years' experience from an Italian pediatric emergency department

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Objective: Childhood poisonings represent an important cause of evaluation in Pediatric Emergency Departments (PED). When and how long to hospitalize these patients may be a complex issue. The objectives of this study were the assessment of factors (time-latency, involvement, substance) associated with occurrence of symptoms and the evaluation of the correlation between Poisoning Severity Score (PSS) at PED admission, type of substance, age and outcome of patients.
Methods: Retrospective study conducted in an Italian PED between January 2015 and December 2019. All children <15 years with poisoning were included. Patients were graded according to PSS. The association between specific factors and occurrence of symptoms was estimated with odds ratio (OR). The correlation between PSS, age, substance and outcomes was evaluated with multiple logistic regression and OR. The absolute risk of hospitalization (AR) was calculated for each category. A P-value <0.05 was considered significant.
Results: Overall, 766 patients were included (0.4% of PED visits); 72.3% were <4 years. PSS 0-1 was present in 94%. Concerning outcomes, 55% were discharged (observation 3.2 ± 2.5 hours), 28% admitted to the Observation Unit (15 ± 6.6 hours), and 17% hospitalized (4.8 ± 8.2 days). There were no fatal cases. In younger children, male patients had a higher incidence (57%) of unintentional poisonings (90%) due to household-products/caustics (57%) and pharmaceuticals (27%). In adolescents (10-14 years), there was a higher incidence in girls (57%), especially for voluntary exposure (53%) to substances of abuse (40%). In children <4 years there was a correlation between the onset of symptoms with late referral to PED (OR 2.9) or with caustic exposure (OR 1.8); a weak association with pharmaceuticals was reported (OR 0.3). The correlation between PSS, age, substance and outcomes showed that no or mildly symptomatic patients (PSS 0-1) with pharmaceutical (OR 3.1, AR 60%) or caustic (OR 9.7, AR 80%) poisoning had a strong association to hospitalization; even alcohol and carbon monoxide had a higher risk of hospital admission (OR 2.1; AR 40% for both). Moderate/severe poisonings (PSS 2-3) had a higher risk of hospitalization, especially with pharmaceuticals (OR 19.5; AR 80%) and substances of abuse (OR 3.6; AR 70%).
Conclusion: In childhood poisonings, clinical presentation alone may not identify patients who can be discharged or hospitalized. Moderate/severe symptomatic patients are at high risk of hospitalization regardless of substance or age. However, asymptomatic or mildly symptomatic patients at PED admission with a history for caustics, pharmaceuticals, ethanol and carbon monoxide poisoning should be hospitalized for prompt treatment and observation for the potential onset of clinical manifestations.

372. Paediatric paracetamol overdose: reducing side-effects with the SNAP 12 hour N-acetylcysteine regime

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Objective: The purpose of this case series was to assess the introduction of a modified 12-hour N-acetylcysteine (NAC) infusion regime (SNAP) as the standard of care for paediatric patients with paracetamol overdose compared to the standard 21-hour regime.
Methods: A paediatric paracetamol overdose guideline including the SNAP protocol was implemented at a single tertiary paediatric centre from April 2019 onwards. Patients were treated with the SNAP regime consisting of IV NAC 100 mg/Kg over 2 hours, then 200 mg/Kg over 10 hours. This retrospectively reviewed case series of patients were compared to historical controls treated with a standard 21-hour regime. Treatment outcomes, admission parameters such as length of stay and rates of side-effects were assessed.
Results: Overall, 17 patients were treated with the 12-hour regime and they were compared to 13 historical controls treated with a 21-hour regime. Median age was 14 with a minimum age of 5 years in each group. The majority of overdoses were single ingestions but staggered overdoses and therapeutic excesses were included. The rate of delayed presentation >8 hours (21-hour 38%, 12-hour 35%), median ingestion dose (21-hour 153 mg/Kg, 12-hour 179 mg/Kg) and median presentation time (21-hour 3h 57m, 12-hour 4h 23m) were similar. Median length of stay was shorter in the 12-hour group (21-hour 49 h, 12-hour 36 h) but time to mental health assessment was longer (21-hour 22h, 12-hour 35h) however neither difference was statistically significant. There was no difference in peak ALT or INR. Mild hepatotoxicity (defined as ALT >150, or >50 and doubled since admission) was higher in the 21-hour group (31% versus 12%) but this was not statistically significant. One patient in each group had peak ALT >1000 and INR >2. There were no cases of anaphylactoid reaction in the 12-hour group compared to 15% in the 21-hour group. Rates of extended treatment were similar (21-hour 54%, 12-hour 41%). No patients died, were transferred to a liver unit or required restarting of NAC.
Conclusion: This case series of children treated with a 12-hour regime demonstrates a reduction in anaphylactoid reactions and no observed difference in rates of liver injury compared a 21-hour regime. This mirrors the findings from a multicentre trial of the 12-hour regime in adults [1] and supports its on-going use in children.

Reference

[1] Pettie JM, Caparrotta TM, Hunter RW, et al. Safety and efficacy of the SNAP 12-hour acetylcysteine regimen for the treatment of paracetamol overdose. EClinicalMedicine. 2019;11:11–17.

373. Altered mental status following a large ondansetron ingestion in a toddler

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Objective: The pediatric range of toxicity for oral ondansetron is not well established. Though rare, there are case reports of significant toxicity resulting from large ingestions of ondansetron. We present a patient who only developed moderate symptoms despite ingesting an amount of ondansetron markedly larger than those in the reported literature.
Case report: A healthy 10 Kg, 21-month-old male presented to the emergency department (ED) with lethargy and ataxia. He had ingested 20 tablets of 8 mg ondansetron rapid dissolving tablets (ODT), and symptom onset occurred 30 minutes later. He had one episode of emesis prior to ED evaluation. On arrival to the ED the patient's heart rate was 186/min; his other vital signs were age appropriate. He was lethargic and ataxic, otherwise his overall exam was unrevealing. Initial labs showed normal electrolytes, glucose, and complete blood count. His venous blood gas showed a pH of 7.29 and pCO_2 of 45 mmHg. Serial electrocardiograms (EKG) over the first several hours showed his QTc progress from 455 to 490 msec. He was then transferred to a tertiary care facility for higher level of care. His neurologic symptoms improved within 4 hours of the suspected ingestion. An EKG 9 hours post-exposure showed a QTc of 440 msec. He was observed overnight and discharged the following day. An ondansetron concentration from a blood specimen at the time of initial presentation, by liquid chromatography tandem mass spectrometry, was 509 μg/L (Cordant Health Solutions, Huntington, NY). Adult peak plasma concentration after 8 mg is 26 μg/L [1].
Conclusion: Reported cases of large overdoses of ondansetron in toddlers are limited. A previous case reported rapid obtundation followed by seizure, serotonin toxicity and QTc prolongation in a 12-month-old after ingesting 7-8 tablets of 8 milligram ondansetron ODT (6.4 mg/Kg) [2]. Our patient had a much larger dose, 16 mg/Kg, resulting in more minor symptoms that resolved within 10 hours of ingestion. His serum ondansetron concentration was nearly 20 fold greater than that seen in adults with usual dosing. Onset of toxicity after ondansetron ODT overdose is rapid and although reports exist of serious neurologic toxicity, our patient had a more benign course with rapid resolution of symptoms.

References

[1] Baselt RC. Disposition of toxic drugs and chemicals in man, 10th edition. Seal Beach, CA: Biomedical Publications, 2014, p. 1505.
[2] George M, Al-Duaij N, O'Donnell KA, et al. Obtundation and seizure following ondansetron overdose in an infant. Clin Toxicol (Phila). 2008;46:1064–6.

374. Severe salicylic acid intoxication with a topical skin preparation in a newborn

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Objective: Although rare, acute salicylate intoxication may occur from topical application. We report the case of complicated salicylism in a newborn.
Case report: A 13-day-old female, 2.7 Kg body weight, was admitted to the emergency department (ED) for tachypnea and periumbilical skin injuries. Her parents, with poor comprehension of the Italian language, had applied a topical powder containing 97% glucose and 3% salicylic acid to the umbilical stump. The estimated total amount of salicylic acid applied was 1.5 g in the week prior to admission. At ED admission, metabolic acidosis (pH 7.0, HCO_3 11 mEq/L) was observed and sodium bicarbonate 1 mEq/Kg IV bolus and fluid therapy were administered with partial improvement. During the following 48 hours, her clinical condition worsened with hypotension and acute respiratory distress syndrome (ARDS) requiring intubation and mechanical ventilation. The plasma salicylate concentration was high (55.9 mg/dL, therapeutic 2-20 mg/dL). Sodium bicarbonate (1 mEq/Kg/hour IV infusion) was started for urine alkalinisation but was minimally effective with a persistently high salicylate concentration (45.3 mg/dL) after 12 hours, and a coagulation disorder (INR 2.7) developed. On day 3, hypercapnia ($PaCO_2$ 70 mmHg) and lactic acidosis (lactate 5 mmol/L) were associated with pulmonary hypertension and infectious encephalitis. On days 4 and 5, the salicylate concentration decreased to 30 and 28 mg/dL, respectively, but hypotension with renal impairment and worsened respiratory failure ($PaCO_2$ 78 mmHg) with non-cardiogenic pulmonary edema and infective pneumonia were observed. A week after admission, extracorporeal membrane oxygenation (ECMO) was started but a severe stroke secondary to ECMO catheter thrombosis occured. On day 20, nuclear magnetic resonance spectroscopy (NMR) showed a large ischemic lesion in left hemisphere, left mesencephalic area and thalamus. At one month follow-up an electroencephalogram (EEG) confirmed organizational anomalies in the left hemisphere and multifocal paroxysmal anomalies in the right hemisphere compatible with a persistent sub-clinical epileptic seizure pattern.
Conclusion: Salicylate containing products with more than 4-10% may result in toxic effects if applied on a large skin surface area and may be associated with salicylate blood concentrations above 50 mg/dL. In our case the percutaneous absorption was increased by the presence of glucose in the compound, the prolonged/inappropriate misuse and the presence of skin injuries. Lung injury and respiratory failure needing extracorporeal support may occur in severe salicylism and specific/supportive treatment may be complex. Parents should be alerted of the potential risks related to salicylate skin application to newborns and should be educated by medical providers on the safe use of topical medication.

375. 38 Weeks pregnant: managing a mother and neonate after a third-trimester acetaminophen ingestion

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Objective: Although acetaminophen is the most common drug overdose in pregnancy, there is limited data regarding the management of a neonate who is delivered shortly after the mother overdosed on acetaminophen. Acetaminophen is known to cross the placenta and maternal overdose puts the neonate at risk of acetaminophen toxicity. We report the case of a young woman who had an emergency cesarean section shortly after presenting with an overdose of APAP and quetiapine.
Case report: A 25-year-old woman at 38 weeks of gestation was brought to the emergency department (ED) after she texted a friend suicidal statements. On arrival, she reported taking an unknown amount of quetiapine. In the ED she became somnolent and hypoxic, requiring intubation. Laboratory examination was significant for an acetaminophen concentration of 68 μg/mL, aspartate aminotransferase (AST) 17 U/L, alanine aminotransferase (ALT) 10 U/L, and urine toxicology screen positive for benzodiazepines, tricyclic antidepressants, and buprenorphine. Due to an unknown time of ingestion, she was started on N-acetylcysteine (NAC). She started having contractions and obstetrics decided to perform an emergent cesarean section to deliver the baby. Prior to delivery, she had received 150 mg/Kg NAC bolus over 60 minutes. The infant was delivered without complication. Due to a laboratory issue, an acetaminophen concentration could not be obtained on the infant after birth so NAC was given (15 mg/Kg/h in sterile water). The acetaminophen concentration 7 hours after birth in the infant was 13 μg/mL with an AST 28 U/L and ALT 6 U/L. The infant was continued on NAC protocol at the same dose until 21.75 hours post-birth with an undetectable acetaminophen concentration. The infant never developed any signs or symptoms of acetaminophen or liver toxicity. The mother was also continued on NAC protocol and was able to be weaned from the ventilator. She continued to improve until she was able to be discharged to a psychiatric facility. She had no hepatotoxicity.
Conclusion: Acetaminophen overdose requiring treatment in both a mother and neonate is rare. Given differences in neonatal pathophysiology, consideration was taken for volume and amount of dextrose the infant received. In this case, we were able to successfully manage both a mother and child born after overdose with NAC.

376. Epidemiology of pediatric benzodiazepine exposures using the National Poison Data System

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Objective: The rate of visits involving benzodiazepine prescriptions increased from 3.8% to 7.4% between 2003 and 2015 in the US. Benzodiazepine-related overdose mortality has risen sharply, from 0.6 per 100,000 adults in 1999 to 4.4 per 100,000 in 2016. The objective of the study was to describe the epidemiology of pediatric benzodiazepines exposures using a near real-time national poison center (PC) database.
Methods: The National Poison Data System (NPDS) was queried for all pediatric (0-19 years) exposures to benzodiazepines from 2011 to 2019 using generic code identifiers. We descriptively assessed the relevant demographic and clinical characteristics. Trends in benzodiazepine frequencies and rates (per 100,000 human exposures) were analyzed using Poisson regression methods. Logistic regression was used to identify important predictors of severe health outcomes (SHO), defined as cases resulting in major medical outcomes or death.
Results: There were 133,704 pediatric exposures to benzodiazepines reported to PCs from 2011 to 2019, with the number of calls decreasing from 16,830 to 11,776 during the study period. Polysubstance exposures accounted for 41.1% of pediatric benzodiazepine exposures. Of the total benzodiazepine calls, the proportion of calls from acute care hospitals and emergency departments (ACH) increased from 45.3% to 59.1% during the study period. Multiple substance exposures accounted for 51.2% of the calls from ACH. Residence was the most common site of exposure (93.6%), and 62.4% cases were en route to the hospital when the PC was notified. Among the patients, 52.2% were females. Suspected suicide (33.6%) was the most commonly reported reason for exposure, mainly attributed to the teenage population. There were 3,209 cases of SHO, with these exposures increasing by 45.2% during this period (334 to 485, $p < 0.001$). This risk of severe health outcomes increased with age, with cases between 6 – 19 years (Adjusted Odds Ratio [AOR]: 3.41, 95% CI: 2.93 – 4.09) demonstrating significantly increased odds. Cases of suspected suicide (AOR: 1.19, 95% CI: 1.07 – 1.34) and abuse (AOR: 1.49, 95% CI: 1.31 – 1.69) were significantly more likely to result in SHO. Multiple substance exposure increased the risk of such outcomes significantly.
Conclusion: Benzodiazepine exposures decreased during the study period. Abuse and diversion of benzodiazepines by teenagers may be as a result of underlying mental or emotional conditions that leads to self-medication. Benzodiazepines have also been increasingly associated with suicidal ideation, the most common reason for exposure in our sample. Increasing prescriber awareness and better screening may be key to reducing such overdoses.

377. Hyperbaric oxygen therapy in loxoscelism skin necrosis: a case report

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Objective: Spider bites belonging to the genus *Loxosceles* can have a very serious evolution both locally and systemically. The therapeutic response requires a multidisciplinary approach that involves general practitioners, toxicologists, emergency doctors, infectivologists, hyperbarists and plastic surgeons. *Loxosceles rufescens* is indigenous to Mediterranean Europe, including Italy where it often takes refuge in homes. Skin loxoscelism is characterized by cutaneous necrosis, sometimes complicated by soft tissue infection or necrotizing fasciitis. We described a severe case of skin necrosis, caused by this spider's bite which was treated with pharmacological therapy, hyperbaric oxygen therapy (HBOT) and rehabilitation.
Case report: A 55-year-old lumberjack was bitten by a spider that had entered one of his gloves. The spider was identified by an entomologist as *Loxosceles rufescens*. After a 7-8 hour asymptomatic period, a burning pain to his left thumb which radiated to his whole hand appeared. Tendonitis was diagnosed and thus, after the hand was immobilized, he was treated with anti-inflammatory drugs and pain relievers. During the next 48 hours, the clinical picture worsened dramatically with intolerable pain and a swelling sensation from the hand up to the forearm. An orthopaedic visit produced a diagnosis of necrotizing fasciitis. The patient underwent surgery and, after other 24 hours, HBOT was performed. At the same time antibiotics and pain relievers were administered. During recovery a total of 36 HBOT sessions were administered along with 3 surgeries. Finally, an autologous skin graft was performed. A regenerative skin substitute was used along with a silk membrane to favour a better wound evolution.
Conclusion: Symptoms of loxoscelism tend to appear late and diagnosis is frequently delayed. These spider bites can worsen with anaerobic bacterial infection and, therefore a broad spectrum antibiotic therapy is necessary. Treatment is initially generic for spider bite with local disinfection, antibiotic and antihistamine therapy, and general pain relief. In cases of dermonecrosis, or necrotizing fasciitis, HBOT is indicated with compression profiles chosen on the basis of signs, symptoms and laboratory tests (LRINEC Score: Laboratory Risk Indicator for Necrotizing Fasciitis). It is worth noting that even if the correct diagnosis is delayed, HBOT may contribute to recovery and prevent loss of the affected limb. HBOT in association with pharmacological therapy may promote reduction of pain intensity, inflammation and edema in loxoscelism.

378. Exotic venomous snakebites in Switzerland reported to the National Poisons Information Centre over 22 years

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Objective: The private keeping of exotic venomous snakes is permitted according to Swiss law. An estimated 2,000-10,000 venomous reptiles are held in the homes of these aficionados [1]. The aim of the present study is to characterize the epidemiologic and clinical features of bites by exotic venomous snakes over a period of 22 years in Switzerland.

Methods: We included all calls related to exotic snakebites in Switzerland and Liechtenstein recorded at the Swiss National Poisons Information Centre (Tox Info Suisse) from 1997 to 2018, where at least the genus of the snake was available. Exclusion criteria comprised indigenous snakes, non-venomous exotic snakes, clinical courses incompatible with a snakebite or calls from Swiss citizens bitten abroad.
Results: Within the study period, 1364 calls related to snakebites were recorded at Tox Info Suisse. Of these 148 (11%) were attributed to exotic venomous snakes and fulfilled the study criteria and 112 of 114 patients (98%) with medical follow-up information exhibited good causality (probable or confirmed). Only adult patients with a median age of 40 (range 16-71 years) were affected, with a predominance of males (n = 136, 92%). Viperidae were involved in 87 (78%) and Elapidae in 25 (22%) cases, respectively; 30% of the vipers belonged to the genus *Crotalus* sp., and 59% of the elapids belonged to the genus *Naja* sp. Overall, the main affected body part was the hand in 89 patients (79%). In the majority of the patients the clinical course was mild (46, 41%) or moderate (40, 36%), a lower proportion was asymptomatic (6, 5%) or exhibited severe symptoms (20, 18%). No fatalities were reported in the study period. Severe symptoms were observed after elapid bites in six patients (24%) and after viper bites in 14 patients (16%), respectively. Besides local effects, neurologic disorders after elapid bites and hematologic disorders after viper bites were most frequently reported. Antivenom was administered in 24% (27 patients (18 Viperidae [20%] and 9 Elapidae [36%]), 5 patients (4%) required multiple doses), overall with good resolution of symptoms. The other 86 patients (76%) were treated symptomatically. The median duration of hospitalization was 1 day (range 0-36).
Conclusion: Considering the number of venomous snakes kept in Switzerland, the number of bites is relatively low. More than half of the patients developed symptoms requiring medical treatment. No fatalities or bites in children were observed.

Reference

[1] Plate A, Kupferschmidt H, Schneemann M. [Bites of venomous snakes in Switzerland]. Praxis (Bern 1994). 2016;105:679–85; quiz 684-5. German.

379. Far from home: compartmental syndrome after envenomation by *Crotalus atrox* in metropolitan France

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Objective: To describe the occurrence of compartmental syndrome and the medical and surgical care of an exotic snakebite in metropolitan France.
Case report: A patient was bitten in the thenar eminence of the right hand while feeding a mature *Crotalus atrox* at 11.45 p.m. He was admitted to the emergency room 15 minutes later in a vagal presentation with pallor and chills that quickly resolved. Locally, two puncture wounds 15 mm apart were observed, associated with swelling of the back of the hand. He received 120 mg of corticosteroids and 1 g of acetaminophen. He was transferred to the intensive care unit (ICU) for further management. At 3 hours the edema had spread to the lower third of the right arm and was associated with paralysis of the hand and motor disability, which was difficult to assess due to pain. Physical examination was otherwise normal. He received 3 vials of Antivipmyn-TRI®, provided by the French exotic antivenom bank. He presented a discrete increase in fibrin monomers (max. 75 µg/mL at 7 hours) and D-dimers (max. 650 ng/mL on day 2). Creatine kinase remained below 250 IU/L and other hemostasis tests were normal. At day 1, the edema had progressed above the elbow, accompanied by local inflammatory signs (erythema and bruising) and hypoesthesia of the thumb. He received 3 further vials of antivenom. At 17 hours a diagnosis of compartmental syndrome was confirmed in the operating room by a pressure measurement of more than 50 mmHg in the thenar, hypothenar and intermetacarpal areas and in the anterior territory of the right forearm. Discharge fascial incisions were immediately made, revealing a fluid collection on the dorsal area of the hand, but preserved muscles. The regression of the edema and the stationary state of the skin sensitivity disorders allowed the patient to be discharged from ICU at day 3. He was discharged home at day 7. At day 20 finger mobility was almost complete except for the right fifth finger and the fascial wounds were in the process of healing.
Conclusion: Among the antivenoms available in the French antivenom bank, ANTIVIPMYN TRI® was the one with the highest paraspecificity in this case, being indicated for envenomation by *Crotalus durissus*. Despite the administration of the antivenom, the patient developed compartmental syndrome, a rare but serious complication of envenomation by exotic viperids. Compartment pressure measurement helps to indicate the need for fasciotomy when antivenom therapy is insufficient.

380. Human exposure to larvae of processionary moths in France: study of symptomatic cases registered by the French Poison Control Centres between 2012 and 2019

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Objective: Contact with the setae of larvae of pine or oak processionary moths (LPPM or LOPM; (*Thaumetopoea pityocampa* and *Thaumetopoea processionea*) can induce severe urticarial or allergic reactions in warm-blooded animals. These species, especially LPPM, are presently expanding towards highly populated areas due to climate change and/or human-mediated translocations, this study aimed to describe human exposures to PM larvae in France.

Methods: We conducted a retrospective study of symptomatic cases of exposures to PM larvae registered by the French Poison Control Centres from 1 January 2012 to 31 July 2019. Toxicologists reviewed all the medical records coded with the agent "larvae" to specify the species when possible.
Results: Of the 1,274 included cases, 59% and 27% corresponded to LPPM and LOPM, respectively; the remaining cases (14%) concerned unspecified PM larvae. While a steady increase characterized the annual trend of exposures to LOPM, exposures to LPPM fluctuated annually. More than 90% of the annual cases occurred between January and May for LPPM, and April and August for LOPM (with a peak in March or June, respectively). For the 1,022 cases for which information was available, the sex ratio was 1.2 and the median age was 11 years old (2 months - 87 years). Patients were exposed directly to the larva (30%, particularly children aged under 5 years), indirectly through airborne setae, tents, contaminated clothes (40%) or through both mechanisms (9%, or unknown). As exposures concerned a dermal route for 93% of cases, alone or in combination with another route, 97% of the 1,022 cases reported skin symptoms (itching, urticarial dermatitis, etc) while 8%, 4% and 3% reported ocular, nasopharyngeal and respiratory manifestations, respectively. Assessment of the case severity was [1]: PSS1 96.3%, PSS2 3.5% and PSS3 0.2%. Ocular or oral exposures led more frequently to severe symptoms (PSS $\geq$2) compared to dermal exposure (respectively, 31% and 18% versus 2%, $p < 0.00110^{-3}$). Finally, considering the low number of occupational cases (2%), the higher proportion of severe cases (PSS $\geq$2) among landscaping sector professionals or forestry workers than in the general population was not statistically significant (12% versus 4%, $p = 0.13$).
Conclusion: Since PM larvae exposure is a growing health concern, which can cause severe injuries particularly after ocular or oral exposure, populations and professionals should be clearly informed of existing recommendations to avoid such events and of actions to take after being exposed.

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.

381. Rattlesnake bite in Austria: a case report

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Objective: Although the keeping of poisonous snakes is forbidden in Austria accidents still occur.
Case report: A 69-year-old man was admitted to hospital after a bite by a North American forest rattlesnake (*Crotalus horridus*), which he kept illegally. He presented with hemodynamic shock, was stuporous and had several bite marks on forearm/wrist/ball of the thumb with bloodstains and swelling. The patient vomited repeatedly and protective intubation was required. The anaphylactic shock was treated with catecholamines and corticosteroids. After consulting the Poisons Information Centre, 10 ampoules of antidote Antivipmyn-TRI (from a private depot in Vienna) were administered. At the intensive care unit the patient received 12 more ampoules (6 from a private depot in Carinthia, 6 from Depot Munich). He had circulatory instability requiring pronounced volume and catecholamine administration. On the following day creatine kinase and myoglobin had increased significantly (68510 U/L and 40650 ng/mL, respectively) as a result of muscular damage. The coagulation values changed only slightly initially. After initial stabilization, he was extubated after 2 days, but had to be re-intubated 1 day later due to sudden cardiovascular arrest and resuscitation. Swelling of the larynx was suspected as an after-effect of the snake bite and 6 more ampoules (from a depot in Zurich) of antiserum were given. Oedema and laboratory values decreased finally and the patient was extubated after 3 more days of mechanical ventilation. He required antihypertensive therapy with urapidil and nitroglycerin. Eight days after the accident he became delirious and consequently comatose. A cerebral computerised tomography (CT) scan was not pathological and "protracted snake venom" was suspected to be the cause of the neurological impairment. Two more ampoules of antiserum (from a depot in Zurich) were administered, which resulted in clinical improvement. On day 17 recurrent myocloni of the upper extremities and face occurred. According to the literature myocloni can occur weeks after a rattlesnake bite and therefore two additional ampoules of Antivipmyn (from a depot in Zurich) were administered. A ventilation-dependent pneumonia was treated with antibiotics. The patient was transferred to an internal ward after 36 days of intensive care.
Conclusion: In this case, a distinction between anaphylactic shock and complications from the snake venom could not be clearly made and lead to the administration of 32 vials of antiserum in total, most of which were transported from abroad. Even though keeping venomous snakes is prohibited in Austria, cases arise. Snake antiserum is expensive, complex to store and there is no generally accessible serum depot in Austria. Fortunately, the cooperation with Germany and Switzerland concerning the acquisition of antiserum was very effective in this case.

382. Bitten abroad, an unforgettable souvenir: bites and stings reported to the UK National Poisons Information Service (NPIS) sustained whilst travelling overseas, 2009–2015

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Objective: International travel has increased steadily over the past 20 years and in 2019 there were 93.1 million visits abroad made by UK residents [1]. We report on cases where advice from the NPIS was sought on the management of patients who sustained bites or stings whilst travelling overseas.
Methods: A retrospective analysis of UK NPIS enquiries between 1 January 2009 and 31 December 2019 was undertaken for enquiries relating to bites and stings and specifically for those that occurred overseas.

Results: There were 142 enquiries regarding 131 patients during this period; 116 (89%) were adults and 15 (11%) were children (under 18 years of age). The travel history was known in 127 cases (97%), and included a total of 41 different countries across six continents, with Europe the most frequently visited (n = 53) followed by North America (n = 28) and Asia (n = 24). The most common regions where exposures occurred were Spain (including Islands) (n = 20), the Caribbean islands (n = 16) and Greece (including Islands) (n = 10). The majority of exposures (n = 79, 57%) involved marine organisms. Jellyfish (n = 25) and sea urchins (n = 25) were the most common, followed by fish (n = 18), 7 of which were stonefish and 4 weever fish. The remaining 11 exposures involved 7 stingrays, 2 sea anemones, one octopus and one fire coral. Of the remaining 52 exposures, 19 involved spiders, 11 insects, 7 scorpions, 6 snakes, 5 monkeys, 1 parrot, 1 dog, 1 worm and a chimpanzee. The site of the bite/sting was known in 94 cases of which 42 occurred on the foot. The maximum poisoning severity score [2] was known in 129 cases and was none in 14, minor in 98, moderate in 15 and severe in 2. The two severe cases involved a bite from a Common Lancehead snake in Trinidad and a sea urchin in Barbados. The advice of a clinical toxicologist was sought in 24 exposures, of which 8 were referred to a clinical toxinologist for further specialist advice.
Conclusion: Bites and stings sustained overseas are an infrequent and unusual type of enquiry for poison centres. Healthcare professionals and poison centre staff need to be aware of the potential for patients to seek medical advice from them upon their return.

References

[1] Office for National Statistics. Travel trends: 2019 (cited 7 October 2020). Available from https://www.ons.gov.uk/peoplepopulationandcommunity/leisureandtourism/articles/traveltrends/2019
[2] Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol. 1998;36: 205–213.

383. Role of decontamination in dogs poisoned by alphachloralose-based rodenticides: a case series

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Objective: In 2014 rodenticides based on alphachloralose were first introduced onto the Dutch market. Alphachloralose (3.4-4.0%) is packaged in 10 g bags with paste or coated grain and is licensed for private indoor use. Here we present a case series of 95 dogs exposed to alphachloralose-containing rodenticides. The influence of decontamination measures on clinical course are evaluated.
Case series: Decontamination by the veterinarian was performed in 64 dogs. In 45 dogs vomiting was induced and in 14 cases (ruptured) bags and in 27 cases coated grains/pasta were visible in the vomitus. Vomiting induction followed by activated charcoal was performed in 17 dogs resulting in 8 cases with (ruptured) bags and 4 with coated grains/pasta retrieved. Two dogs received only activated charcoal. Thirty-one of the decontaminated dogs with a median body weight of 8 Kg (range: 2.7-30.0) developed signs and symptoms (48%). The estimated median dose was 56.7 mg/Kg (range: 2.5-195.1; n = 29). Mild symptoms (e.g., drowsiness) which resolved within 4 hours were seen in 9 dogs (29%). The remaining 22 dogs developed predominantly signs of CNS excitation (often sensory induced), i.e., tremors/cramps (n = 8), and seizures (n = 1), ataxia (n = 12), and CNS depression e.g., drowsiness (n = 7), stupor (n = 4), and coma (n = 2). Hypothermia was noted in one dog. All symptoms resolved within 24 hours. No decontamination was performed in 31 dogs. Twenty-two of the 31 dogs with a median body weight of 6.5 Kg (range: 2.5-31.0, n = 21) developed signs and symptoms (71%). The estimated median dose was 62.6 mg/Kg (range: 12.9-300.0; n = 20), mild symptoms (e.g., drowsiness) which resolved within 4 hours were seen in 4 dogs (13%). The remaining 18 dogs developed predominantly signs of CNS excitation, often sensory induced (i.e., tremors/cramps (n = 13), and seizures/status epilepticus (n = 8), and CNS depression (i.e., drowsiness (n = 5), stupor (n = 2), coma (n = 4) and ataxia (n = 11). Hypothermia was noted in 6 dogs. Five dogs vomited spontaneously retrieving (partially) the ingested rodenticide in 4 cases. One 10-year-old dog (2.8 Kg) was euthanized. All other dogs survived the poisoning and all symptoms resolved within 60 hours.
Conclusion: Decontamination measures such as induction of vomiting are effective in reducing exposure if they can be performed before signs develop, and thereby reduce the severity of alphachloralose-based rodenticide poisoning in dogs.

384. "Curiosity killed the cat": cats poisoned by alphachloralose-containing rodenticides

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Objective: In 2014 rodenticides based on alphachloralose were first introduced on the Dutch market. Alphachloralose (3.4-4.0%) is packaged in 10 g bags with pasta or coated grain and are licensed for private indoor use. Here we present a case-series of 18 cats exposed to alphachloralose-based rodenticides.
Case series: During the night three, nine months old cats entered the garage after the door was left open accidentally. In the garage, the cats found an open box with twelve 10 g bags containing 4% alphachloralose paste. The next morning, the pet-owner found one cat lying dead in its urine and stool. The second cat displayed neurological signs while the third cat seemed healthy. Neurological signs consisted of generalized tremors and ataxia. After activated charcoal was given and intravenous fluid therapy was started, this cat was hospitalized for observation in a warm, quiet environment. After 24 hours, the cat was almost recovered and discharged. In addition to the above-mentioned case history we have follow up information for another 15 cats. One cat remained asymptomatic after vomiting was induced. The estimated dose was 11 mg/Kg body weight. Fourteen cats with a median age of 0.4 years (range: 0.1-19; n = 12) and median body weight of 2.8 Kg (range 0.5-4.0; n = 14) developed signs and symptoms. It was possible to estimate the exposure dose in 8 cats; median dose 83 mg/Kg (range: 34-320).

Symptoms consisted predominantly of signs of CNS excitation, often sensory-induced i.e., tremors/cramps (n = 12) and seizures (n = 3), and CNS depression i.e., drowsiness (n = 2), lethargy/stupor (n = 2), coma (n = 1) and ataxia (n = 6). Hypothermia was noted in six cats; the median body temperature was 35.3 °C with a minimum of 32.0 °C. Gastrointestinal symptoms were seen in three cats; two vomited spontaneously and the rodenticide was visible in the vomitus. Salivation was seen in another cat. In one cat, vomiting was induced followed by activated charcoal. Treatment of the CNS excitation signs was necessary in 6 cats, diazepam (n = 3), midazolam (n = 1) and midazolam followed by propofol constant rate infusion (n = 2) was used. One, an 8-week-old kitten with a body weight of 0.6 Kg did not survive the poisoning. It was found hypothermic (32 °C) and deeply sedated next to a ruptured bag of rodenticide and died one day later.
Conclusion: In this case-series predominantly young cats (median age: 0.7 years; n = 15) were exposed to alphachloralose containing rodenticides. Due to their small body weight, cats may develop a severe, potentially life-threatening poisoning.

385. A case series of hypothermic, sedated cats with sensory-induced CNS excitation: alphachloralose poisoning?

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Objective: In the autumn of 2018, the Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) announced that the registration of rodenticides based on anticoagulants will not be renewed for use by a lay-person in the Netherlands. As a consequence the use of rodenticides based on alphachloralose is increasing rapidly.
Case series: Between December 2018 and October 2020, the Dutch Poisons Information Center (DPIC) received 15 information requests concerning 21 predominantly hypothermic, sedated cats experiencing CNS excitation who were found outside. In four cases, multiple cats (2 or 3) from different households were found in the same neighborhood and presented at the veterinary clinic within a few hours of one another. Symptoms consisted predominantly of signs of CNS excitation, often sensory-induced i.e., ataxia (n = 4), tremors/cramps (n = 17), seizures (n = 3), and CNS depression i.e., drowsiness (n = 3), lethargy/stupor (n = 3) and coma (n = 13). Sixteen cats were hypothermic with a median body temperature of 36.0 °C (n = 8) with a minimum of 32 °C. Miosis during CNS depression was noted in eleven cats and mydriasis (n = 3) during CNS excitation. Two cats appeared (temporarily) blind during their recovery. Other reported symptoms were respiratory distress (n = 3) and bradycardia (n = 3). Blood analysis was generally unremarkable. After activated charcoal was given (n = 3), intravenous fluid therapy (n = 14) was started and the cats were observed in a warm, quiet environment. Additional treatment was necessary in 12 cats; diazepam (n = 6), midazolam (n = 4) and propofol constant rate infusion (n = 2) were used. All cats except one, survived and fully recovered; twelve cats within 24 hours and seven cats in 48-72 hours. Length of recovery was unknown in one.
Conclusion: Suspected alphachloralose poisoning is characterized by CNS depression combined with often sensory-induced CNS excitation. Small animals are at greater risk of developing hypothermia. Recognition of this typical clinical picture by veterinarians is important, because with proper treatment full recovery is possible. Whether these cats were poisoned by alphachloralose containing bait or indirectly by eating alphachoralose-sedated mice is unknown. However, the DPIC did receive one information request (left out of this case series) concerning a cat developing symptoms within 15 minutes after it was seen eating a alphachloralose sedated mouse.

386. When does xylitol-induced hypoglycaemia occur in dogs?

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Objective: Xylitol is a sugar substitute present in many foods and medicines. In dogs it causes non-dose-related hypoglycaemia due to insulin release. We investigated the time to onset of hypoglycaemia in dogs reported to the Veterinary Poisons Information Service (VPIS).
Methods: All symptomatic cases of xylitol ingestion in dogs reported from 2009 to the end of October 2020 were extracted from the VPIS database. Three sets of time data were used: the time hypoglycaemia was measured; the time to signs consistent with hypoglycaemia (weakness, collapse, coma or convulsions) and the signs reported at the time of the enquiry with the time since exposure.
Results: There were 715 symptomatic cases of xylitol ingestion in dogs. Information on time to hypoglycaemia or markers of hypoglycaemia was available in 84 cases. The time hypoglycaemia was measured was available in 38 cases, in 12 cases the time to onset of signs consistent with hypoglycaemia was available and the time since ingestion and hypoglycaemia or signs of hypoglycaemia in 34 cases. Overall, the average time to onset of hypoglycaemia was 1.9 hours (range 0.25 to 12 hours). Cases of hypoglycaemia within 1 hour occurred with all product types except nicotine replacement gum (Table 1). In 77.4% of cases hypoglycaemia occurred within 2 hours of ingestion and in 4.8% it occurred after more than 4 hours.
Conclusion: Xylitol typically causes hypoglycaemia within 2 hours of ingestion in dogs, but it can occasionally be delayed up to 12 hours. The delay in onset with chewing gum may be because

Table 1. The number of cases and time to onset of hypoglycaemia in dogs after ingestion of various products containing xylitol.

	Product type							
Time to onset of hypoglycaemia	Chewing gum (n = 38)	Sugar replacement/ baked goods (n = 20)	Starburst® (n = 10)	Pharmaceutical products/ supplements (n = 7)	Nicotine replacement gum (n = 3)	Sweets (n = 3)	Unknown (n = 3)	Total (n = 84)
0-1 hours	20	9	4	2		2	2	39
>1-2 hours	11	3	5	5	1		1	26
>2-4 hours	5	7	1		2			15
>4 hours	2	1				1		4

Note: Starburst® is marketed as a cross between a gum and a sweet.

Table 1. Call numbers to the Veterinary Poisons Information Service (VPIS) and Animal PoisonLine (APL) in 2019 and 2020 with calculated percentage change.

	Total Calls			VPIS calls			APL calls		
Month	2019	2020	% Change	2019	2020	% Change	2019	2020	% Change
January	978	1020	4	789	767	−3	189	253	34
February	995	1028	3	826	793	−4	169	235	39
March	1083	1143	6	893	883	−1	190	260	36
April	1081	1219	13	877	822	−6	204	397	95
May	1072	1252	17	825	809	−2	247	443	79
June	1052	1305	24	824	870	6	228	435	91
July	1152	1319	14	899	919	2	253	400	58
August	1107	1242	12	843	815	−3	264	427	61
September	1101	1277	16	858	830	−3	243	447	84
Total	**9621**	**10805**	**12**	**7634**	**7508**	**-2**	**1987**	**3297**	**66**

Table 1. Number of cases of disinfectant, dough and home decorating products in the first 6 months of 2019 and 2020 reported to the Veterinary Poisons Information Service (VPIS) and Animal PoisonLine (APL).

Agent	2019	2020	% Change
Disinfectant products			
Disinfectant wipes	8	12	50
Benzalkonium chloride (BAC) containing products	67	80	19
Didecyldimethyl ammonium chloride (DDAC) containing products	10	21	110
Disinfectants not specified	9	12	33
Sodium hypochlorite (bleach)	20	19	−5
Soap	15	17	13
Hand cleanser/sanitiser	0	8	N/A
Home decorating products			
Paints	45	55	22
White spirit/turpentine substitute	10	21	110
Doughs			
Bread dough	4	23	475
Salt modelling dough	5	13	160
Total Call	6262	7010	12

the product is not chewed before swallowing. With home baked goods and sweets, the delay may be due to the presence of other carbohydrates including sugars. Monitoring for at least 12 hours is recommended for dogs after ingestion of a toxic dose of any form of xylitol.

387. The effect of the COVID-19 pandemic on call numbers to the Veterinary Poisons Information Service (VPIS) and Animal PoisonLine (APL)

Zoe Tizzard, Nicola Bates and Nick Edwards

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Objective: The COVID-19 pandemic and subsequent lockdowns have had an impact on all parts of our lives. Veterinary practices in the UK have had to adapt, including temporary closure of branches, pausing non-essential services and telephone screening cases that physically attend practices. Emergency cases of potential poisoning in animals are still occurring but may be dealt with differently given the current situation. The VPIS provides a telephone poisons information service to veterinary professionals but also a direct triage service to owners via APL.
Methods: A retrospective study of records of enquiries to VPIS (a service for veterinary professionals) and APL (a triage service for owners) in 2019 and 2020 between 1 January to 30 September.

Results: During the 2019 study period there were a total of 9621 calls, of which 7634 (74%) were to VPIS and 1987 (21%) to APL. During the 2020 study period there were a total of 10805 calls, of which 7507 (69%) were to VPIS and 3297 (31%) to APL. VPIS call numbers have remained relatively stable, dropping by just 127 cases in 2020 compared to the same period in 2019, despite practice closures. While APL calls have slowly increased since it's inception in 2017 consistent with increased awareness of the service, in 2020 there was a marked increase in APL cases from April 2020.
Conclusion: The number and proportion of calls to VPIS and APL has been affected by the COVID-19 pandemic. The number of calls directly from pet owners to APL has increased, particularly from April following the national lockdown from 23 March 2020, increasing the proportion of APL calls from 21% of all calls in the 2019 study period to 31% of all calls in the same period of 2020.

388. The effect of the COVID-19 pandemic on animal poisons cases reported to the Veterinary Poisons Information Service (VPIS) and Animal PoisonLine (APL)

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Objective: The COVID-19 pandemic and subsequent lockdowns have had an impact on all parts of our lives. We are washing hands and using sanitisers and disinfectants more. Disinfectant exposure is a concern in pets, particularly cats, as they can develop significant local tissue injury. Exposure may occur through spills and splashes but also during normal use where pets walk over cleaned surfaces and groom feet and fur. This can result in pain, oral ulceration and pyrexia. Large numbers of people have also spent more time than ever at home. We examined whether there was any reflection of these circumstances in animal poisons cases in the UK.
Methods: A retrospective study of the records of enquiries to VPIS (service for veterinary professionals) and APL (triage service for owners) in 2019 and 2020 between 1 January and 30 June, examining specifically COVID-19 related agents (disinfectants and hand cleaners) as well as home decorating products, and home-made bread and salt modelling doughs.
Results: We have seen an increase in the number of cases relating to disinfectant products and alcohol-based hand cleaners. Bleach exposures have not increased. There has been an increase in the number of pets exposed to paints and white spirit. Additionally, there has been a large increase in the number of cases of ingestion of home-made bread dough (risk of gastric distension and obstruction) and salt modelling dough (risk of hypernatraemia).
Conclusion: The increased number of exposures to disinfectant products likely reflect their increased use and availability during 2020. The increases in exposures to DIY products and home-made bread and salt modelling dough perhaps reflect changes in habits as we spend more time at home.

389. The successful treatment of thallium sulfate toxicity in a dog using Prussian blue

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Objective: Thallium sulfate, once commonly used as a household rodenticide, is a poisonous heavy metal banned in most countries due to its high toxicity. We report a case of thallium poisoning in a dog which was successfully treated using Prussian blue.
Case report: An 8 Kg, 5-year-old female miniature schnauzer was presented to a veterinary clinic four days after eating corn soaked in an old liquid rodenticide containing 5 g/L thallium sulfate. The maximum estimated ingested dose was 1.25 grams thallium sulfate (156 mg/Kg). The reported minimal lethal dose of thallium sulfate in dogs is 12-15 mg/Kg [1]. The dog presented with signs of lethargy, anorexia, ataxia, abdominal pain and hair loss. Treatment of thallium toxicity is most effective using a specific chelator, Prussian blue. Availability of this antidote can be problematic, especially in a veterinary setting. In the Netherlands Prussian blue (Radiogardase-CS®, ferric hexacyanoferrate(II)) is available via the National emergency stock of antidotes, this stock is not for veterinary use. Fortunately, the stock of Prussian blue was close to its expiration date however, and therefore it was made available for this dog. The dog received a human dose of 250 mg/Kg Prussian blue per day for 15 days. Additional treatments included butylscopolamine bromide (Buscopan®) as an antispasmodic to treat the abdominal pain, dexamethasone to aid the Buscopan injections, lactulose as a laxative (Prussian blue can cause obstipation), and four days of activated charcoal following the Prussian blue treatment. Over the course of the poisoning the alopecia progressed, most markedly over the abdominal area and around the muzzle. Furthermore, dermal lesions appeared primarily situated at the soles of the paws. Behaviourally, the dog became more withdrawn and irritable. Blood thallium concentrations were determined 9, 18, and 38 days after exposure and were 196 μg/L, 20 μg/L, and 21.5 μg/L, respectively. After approximately six to eight weeks hair began to grow back and behaviour started to normalize. Three months after the exposure the dog was completely recovered, without any sequelae.
Conclusion: To our knowledge this is the first documented case of a potentially severe thallium poisoning in a dog, successfully treated with Prussian blue. We propose that this treatment contributed significantly to the recovery of the dog. Our case demonstrates that, when available, Prussian blue can be safely administered to dogs to treat thallium toxicity.

Reference

[1] Gettler AO, Weiss L. Thallium poisoning. III. Clinical toxicology of thallium. Am J Clin Pathol. 1943;13:422–429.

390. Pharmacovigilance for identification and prevention of therapeutic errors

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Objective: Poison centers have a central role in the management of therapeutic errors and in their prevention through analysis of the cases in order to promptly identify critical issues.
Methods: In the period between 1 January 2018 and 8 June 2020, a total of 5876 therapeutic errors that required the consultation of the Milan Poison Center were analyzed and follow-up calls were performed. Data was collected and analyzed in order to identify the most frequently involved age groups and drugs, symptom severity, and to verify if there was a predominant type of error in the different age groups.
Results: Of 5876 cases, 5243 (89.2%) were asymptomatic, whereas the severity of the symptoms was mild (n = 478, 8.1%); moderate (n = 127, 2.2%), severe (n = 16, 0.3%) or not evaluated (n = 12, 0.2%). The majority of cases involved patients aged 0-4 years (n = 2076, 35.3%) and patients over 70 years (n = 1143, 19.5%). See Table 1. The most frequently involved drugs were: acetaminophen (n = 586), amoxicillin/clavulanate (n = 255), colecalciferol (n = 172), amoxicillin (n = 232), cetirizine (n = 124), ibuprofen (n = 257), azithromycin (n = 157), and salbutamol (n = 99). The most common errors involved the wrong dosage (n = 3696, 62.9%), followed by the wrong drug (n = 1920, 32.7%), wrong administration route (n = 311, 5.3%) and wrong preparation (n = 203, 3.5%). In 97 cases (1.7%) the drug was expired.
Conclusion: Monitoring therapeutic errors is important in order to avoid preventable mistakes. Overall, more than 89% of the cases were asymptomatic or presented with mild symptoms. Pediatric patients are particularly at risk and the majority of the errors involved the wrong dosage. The collaboration with

Table 1. Symptom severity, age class and type of error in therapeutic errors reported to the Milan Poison Center (2018-June 2020).

	Wrong dosage		Wrong drug		Wrong administration route	
Age	N	Symptom severity	N	Symptom severity	N	Symptom severity
<1 year	319	No symptoms	196	No symptoms	34	No symptoms
	26	Mild	10	Mild	3	Mild
	9	Moderate	2	Moderate	0	Moderate
	1	Severe	0	Severe	0	Severe
1-4 years	4	Unknown	0	Unknown	0	Unknown
	874	No symptoms	402	No symptoms	65	No symptoms
	45	Mild	20	Mild	2	Mild
	12	Moderate	10	Moderate	2	Moderate
	2	Severe	0	Severe	0	Severe
5-9 years	1	Unknown	0	Unknown	0	Unknown
	448	No symptoms	225	No symptoms	28	No symptoms
	29	Mild	17	Mild	3	Mild
	4	Moderate	7	Moderate	0	Moderate
	0	Severe	1	Severe	0	Severe
10-14 years	182	No symptoms	89	No symptoms	9	No symptoms
	5	Mild	9	Mild	1	Mild
	4	Moderate	2	Moderate	0	Moderate
15-17 years	1	Unknown	0	Unknown	0	Unknown
	33	No symptoms	29	No symptoms	3	No symptoms
	4	Mild	4	Mild	0	Mild
	2	Moderate	1	Moderate	0	Moderate
18-29 years	87	No symptoms	44	No symptoms	10	No symptoms
	16	Mild	7	Mild	3	Mild
	2	Moderate	7	Moderate	0	Moderate
30-39 years	120	No symptoms	64	No symptoms	7	No symptoms
	14	Mild	8	Mild	3	Mild
	7	Moderate	2	Moderate	0	Moderate
40-49 years	0	Unknown	2	Unknown	0	Unknown
	166	No symptoms	81	No symptoms	10	No symptoms
	20	Mild	22	Mild	3	Mild
	2	Moderate	1	Moderate	0	Moderate
	0	Severe	1	Severe	0	Severe
50-59 years	2	Unknown	2	Unknown	0	Unknown
	194	No symptoms	115	No symptoms	15	No symptoms
	20	Mild	17	Mild	3	Mild
	4	Moderate	5	Moderate	0	Moderate
	2	Severe	0	Severe	0	Severe
60-69 years	243	No symptoms	117	No symptoms	13	No symptoms
	15	Mild	27	Mild	0	Mild
	2	Moderate	8	Moderate	0	Moderate
	1	Severe	1	Severe	0	Severe
70-79 years	346	No symptoms	148	No symptoms	35	No symptoms
	37	Mild	19	Mild	4	Mild
	8	Moderate	5	Moderate	0	Moderate
	2	Severe	2	Severe	1	Severe
80-89 years	251	No symptoms	98	No symptoms	38	No symptoms
	23	Mild	19	Mild	5	Mild
	9	Moderate	7	Moderate	0	Moderate
	2	Severe	0	Severe	0	Severe
> 90 years	65	No symptoms	38	No symptoms	7	No symptoms
	9	Mild	9	Mild	0	Mild
	3	Moderate	1	Moderate	0	Moderate
Unknown	18	No symptoms	19	No symptoms	4	No symptoms
	1	Moderate	0	Moderate	0	Moderate

pharmaceutical companies, healthcare professionals and citizens is crucial to implement effective preventive strategies and would allow consideration of these data in the context of the prevalence of use of these drugs.

391. Lamotrigine-induced Stevens-Johnson syndrome: a case report

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Objective: Stevens-Johnson syndrome is an immune-complex-mediated hypersensitivity reaction that involves skin and mucous membranes. The main known causes are hypersensitivity to drugs, viral infections, systemic lupus erythematosus and, rarely, malignancies. We present a case where a patient developed Stevens-Johnson syndrome after three weeks of treatment with lamotrigine for mood disorder.

Case report: A 21-year-old pregnant woman at 7 weeks' gestation with a medical history of mood disorder presented to the emergency department with a severe generalized skin reaction. Four days prior to admission she noted bumps on her lips that spread to the oral mucosa and began to appear vesicular. Drug

history revealed that she had started lamotrigine 50 mg three weeks before. On the basis of history and clinical examination, a diagnosis of Stevens-Johnson syndrome due to lamotrigine was made. All routine blood tests were normal; other causes such as viral infection, autoimmune disorders and malignancies were excluded. During the first two days after admission, she developed pseudomembranous conjunctivitis and a worsening swelling of the face and lips. She also developed erosion of the mucous membranes inside the mouth and vulva, as well as erythematous papules and bullous eruptions over the body, particularly serious on feet where detachment of the epidermis occurred. Histopathological examination confirmed Stevens-Johnson syndrome. Herpes simplex II eruption complicated the hospitalization. Lamotrigine was discontinued immediately and replaced by trazodone 30 mg/day and flurazepam 15 mg/day. She also received prednisone 50 mg and intravenous fluids. Oxatomide 30 mg was given for pruritus and intravenous aciclovir 500 mg, three times/day was added. Dexamethasone plus netilmicin eye drops, aciclovir cream topically 5 times per day, nystatin vaginal tablets, mupirocin cream and aciclovir oral gel were applied. She had a slow but favorable course and was discharged from hospital on day 17; the pregnancy was terminated at the patient's request.
Conclusion: Lamotrigine, a commonly used antiepileptic drug, is also approved by the US Food and Drug Administration (FDA) for the treatment of bipolar disorders. There are few case reports linking lamotrigine to Stevens-Johnson syndrome and the German Rash Registry reports rates of 0.02% in adults. Although the risk of developing Stevens-Johnson syndrome with lamotrigine is rare, the use of this drug in psychiatry is increasing and clinicians prescribing this medication should be aware of this potentially lethal disorder.

392. Dimethyl fumarate-induced hepatotoxicity confirmed by biopsy

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Objective: To report a case of a multiple sclerosis patient that developed dimethyl fumarate-induced clinically significant acute hepatotoxicity, which was confirmed by liver biopsy.
Case report: A 26-year-old woman was diagnosed with relapsing multiple sclerosis. Serum liver enzyme activities were in the normal range on diagnosis. After a failed treatment attempt with glatiramer acetate and a washout period of a few weeks, she started treatment with dimethyl fumarate. Ten days after doubling the initial dose of 120 mg BID, liver transaminases activities were elevated (aspartate aminotransferase (AST) 372 IU/L, aspartate aminotransferase (AST) 674 IU/L). Treatment with dimethyl fumarate was stopped, but the patient developed nausea, vomiting, lack of appetite, malaise and fatigue. Liver enzymes continued to increase (ALT 1864 IU/L, AST 1242 IU/L, alkaline phosphatase (ALP) 165 IU\L) with slightly increased serum total bilirubin (1.94 mg/dL). Coagulation factors were within normal limits. Viral serology was negative. Hepatic ultrasound demonstrated normal liver size with fatty texture. Liver biopsy was performed successfully and showed disordered architecture due to extensive perivenular necrosis with fibrin deposits and mostly mixed mononuclear inflammatory infiltrates. Occasional apoptotic bodies were seen. The preserved hepatocytes demonstrated nuclear pleomorphisim, occasional binucleation and rare mitoses. Portal spaces were expanded with mixed inflammatory infiltrate containing rare eosinophils. The native bile ducts were diminished in number, and small distorted ducts appeared at the periphery of portal spaces suggesting mild ductal proliferation. The patient recovered gradually with liver enzyme values returning to the normal range within 10 weeks. The patient was discharged from the hospital without sequelae. The calculated probability of dimethyl fumarate-induced significant hepatic toxicity was high (Naranjo scale score 7, at the minimum).
Conclusion: Dimethyl fumarate has been associated with a low rate of transient serum enzyme elevations during treatment, with only rare reports of suspected dimethyl fumarate-induced clinically significant liver injury. The presented case clearly indicates the high probability of dimethyl fumarate-induced significant hepatotoxicity. The liver biopsy revealed acute hepatitis with massive parenchymal necrosis, ductal injury, third zone changes and apoptotic transformation, which are consistent with drug-induced acute liver injury. It is advised to routinely monitor liver enzymes prior to and during dimethyl fumarate treatment. Acute significant hepatic injury should be emphasized as a potential severe adverse reaction in dimethyl fumarate medication information.

393. Iodoform medications may cause iodine toxicosis: two case reports

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Objective: Iodine is an essential oligoelement involved in the synthesis of thyroid hormones. Iodine is also used to promote antisepsis and iodoform medications release iodine and are commonly used for septic ulcers and surgery lesions. Few cases of iodine/iodoform toxicity due to systemic absorption from topical/dermal application have been reported [1,2]. We report two cases of neurologic impairment and transient hypothyroidism induced by excess systemic absorption of iodoform after prolonged and extensive medications.
Case series: Case 1. A 64-year-old male hospitalized for COVID-19 pneumonia, presented *Klebsiella pneumoniae* carbapenemase sepsis associated with decubitus ulcers, that were treated with iodoform gauze medication. After three medications, he developed diarrhoea, xerostomia and lethargy. Blood analysis showed renal impairment with creatinine 3.1 mg/dL and a total calcemia of 11 mg/dL. Suspecting iodine poisoning, urine and serum concentrations were performed and were respectively 14,517 μg/L and 2,400 μg/L. Free thyroxine (FT4) was 13.80 ng/L (normal 9.30-17.00), thyroid stimulating hormone (TSH) 6.160 mIU/L (normal 0.270-4.200). A few days later, he died from multiorgan failure. Case 2. A 56-year-old male was admitted to hospital for severe traumatic perianal injury. After surgery, he was stable and treated with iodoform gauze medications, but presented with acute inhibition of thyroid hormone synthesis (Wolff-Chaikoff effect) with TSH 10.500 mIU/L and FT4 16.70 ng/L. Urinary and serum iodine concentrations were 53,500 and 1,087 μg/L, respectively. The patient gradually recovered normal thyroid function after discontinuation of iodoform treatment.
Conclusion: Iodine/iodoform poisoning is an underestimated clinical event. Extensive surface and prolonged application are risk factors for developing toxicity. Thyroid function is efficiently regulated even with excessive iodine (Wolff-Chaikoff mechanism). However, in these patients, iodine/iodoform toxicity may be suspected when a new impairment occurs, including disturbance of

consciousness, diarrhoea, liver dysfunction, renal failure, and metabolic acidosis. Iodoform (CHI_3) is similar to chloroform ($CHCl_3$) in molecular structure and has a similar anaesthetic effect [1]. Moreover, it is lipid soluble and may easily pass the blood-brain barrier, causing headache, disorientation, delirium and coma. Urinary and serum iodine concentration can be useful in clinical practice to confirm and estimate the degree of toxicity; however, it seems that these values may be higher in iodine and lower in iodoform toxicity.

References

[1] Nakamura K, Inokuchi R, Fujita H, et al. Intoxication caused by iodoform gauze packing in necrotizing fasciitis. J Jpn Soc Intensive Care Med. 2011;18:629–631.
[2] D'Auria J, Lipson S, Garfield JM. Fatal iodine toxicity following surgical debridement of a hip wound: case report. J Trauma. 1990;30:353–5.

394. Fooled by adrenaline: a pyrogenic-like reaction during treatment of a common European viper bite

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Objective: Snake antivenoms have historically been reported to cause pyrogenic reactions and although once common, improvements in manufacturing processes have made this reaction exceedingly rare. Testing for pyrogenicity is now mandated by European regulatory authorities and in a review from 2017 including 2602 patients with European viper bites treated with modern antivenoms, no pyrogenic reactions were reported [1,2]. Furthermore, the Swedish Poison Centre (PC) has not recorded a single case of pyrogenic reaction after antivenom treatment for *Vipera berus* bites, despite more than 25 years of extensive use of ViperaTAb. We describe a case that was initially erroneously perceived as a first instance of this ancient complication in our practice.
Case report: A 29-year-old man was bitten on his right index finger by a common European adder (*Vipera berus*). He developed gastrointestinal symptoms, a swelling of the tongue and of the bitten limb that had spread to the wrist upon hospitalization two hours after the bite. An infusion of ViperaTAb (200 mg over 30 minutes) was started at three hours. During the infusion, the patient started shivering intensely and was described as "bouncing around" on his gurney. The PC was consulted by telephone and a pyrogenic reaction to the serum was suspected. However, the reaction subsided within an hour, the patient remained normothermic and normotensive and although his leukocyte count rose from 6 (on admission) to 20 x 10^9/L, his C-reactive protein (CRP) remained <5 μg/L and procalcitonin reached a modest peak of 0.65 μg/L. The initial diagnosis now seemed unlikely and it was recalled that an intramuscular injection of 0.5 mg adrenaline had been given for the tongue swelling and that the "bouncing" followed shortly thereafter. It was concluded that the adrenaline and not the antivenom had caused the reaction. The limb swelling progressed further and another infusion of ViperaTAb was given nine hours after the first without complications. A serum tryptase taken during the rigors was not elevated (4.6 μg/L).
Conclusion: Adrenaline is often used alongside antivenoms when treating toxic reactions to snakebites and, as this case demonstrates, can cause symptoms resembling a pyrogenic reaction if the dose is high enough.

References

[1] European Medicines Agency. EMA/CHMP/BWO/3354/1999. Guideline on production and quality control of animal immunoglobulins and immunosera for human use, 2016 [cited 20 October 2020]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-production-quality-control-animal-immunoglobulins-immunosera-human-use-revision-1_en.pdf
[2] Lamb T, de Harlo L, Lonati D, et al. Antivenom for European *Vipera* species envenoming. Clin Toxicol. 2017;55:557–68.

395. Symptomatic therapeutic errors in the elderly: a case study

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Objective: Therapeutic error (TE) is defined as any preventable medication event that may cause or lead to patient harm following inappropriate medication use. It includes taking the wrong dose, missing a dose, incorrect timing, administration to the wrong patient, administration of the wrong substance or via the wrong route [1]. The elderly, who take a large number of medications, are at greater risk. Our Poison Center contributes TE reports to the National Pharmacovigilance Network (NPN). Our objective was to characterise the exposures due to TE in elderly patients reported to PC.
Methods: We analysed all symptomatic cases due to TE reported to NPN by our PC from December 2017 to October 2020. All events involving patients older than 64 years were included. Data including clinical manifestations, type of error and patient characteristics were analysed.
Results: From 1380 symptomatic adverse drug reactions (ADR) reported to the NPN, 258 (18.7%) were due to TE in elderly patients. Females were more commonly involved (67.4%). Young elderly (65-74 years) represented 34.9%, while elderly (75-84 years) and ultra-elderly (85-99 years) patients were involved in 46.1% and 19.0%, respectively. TE were mainly related to accidental overdose (35.7%, n = 92), drug exchange (34.5%, n = 89), taking another patient's therapy (9.7%, n = 25) or misunderstanding medical prescription (7.0%, n = 18). The most frequent involved are psychotropic (66.3%) and cardiovascular medications (12.2%). The most represented active principle was clonazepam (5.0%, n = 16), followed by chloramine, quetiapine and tramadol, each representing 3.4% of the sample (n = 11). Tablets and drops where the formulation most commonly involved (49.7%, n = 159

and 34.1%, n = 109, respectively). Clinically severe TE occured in 219 patients (84.9%), but only two with life-threatening conditions. No fatal cases were registered. The most common symptoms were drowsiness (21.5%, n = 96), vomiting (8.5%, n = 38), nausea (7.0%, n = 31) and bradycardia (4.0%, n = 18). Follow-up was done 48 hours after TE, and patients had complete resolution (13.6%, n = 35) or improvement (77.1%, n = 199) of clinical conditions. One patient had not yet recovered, and 23 cases (8.9%) were lost at follow-up.
Conclusion: We noticed that young elderly and elderly were more prone to accidental overdose or exchange medication errors. Psychotropic and cardiac medications represented the most common agents in all groups. PC data are important to identify the most frequent TE. Close collaboration between healthcare professionals, pharmaceutical companies and consumers is important to reduce the risk of TE, especially in a vulnerable population such as the elderly.

Reference

[1] National Pharmacovigilance Network. Available from https://www.agenziafarmaco.gov.it/Farmacovigilanza/

396. Severe adverse effects after a second dose of paliperidone palmitate long-acting injectable administration: a case report

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Objective: Long-acting injectable paliperidone palmitate (PP-LAI) is an antipsychotic used to treat patients with poor adherence to medications. The long-acting effect of PP-LAI properties is due to a microcrystal drug formulation that maintains a therapeutic plasma concentration for 4 weeks. Only two single cases of persistent side effects are described in the medical literature [1,2]. The dosage regimen suggested by the manufacturer (deltoid IM injection) is 150 mg +100 mg (day 8) + 75 mg (one month after the second dose), then a monthly maintenance dose of 75 mg (range 25-150 mg dependent on patient response). We describe a case of PP-LAI-induced extrapyramidal symptoms (EPS) with measured paliperidone plasma concentrations.
Case report: A 37-year-old man with a history of severe psychiatric disorder (mental retardation and schizophrenia) previously treated with oral olanzapine and paliperidone without clinical response started PP-LAI. The patient received PP-LAI 150 mg (day 1) and 100 mg (day 8) without acute adverse events but he was admitted to the emergency department at day 10 due to worsening dyspnoea, hyperthermia (38.5 °C), severe EPS associated with agitation and mental confusion. His fever was successfully treated with antipyretics but he required pharmacological sedation and mechanical ventilation for a week. Biochemical results (including creatine kinase) were normal. During intensive care unit (ICU) stay, the clinical course was complicated by pneumonia (*Streptococcus pneumoniae*). Clinical manifestations slowly improved and biperiden (5 mg bid, IM) was started 15 days later with partial clinical response. The paliperidone plasma concentration measured at day 10 by liquid chromatography-tandem mass spectrometry (LC-MS/MS) was 89.1 μg/L (therapeutic range 20-60 μg/L).
Conclusion: EPS can occur despite correct administration of PP-LAI and are related to the serum concentration of paliperidone. Few clinical experiences are available in the medical literature, but the long-lasting property of this specific formulation can cause long-lasting and severe side effects. There may be predisposing factors (e.g., D_2-receptors occupancy). Identification of a D2-receptor disorder during evaluation could lead to identification of patients vulnerable to EPS. Clinical monitoring supported by paliperidone plasma concentrations during the first PP-LAI administrations could be useful to identify and prevent overdose, and to adjust the dosage regimen.

References

[1] Jang S, Woo J. Five month-persistent extrapyramidal symptoms following a single injection of paliperidone palmitate: a case report. Clin Psychopharmacol Neurosci. 2017;15:288–291.
[2] Omi T, Kanai K, Kiguchi T, et al. The possibility of the treatment for long-acting injectable antipsychotics induced severe side effects. Am J Emerg Med. 2017;35:1211.e1-1211.e2.

397. Soft capsules formulated with ethanol: unexpected disulfiram-ethanol reaction after one dosage of ciclosporin

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Objective: As solid ciclosporin is practically insoluble in water, its biological availability is limited. To increase this biological availability, some ciclosporin medicines are formulated as a soft capsule containing a solution of ciclosporin in anhydrous ethanol. We report an unexpected disulfiram-ethanol reaction (DER) after exposure to ciclosporin formulated as a soft capsule containing ethanol in a patient under disulfiram treatment.
Case report: A patient, treated for ethanol dependence with disulfiram, was prescribed ciclosporin, commercialised as Neoral-Sandimmun®, for a rheumatoid disease. After his first dosage, he presented with facial flushing, nausea and headache. The patient clearly recognised these symptoms as an initial stage of DER since he had suffered this before. His symptoms diminished gradually an hour later. Uncertain about the origin of the ethanol responsible for his DER, he consulted the Poison Centre.
Conclusion: It is common for liquid medicines like syrups and droplets to contain ethanol. However some drugs like ciclosporin or some food supplement can also contain ethanol even though they are formulated as soft capsules. One dosage of Neoral-Sandimmun® has equal mass amounts of ciclosporin and ethanol which results in a 12% (v/v) ethanol concentration in each soft capsule [1]. In this case, there was enough ethanol in the soft capsules with ciclosporin to provoked an unexpected initial stage of a DER. We would like to warn our colleagues, especially those working with alcoholics of the risks of a disulfiram-ethanol reaction with ethanol-containing medicines.

Reference

[1] Summary of product characteristics; Neoral-Sandimmun ® 100 mg soft capsules. N.V. Novartis Pharma, Vilvoorde, February 2020.

398. Effect of a 12-hour intravenous acetylcysteine (SNAP) regimen on the International Normalized Ratio (INR)

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Objective: Acetylcysteine can cause an isolated increase in the INR in the absence of paracetamol-induced hepatotoxicity [1]. We measured the effect of NAC on the INR in patients treated with a modified 2-bag 12-hour intravenous acetylcysteine (NAC) regimen ("SNAP").
Methods: The modified 12-hour "SNAP" regimen, consisting of intravenous NAC 100 mg/Kg over 2 hours, then 200 mg/Kg over 10 hours, was introduced in 2016 in two UK hospitals to treat all patients requiring NAC for paracetamol overdose. Those patients who had an isolated INR rise at the end of the 12-hour NAC infusion (INR >1.3, ALT ≤40) had an additional blood sample at least 24 hours post-ingestion prior to discharge if they completed the infusion less than 24 hours post-paracetamol ingestion.
Results: Overall 182/1813 (10%) of all patients treated with the SNAP regimen had an isolated INR rise at the end of the 12-hour infusion. Five patients taking anticoagulants were excluded. The median change in INR from admission to end-of-infusion was 0.3 (range −0.2 to 0.9). Of the remaining 177 patients, 34 received additional NAC treatment and 75 were discharged as they were more than 24 hours post-ingestion. None of the 75 patients who were discharged was readmitted within 7 days with acute liver injury; 68 patients did not receive additional NAC and had a repeat blood sample at least 24 hours post-ingestion. The median change in INR from end-of-infusion to the 24 hour post-ingestion sample was −0.2 (range −0.6 to 0.1). The INR was unchanged or decreased in 66/68 patients and increased from 1.4 to 1.5 in 2 patients. In all 68 patients, the ALT remained normal.
Conclusion: The effect of the SNAP acetylcysteine regimen on the INR should be taken into consideration when interpreting the end-of-infusion results. In patients with an isolated INR increase, unnecessary additional NAC treatment may be avoided by repeating the INR 4-6 hours later.

Reference

[1] Schmidt LE, Knudsen TT, Dalhoff K, et al. Effect of acetylcysteine on prothrombin index in paracetamol poisoning without hepatocellular injury. Lancet. 2002;360:1151–2.

399. Severe gasoline poisoning and its treatment. The autonomy of the lung response facing different pathogenic agents

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Objective: Aliphatic hydrocarbon poisoning whether by inhalation, ingestion or injection, is not frequently seen in the intensive care unit (ICU). We present a case of gasoline poisoning after a siphoning accident at the workplace that presents a near-lethal course and benefited from treatments that have been implemented for COVID-19 cases.
Case report: A 53-year-old male was admitted to the ICU after accidental gasoline exposure while attempting transfer of the liquid from one container to another by sucking with the mouth through a "tube" connected to the gasoline container. Paramedics were called due to a sudden loss of consciousness immediately after performing this manoeuvre. They proceeded to intubation and transfer the patient to hospital. Upon his arrival at the ICU, he presented severe acute kidney injury without other initial organ dysfunction. During the first hours he developed acute respiratory distress syndrome (ARDS) associated with chemical pneumonitis, distributive shock, mild metabolic hyperlactacidemic and hyperchloremic acidosis, severe hypokalaemia and hypoglycaemia and persistent severe fever. Norepinephrine, fluid replacement and ceftriaxone as prophylaxis for early ventilator-related pneumonia were initiated. A computerised tomography (CT) scan at day 5 showed lipoid pneumonia. With a progressive general worsening, on day 15 the patient was diagnosed by CT with necrotizing pneumonia. Antibiotic therapy was directed by the results from cultures. He required protective ventilation due to severe hypoxemia, with continuous neuromuscular blockage; nitric oxide and several prone sessions were needed. On day 7, high ARDS-dose corticoids were initiated (methylprednisolone 1 mg/Kg/d). During the following days he showed a slow respiratory improvement and hemodynamic stabilization. He finally received 15 days of neuromuscular blockage, 1 month of steroids and targeted antibiotic therapy with piperacillin/tazobactam and vancomycin, for 4 weeks and 2 weeks, respectively. Vasoactive support could be removed on day 22 and a CT control showed general improvement with persistence of ground glass images. Percutaneous tracheostomy took place on day 11. Eventually, the patient could be decannulated on day 30 and discharged to medical hospitalization on day 40. Follow up X-ray showed a persistent image of bilateral infiltrates consistent with fibrosis.
Conclusion: This case, which occurred at the time of the peak of the COVID-19 pandemic, reveals a common pattern of pulmonary response and its complications, showing a relative independence with respect to causal agents as disparate as an aspirated hydrocarbon or a virus, and that were treated in a similar way.

400. The health and blood aluminium concentrations in firefighters following the Alytus tyre recycling factory fire

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Objective: A large industrial fire at a tyre recycling factory in Alytus, Lithuania, lasted 10 days. A sample of firefighters who were exposed to harmful conditions were tested and examined for concentrations of metals and fire products, including

aluminium. The aim of the research was to evaluate the correlation of the health with blood aluminium concentrations in firefighters.
Methods: A retrospective study of hospital medical records of firefighters who visited the Toxicology Center during February-September 2020 was conducted. Information such as fire exposure time, age, symptoms/complaints, general health status and blood aluminium concentration 6 weeks and 6 months following exposure to the fire was collected and analysed. Data analysis was performed with IBM SPSS 22.0.
Results: All firefighters were male, aged 26 to 63-years-old (mean 43.7 ± 10.8 years). In all 6-week blood samples the concentration of aluminium were found to be increased, averaging 14.9 ± 5.2 μmol/L (highest concentration 25.2 μmol/L). In blood samples taken 6 months after the incident, the aluminium concentrations were significantly lowered ($p < 0.0001$), mean concentration 1.08 ± 0.65 μmol/L. However, in 93.1% of firefighters the blood concentration of aluminium remained above the normal range (>0.28 μmol/L) and in 6.9% remained clinically significantly elevated (>2.2 μmol/L). Exposure time and blood aluminium concentration had very weak positive correlation (Spearman coefficient 0.117) and it was statistically insignificant.
Conclusion: Even though the firefighters all had an increased concentration of aluminium (for some it was more than 11 times the normal concentration), in initial blood samples there were no significant clinical symptoms associated with aluminium toxicity. Therefore, no chelation therapy was administered. Considering all the patients continued their work as firefighters, an assumption can be made that the increase of aluminium concentration in blood is specific to this incident. However, in order to fully understand if aluminium concentrations are specific to the type of fire or firefighters daily work, a more detailed epidemiologic investigation is required.

401. A case of acute occupational exposure to sodium molybdate with determination of molybdenum concentration

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Objective: Molybdenum (Mo) does not exist naturally in the pure metallic form and, of the 5 oxidation states (2-6), the predominant species are Mo(IV) and Mo(VI). The majority of molybdenum is used in metallurgical applications, but sodium molybdate is an experimental chelating agent for Wilson's disease. Molybdenum elimination occurs via the kidney and is usually complete within several weeks [1]. Human toxicological data are mainly related to chronic exposure; acute exposure reports are lacking, particularly evaluation of plasma/urinary Mo concentration. We report a case of acute occupational exposure to sodium molybdate with related plasma and urine molybdenum concentrations.
Case report: A 36-year-old man was admitted to the emergency department (ED) following a work accident causing accidental ingestion of a sip of an industrial product containing sodium molybdate 10%. At admission he was asymptomatic. Due to the lack of clinical data about acute molybdenum exposure, he was hospitalized in order to monitor the possible development of clinical manifestations and/or biochemical alterations. Blood and urine molybdenum concentrations collected 2 hours after ingestion were 50 μg/L (reference range: 0.43-1.8 μg/L) and 630 μg/L (reference range: up to 116 μg/L), respectively. Despite these high Mo concentrations, the patient remained asymptomatic for 48 hours and biochemistry did not show alterations except for elevated total bilirubin (3.5 mg/dL). He was discharged well on day 3. Seven days later, plasma and urine Mo concentration were 2.5 μg/L and 73 μg/L, respectively. Considering these last results, no further molybdenum measurements were undertaken. At the last biochemistry evaluation 1 month after ingestion, bilirubin was within the normal range.
Conclusion: Molybdenum exposure is rare and occurs primarily as an occupational exposure. The few available data on its toxicity come mainly from animal studies and from a small number of reports of occupational and environmental chronic exposure that reported gout-like symptoms, hypertension and a possible decrease in testosterone concentrations. There are no reports of acute exposure. Our case, even if without clinical evidence of toxicity, is the first to evaluate Mo concentrations in blood and urine. This case needs to be supported by other reports but, due to the rarity of the event, it may be helpful for the clinician the management of similar cases.

Reference

[1] Barceloux DG. Molybdenum. J Toxicol Clin Toxicol. 1999;37:231–7. Erratum in: J Toxicol Clin Toxicol 2000;38:813.

402. Acute poisoning in Moscow during COVID-19 restrictive measures

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Objective: To identify the impact of COVID-19 restrictive measures on acute poisoning in Moscow.
Methods: Statistical analysis of hospitalizations to the Toxicological Department of the Sklifosovsky Research Institute for Emergency Medicine, Moscow in March-May 2020 compared to the same period in 2019.
Results: The number and gender composition of patients with poisoning did not differ significantly in the compared periods. In 2020, the number of people admitted aged 30-39 increased by 23%, while patients over 50 decreased by 7%. In 2020, the

Table 1. Acute poisoning in Moscow in March-May 2020 compared to March-May 2019.

			Number / percentage of poisoning with toxicant (n/%)				
Year	No. of persons	Gender M/F	Medicines	Narcotics	Alcohol	Chlorine	Other
2019	786	413/373	377 (48%)	144 (18.3%)	23 (2.9%)	7 (0.9%)	135 (29.9%)
2020	774	437/337	294 (38%)	181 (23.4%)	92 (11.9%)	13 (1.7%)	194 (25.0%)

Table 1. Cases of exposures to alcohol-based hand sanitisers during March-July 2020 and 2019.

Parameter	Year		Difference
Age (years)	**2020**	**2019**	p = 0.795512
0-15	102	17	
≥16	28	4	
Circumstances			p = 0.042663
Accidental	122	17	
Other / Unknown	8	4	
Route of exposure			p = 0.697406
Ingestion	116	21	
Other / Unknown	15	2	
Poisoning Severity Score			p = 0.533369
None	106	15	
Minor	21	5	
Unknown	3	1	

frequency of poisoning caused by medicines decreased, with sedatives and antidepressants prevailing. There were 46 cases of overdose with NSAIDs, paracetamol, antibiotics and antiviral drugs, due to attempts of self-treatment against COVID-19. Cases of narcotic poisoning increased. Their significant growth is a result of consumption of designer drugs (mephedrone, 4-methcathinone, MDMA, α-PVP) and combinations of different narcotics. In 2020 the number of poisoning cases caused by drugs (pregabalin, baclofen, others) taken together with other narcotics and/or alcohol to overcome "withdrawal syndrome" decreased 2.4 times compared to 2019. In 2020, the number of patients with severe poisoning caused by alcohol increased 4 times, and the number of people with other forms of poisoning hospitalized with alcohol intoxication increased 2.7 times. This is probably due to the myth of a reduced risk of COVID-19 infection through alcohol consumption, and high stress levels. Additionally, twice as many household poisoning cases caused by chlorine vapor occurred, attributable to a frequent improper use of disinfectants.

Conclusion: The introduction of COVID-19 restrictive measures affected the structure of poisoning in Moscow. In most of the reported cases, poisoning with antidepressants and sedatives, as well as medications used for colds and viral diseases, was detected. There has been a significant increase in the number of severe alcohol and drug poisoning, especially cases involving their combinations.

403. Unintended consequences of public health measures: exposures to alcohol-based hand sanitisers during the COVID-19 pandemic 2020

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Objective: Hand hygiene, using soap and water or an alcohol-based hand sanitiser (AHS), is an important measure to slow the spread of COVID-19 and there was rapid growth in the number of AHS products placed on the market in March/April 2020. This study was performed to see if there were changes in the number and type of calls to the National Poisons Information Centre (NPIC) about AHS during the early months of the COVID-19 pandemic.

Methods: This was a retrospective observational study using routine data collected by the NPIC. We identified all enquiries about human cases of exposure to AHS between March and July inclusive, in 2020 and 2019. We excluded calls about patients exposed to alcohol-free hand sanitisers, animal exposures and requests for statistics. We extracted data on the patient's age, circumstances of exposure, routes of exposure and Poisoning Severity Score (PSS) at the time of the call. Cases in 2020 were compared to those during the same period in 2019 using the chi-square test.

Results: The NPIC answered 134 calls about 130 patients exposed to AHS during March-July 2020 (2.6% of 5165 calls) compared to 21 calls and cases during the same period in 2019 (0.4% of 4844 calls), a significant increase ($p < 0.00001$). There were no significant differences in patient age, circumstances of exposure, route of exposure or PSS during the two periods (Table 1). The majority of patients in both periods analysed were children, exposed accidentally, had ingested the product and were asymptomatic.

Conclusion: There was a five-fold increase in calls about patients exposed to AHS during March-July 2020 compared to the same months in 2019. There were no differences in patient age, route of exposure or PSS during the two time periods.

404. Increased exposures to alcohol-based hand sanitizers reported by an Italian Poison Center during the COVID-19 pandemic

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Objective: During the COVID-19 pandemic, public health messaging emphasized the use of hand sanitizer products to reduce SARS-CoV-2 exposure, the agent responsible for COVID-19. Our aim was to analyse these exposures and compare to the same period in 2019.

Methods: We used descriptive statistics to analyse Milan Poison Center exposures to alcohol-based hand sanitizers for the period 1 January 2019 to 30 September 2019 to the same period in 2020.

Results: During the 2020 study period a total of 474 exposures were collected and in the same period in 2019 there were 211 exposures. During the COVID-19 pandemic in 2020 an increase in exposures of 124.6% compared to 2019 was observed. In relation to the year 2020, the age group distribution was: < 1 year 5.5% (n = 26), ≥ 1 < 5 years 49.6% (n = 235), ≥ 5 < 18 years 6.5% (n = 31); ≥ 18 years 50.4% (n = 239) and age unknown 7% (n = 33). The circumstance of exposure was unintentional for 77.2% (366 cases), intentional 2.1% (n = 10), transfer from original container 5.9% (n = 28), other 13.3% (n = 63), and therapeutic error instead of medicament 1.5% (n = 7). In one of the therapeutic error cases, the hand sanitizer was mistaken for vitamins and was administered to a baby of one week and in a second case a man of 78 years mistook the hand sanitizer for ophthalmic gel and presented pain and ocular inflammation. The oral route was involved in 79% of cases, ocular in 4.9%, skin in 3.8%, and multiple routes in 12.3%. Most exposures were managed at home (86.5%) and 13.5% in hospital. The most frequently reported clinical effects were nausea, vomiting, diarrhea, heartburn, pharyngodynia, ocular pain and inflammation. Overall, 377 patients (79.5%) had no effects, 79 had minor effects (16.7%) and 18 (3.8%) had moderate effects.

Conclusion: The public health messaging advocating the use of these products was necessary to mitigate COVID-19 health effects. Messaging should also emphasize proper use of these products. The increased availability at home was temporally associated with an increase in exposures. The analysis of data reveals the role of poison control centers in the identification of risk factors for prevention and for reducing unnecessary emergency medical attention.

405. Pediatric eye injuries related to public location of alcohol-based hand sanitizers during the first pandemic COVID-19 context: French Poison Control Centers data

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Objective: To fight against the transmission of SARS-CoV-2, alcohol-based hand sanitizers (ABHS) were widely available in public places. We aim to describe pediatric eye exposures to ABHS occurring in a public location.

Methods: We reviewed all cases of ocular exposure to chemical agents in children under 18 using data from the French National Database of Poisonings (FNDP) between 1 April 2020 and 24 August 2020, as well as those occurring in the same period in 2019. We further analyzed ABHS exposures occurring in a public location.

Results: In the FNDP for the two study periods, ABHS were involved in 33 cases in 2019 (1.3% of eye chemical exposure, mean 3.4 ± 3.8 years old) and in 232 cases in 2020 (9.9%, 4.5 ± 3.5 years old). Cases occurring in a public location represent 0% in 2019 and regularly increased in 2020, from 16.4% of ABHS in May to 52.4% in August. Most of the cases were of low or no severity (n = 269, 97.8%). Symptoms reported were pain, tingling sensation and conjunctival hyperemia. Six cases of moderate severity with limited keratitis were also reported.

Conclusion: In order to maintain good public compliance with hand disinfection, health authorities must ensure the safe use of ABHS, for example, exercise caution in positioning and use of

Table 1. Comparison of poisoning cases in the first 6 months of 2019 and 2020 (abstract 406).

	2019 cases		2020 cases		
	n	(%)	n	(%)	p
ED total cases	72745		52511		
Poisoning cases	455	0.6	376	0.7	ns
Male	244	53.6	198	52.7	ns
Female	211	46.4	178	47.3	ns
Median age (years)	36.4		36.3		ns
Intentionality					
Recreational use	228	50.1	208	55.3	ns
Suicidal intent	150	33	113	30.1	ns
Accidental exposure	52	11.4	36	9.6	ns
Substances involved					
Benzodiazepines	116	25.5	93	24.7	ns
Antidepressants	28	6.2	33	6.9	ns
Other medicine including psychoactive drugs	15	3.3	24	6.4	<0.05
Non-steroidal anti-inflammatory drugs (NSAIDs)	17	3.7	9	2.4	ns
Paracetamol	16	3.5	12	3.2	ns
Ethanol	207	45.5	169	44.9	ns
Cannabis	54	11.9	64	17	<0.05
Amphetamines	29	6.4	26	0.9	ns
Cocaine	27	5.9	24	6.4	ns
Opiates	5	1.1	3	0.8	ns
Carbon monoxide	11	2.4	3	0.8	ns
Irritant gases	5	1.1	4	1.1	ns
Caustics	14	3.1	6	1.6	ns
Solvents	8	1.8	4	1.1	ns
Pesticides	6	1.3	1	0.3	<0.05
Outcome					
Hospital admission 24 h	175	38.5	156	41.5	ns
ICU admission	14	3.1	9	2.4	ns
Death	2	0.4	3	0.8	ns

automatic devices dispensing ABHS in public places, and provide immediate care advice.

406. Has the COVID-19 pandemic changed the pattern of poisoning cases attending Emergency Departments?

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Objective: The current COVID-19 pandemic has impacted emergency departments (EDs) heavily. The rise of infectious cases has seen a decrease in other pathologies usually attending the ED. This was particularly intense during lockdown periods. We aimed to verify the way this change of pattern has included poisoned patients and we compared the poisoning cases attending our ED during the first 6 months of the year in 2019 and 2020 looking at frequency, cause of poisoning and severity.
Methods: We analysed the main characteristics of these cases as recorded in the Unit of Clinical Toxicology database gathered prospectively on a daily basis. The evaluated data were demographics, intentionality of poisoning, main agents, severity and evolution. We have also compared the relative rate of poisoning cases reported compared to total ED cases over the same period.
Results: There were 72,745 total ED cases in 2019 and 52,511 in the same period in 2020, including 455 and 376 poisoning cases, respectively (Table 1). The only significant changes were an increase in cases involving other medicines and a decrease in pesticide cases.
Conclusion: The great sociologic changes affecting the whole population in terms of current habits and behaviour should *a priori* be expected to produce some changes in the pattern of poisoning as seen at the ED. These changes could be anticipated to take into account the voluntary origin of most of them as suicidal or recreational events. Nevertheless, only very minor differences were observed in relation to some of the etiologic agents, and no differences at all in terms of demographics, intentionality or severity.

407. The only thing we have to fear is fear itself: inadvertent disopyramide toxicity during the COVID-19 pandemic

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Objective: Disopyramide is a Class 1a antidysrhythmic used to treat ventricular and atrial arrhythmias. Its side effects include antimuscarinic symptoms, sodium channel blockade, QT prolongation, negative cardiac inotropy, and hypoglcyemia. Disopyramide is the most likely of the Class IA antidysrhythmic agents to cause congestive heart failure [1]. Disopyramide is 70% renally eliminated and requires a dosage reduction in renal dysfunction. We describe an elderly patient prescribed oral disopyramide as an outpatient due to the concern of hospitalization and COVID-19 exposure who developed toxicity.
Case report: A 96-year-old female with a past medical history of atrial fibrillation, hypertension, and chronic diastolic heart failure, was diagnosed as an outpatient with paroxysmal atrial fibrillation and prescribed oral disopyramide 100 mg every 6 hours to avoid hospitalization. Four days later she presented with lethargy, alteration in mental status (alert to person only), antimuscarinic symptoms (hypoactive bowel sounds, urinary retention, dry mucous membranes), and bradycardia with evidence of sodium channel blockade and QT prolongation on electrocardiogram (ECG). Initial vital signs were: BP 106/69 mmHg, heart rate 58 bpm, respiratory rate 25 bpm, oxygen saturations 88% (room air), and temperature 35.6 °C. Labs was remarkable for potassium 6.5 mmol/L, bicarbonate 9 mmol/L, BUN 81 mmol/L, creatinine 247.6 μmol/L (baseline 106.1 μmol/L), glucose 2.6 mmol/L, pH 7.04, PCO_2 50 mmHg, and lactate 12.4 mmol/L. She was emergently treated with 100 mEq sodium bicarbonate, 2 g calcium gluconate, insulin, and 50% dextrose. Her initial ECG showed a QRS 160 msec which narrowed to 126 msec. She was admitted to the cardiac intensive care unit where she required pressor support with norepinephrine and dopamine for 2 days. Broad-spectrum antibiotics were also administered. Hemodialysis was attempted for hyperkalemia and elevated lactate, but was stopped due to hypotension. Repeat calcium gluconate (2 g) was administered with a bicarbonate infusion. She was discharged home after a 15-day hospitalization at baseline functional status with normalization in electrolytes and creatinine. Her initial disopyramide concentration was 21.83 μmol/L (5.89-14.73 μmol/L reported range).
Conclusion: Our patient developed significant disopyramide toxicity after an attempt to treat her atrial fibrillation at home to avoid hospitalization due to her fear of COVID-19. Outpatient prescribing of disopyramide is risky because of prominent side effects and dose reduction required in renal dysfunction. Patients with critical illness, despite the COVID-19 pandemic, should be encouraged to come to the emergency department.

Reference

[1] Pfisterer M. Negative inotropic effects of antiarrhythmic drugs: a clinical point of view. J Cardiovasc Pharmacol. 1991;17Suppl 6: S44–S7.

408. Nicotine does not affect SARS-CoV-2 in-host viral kinetics in a modeling and simulation study

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Objective: A potential protective effect of smoking on coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been reported [1]. One of the postulated hypotheses suggested SARS-CoV-2 as a nicotinic agent, interacting with the alpha7-nicotinic receptor (α7-nAChR) [2], thus suggesting a protective effect of nicotine by competitive binding to α7-nAChR. With this modeling and simulation study, we aimed to investigate this hypothesis by exploring the influence of nicotine action and timing of interventions on key parameters of viral kinetics (peak load, duration of positivity, and total viral exposure (measured by area under the curve)).
Methods: We created viral kinetics models driven by simulated pharmacokinetic profiles of nicotine. Different dose regimens of nicotine transdermal patches were simulated: 21 mg, 14 mg and 7 mg, for 1, 3 or 5 days. Daily nicotine dosing was modelled with 8 h intervals between applications. Nicotine's half-maximal effective concentration (EC_{50}) to activate α7-nAChR (125 μM) [3] was entered as an effect on the reduction of cellular infection rate. We evaluated treatment initiation 1, 3 or 5 days before inoculation, on presentation, on positivity (5.4 days post infection, dpi) in reverse transcriptase polymerase chain reaction (RT-PCR), and on viral peak load (10.2 dpi).
Results: Total viral exposure was 12'003 days*log(copies/mL) for untreated patients. Nicotine 21 mg patch for 3 or 5 days administered before infection or on exposure reduced total viral exposure (11'996 days*log(copies/mL)), similar to the 14 mg patch (11'998 days*log(copies/mL)). Other treatments had no appreciable effect on peak viral load, duration of positivity or exposure.
Conclusion: Our results based on a viral kinetics model and assuming a SARS-CoV-2 interaction over α7-nAChR did not indicate a protective effect of transdermal nicotine application. If smoking has a protective effect on SARs-CoV-2 infection, it may be due to nicotine influencing viral-in-host kinetics through other mechanisms, such as modulation of the angiotensin-converting enzyme 2 (ACE2) receptor or the host's autonomic nervous system response. The effects might also be mediated by non-nicotine tobacco components or other confounding factors.

References

[1] Farsalinos K, Barbouni A, Niaura R. Systematic review of the prevalence of current smoking among hospitalized COVID-19 patients in China: could nicotine be a therapeutic option? Intern Emerg Med. 2020;15:845–852.
[2] Changeux JP, Amoura Z, Rey FA, et al. A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications. C R Biol. 2020;343(1):33–39.
[3] Fu XW, Lindstrom J, Spindel ER. Nicotine activates and up-regulates nicotinic acetylcholine receptors in bronchial epithelial cells. Am J Respir Cell Mol Biol. 2009;41:93–9.

409. A human exposure to chlorine dioxide solution … not the solution

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Objective: Viruses have caused many epidemics throughout history. The novel coronavirus SARS-CoV-2 is the latest, and initially no clinically approved drugs were available for the management of infection. As a result, many "miraculous remedies" have been promoted [1], including chlorine dioxide solution. The FDA has warned consumers not to purchase or drink chlorine dioxide products sold as medical treatments [2]. We present a case of a patient who decided to face coronavirus by drinking chlorine dioxide solution and attended in our emergency department.
Case report: A 57-year-old male presented due to generalized bruising on the extremities, chest and back. He also had asthenia, anorexia, back pain and thigh pain. No external bleeding was reported. He reported that he had been taking a chlorine dioxide solution (20-30 ppm) daily for a month, as a preventive treatment for COVID-19. His blood pressure was 136/71 mmHg and heart rate 59 beats/min. Blood tests evidenced a severe thrombocytopenia (2 x 10^9/L platelets) with no anemia or leukopenia (haemoglobin 14.4 g/dL, white cell count 7.3 x 10^9/L). Other coagulation parameters were normal (prothrombin time, activated partial thromboplastin time). Two packs of platelets were transfused and he was admitted to the hematology service for further investigation. A bone marrow aspirate (which showed megakaryocytic hypoplasia), autoimmunity study, and abdominal ultrasound were performed. His platelet count improved (40000/μL) without drug treatment after discontinuation of chlorine dioxide. He was discharged after 5 days with the diagnosis of possible hematological toxicity (megakaryotic hypoplasia) from chlorine dioxide.
Conclusion: During the global COVID-19 pandemic, the oral consumption of chlorine dioxide solutions has been promoted through social media. It is fraudulently claimed to treat or prevent COVID-19. Chlorine dioxide, a strong oxidant, can inhibit or destroy microbes. Studies have investigated the application of chlorine dioxide in numerous fields such as water or wastewater treatment, environment and food disinfection, and medicine, however, the oral consumption of such antimicrobial solutions may be associated with harm related to the toxicity of the solutions themselves. Hematological toxicity (hemolytic anemia) has been described in patients with chronic use of chlorine dioxide in addition to other severe side effects such as QT prolongation or methemoglobinemia.

References

[1] Bramstedt KA. Unicorn Poo and Blessed Waters: COVID-19 Quackery and FDA Warning Letters. Ther Innov Regul Sci. 2021; 55:239–244.
[2] Food and Drug Administration (FDA). Coronavirus (COVID-19) Update: FDA Warns Seller Marketing Dangerous Chlorine Dioxide Products that Claim to Treat or Prevent COVID-19 [cited 15 November 2020]. Available from https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-warns-seller-marketing-dangerous-chlorine-dioxide-products-claim

410. Changes in the epidemiological profile of poisonings during COVID-19: differences between the first half of 2019 and 2020

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Objective: The COVID-19 pandemic has changed the epidemiological profile of acute poisonings, due to social changes related to preventive measures for protection against SARS-CoV-2 [1]. The purpose of this analysis is to compare the changes in the

epidemiological characteristics of acute poisonings between the first half of 2019 and 2020.
Methods: A retrospective study analyzing the data from the Register for poisonings, of the Poison Information Center, University Clinic of Toxicology, Skopje, Macedonia.
Results: During the first half of 2020, a total of 564 cases of acute poisoning were registered presenting a decrease of 23.7% compared to the same period in 2019. The monthly percentage distribution of patients in the first half of 2020 showed more patients in January and February, and a decrease in the remaining 4 months, which coincided with the onset of the COVID-19 pandemic. The lowest prevalence was registered in March and April with a percentage decrease (23.6% and 24.1%, respectively), when quarantine measures were introduced in Macedonia. Although there was no significant difference in out/inpatient treatment groups between 2019 and 2020 year ($X^2 = 0.605$, df $=1$, $P = 0.437$), in April 2020, during quarantine, the percentage difference between inpatients and outpatients was the lowest (6%) of all months in 2019 and 2020. The distribution of poisonings by motive (suicidal, abuse and accidental) did not differ significantly between the first half of the last 2 years ($X^2 = 0.178$, df $=2$, $P = 0.915$). The percentage of ethanol abuse, medicines and mushroom poisoning cases was reduced in 2020 compared to 2019 by 2.2%, 7.4% and 79.3%, respectively. In contrast, psychoactive substance cases increased by 51.5% in the first half of 2020 compared to the first half of 2019. In the group of recreational drug abuse cases, the largest increase was observed in heroin (141.2%) and methadone (125.1%) overdose. For chemicals, there was a large increase in cases involving disinfectants (681.0%) in 2020. There was no change in the case fatality ratio of total (1.8%) and hospitalized patients (4.8%) between 2019 and 2020.
Conclusion: The first half of 2020 compared to the same period in 2019 was characterized by an increase in poisonings with disinfectants and psychoactive substances. The decrease in the total number of poisonings, with the largest decrease in the quarantine months, stress the need to examine family dynamics and communication as a social key to reducing the number of poisonings.

Reference

[1] Chang A, Schnall AH, Law R, et al. Cleaning and disinfectant chemical exposures and temporal associations with COVID-19 – National Poison Data System, United States, January 1, 2020-March 31, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:496–498.

411. Multiple factors in a COVID-19 patient leading to an elevated 5-oxoproline as a cause of high-anion gap metabolic acidosis: a case report

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Objective: High anion gap metabolic acidosis (HAGMA) is one of the most common metabolic derangements seen in critical care patients. With this report we want to raise awareness of the rare, but clinically important HAGMA due to elevated 5-oxoproline caused by concomitant therapy with acetaminophen and flucloxacillin in a patient with a confirmed COVID-19 infection.
Case report: A 69-year old malnourished patient was referred to the emergency department due to complaints of lower back pain, malaise and laboratory evidence of inflammation. He was recently diagnosed with mitral valve endocarditis due to *Staphylococcus aureus* for which he was treated with flucloxacillin. Positron emission tomography – computed tomography (PET/CT) confirmed spondylodiscitis. Acetaminophen was started for pain relief. At admission, screening for COVID-19 with polymerase chain reaction (PCR) was positive and chest CT showed small ground glass infiltrations. On the rehabilitation ward, 21 days after his initial presentation, the patient became confused accompanied by abdominal pain and vomiting. Laboratory work-up showed a metabolic acidosis with respiratory compensation (pH 7.31, pCO_2 18.6 mmHg, pO_2 104.5 mmHg, bicarbonate 9.1 mmol/L, lactate 3.2 mmol/L) and a high anion gap (17 mmol/L). Glucose was normal, ethanol was negative and there was no ketonuria. Since the patient received flucloxacillin and acetaminophen, which are known causes of elevated 5-oxoproline, this was determined with gas chromatography-mass spectrometry (GC/MS) revealing a strongly elevated serum and urine 5-oxoproline of 945.7 mg/L and 7.54 mg/mg creatinine, respectively. Acetaminophen was discontinued and the patient was treated with piperacillin/tazobactam and the HAGMA resolved.
Conclusion: Although it is uncommon, simultaneous treatment with acetaminophen and flucloxacillin can lead to glutathione depletion in the γ-glutamyl cycle causing accumulation of 5-oxoproline. Other important elements which possibly contributed to higher 5-oxoproline concentrations in our case are malnutrition, vitamin B832 deficiency in the past, diabetes mellitus, chronic inflammation and a COVID-19 infection [1]. It has been suggested that glutathione deficiency is associated with higher morbidity and mortality in COVID-19 patients [2]. With this case report we wanted to raise awareness of multiple risk factors contributing to an elevated 5-oxoproline as a cause of HAGMA in a COVID-19 patient.

References

[1] Berbee JK, Lammers LA, Krediet CTP, et al. Metabolic acidosis caused by concomitant use of paracetamol (acetaminophen) and flucloxacillin? A case report and a retrospective study. Eur J Clin Pharmacol. 2017;73:1459–1465.
[2] Polonikov A. Endogenous deficiency of glutathione as the most likely cause of serious manifestations and death in COVID-19 patients. ACS Infect Dis. 2020;6:1558–1562.

412. An unsolved mystery: idiopathic thallium exposure resulting in clinically significant toxic effects

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Objective: Thallium rodenticide was banned in the US in 1972 but poisoning cases persist due to suicide, homicide, herbal product contamination, depilatories, and illicit drug adulteration. We present a report of a thallium exposure resulting in significant toxicity.

Case report: A 41-year-old male with a history of juvenile myoclonic epilepsy on divalproex sodium, amlodipine, gabapentin and hydrocodone/acetaminophen presented with generalized weakness, difficulty ambulating, vague gastrointestinal symptoms, and progressive distal paresthesias. Diagnosed with atypical Guillain-Barré syndrome he received IV immunoglobulin (IVIG) and corticosteroids and was discharged to a rehabilitation facility. He was re-admitted with visual and auditory hallucinations, disorientation, memory deficiencies, encephalopathy, seizures, and worsening neuropathy with four limb weakness. He was given IVIG and corticosteroids. Magnetic resonance imaging (MRI) of brain and spine were unremarkable. Electromyography-nerve conduction velocity studies showed progression of subacute distal motor neuropathy greater than sensory axonal peripheral neuropathy. He also developed alopecia and a serum thallium concentration was sent (Table 1). Family, social, and occupational history were unremarkable. Vital signs were blood pressure 141/93 mmHg; heart rate 96 bpm; respiratory rate 16 breaths/min; oxygen saturation 97% (room air); temperature 36.4 °C. Physical examination was remarkable for encephalopathy and bradykinesis with visual hallucinations, short-term memory deficit, tremors and profound weakness with areflexia, and painful hyperesthesias. A comprehensive metabolic panel and initial heavy metal screen were unremarkable with normal thyroid testing. He received multi-dose activated charcoal, and Prussian blue (3 g 8 hourly via a nasogastric tube) over 3 weeks until concentration of thallium were <20 ng/mL. He was hospitalized for 3.5 months then transferred for rehabilitation for residual motor weakness. He had total body alopecia. The source of thallium remains undetermined.

Table 1. Serum and urine thallium concentrations in a patient with pronounced effects. The source of thallium was unknown.

Date	Serum thallium (ng/mL)	Urine thallium (μg/L)
10 August	158	–
12 August	197	>800
13 August	103	727
14 August	83	413
15 August	62	>800
16 August	53	–
17 August	37	177
20 August	22	33
22 August	20	34

Conclusion: This is a case involving thallium exposure of unknown etiology resulting in elevated serum concentrations with pronounced clinical toxicity. It remains an open investigation.

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