CLINICAL TOXICOLOGY
2023, VOL. 61, NO. S1, 1–129
https://doi.org/10.1080/15563650.2023.2192024

Taylor & Francis
Taylor & Francis Group



# 43rd International Congress of the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT), 23–26 May 2023, Palma de Mallorca, Spain

## 1. Postgraduate Diploma in Medical Toxicology: a first for Africa

Catharina E. Du Plessis and Carine J. Marks
Stellenbosch University, Cape Town, South Africa

**Objective:** There is currently a lack of trained staff that can deal with poisonings relevant to the African continent. To this end, a Postgraduate Diploma in Medical Toxicology was registered at Stellenbosch University, with the aim of providing training for students from South Africa, as well as other African countries. This course is the first of its kind in Africa. The 18-month programme is offered through a hybrid model. The programme also has a formal synchronous online week, and a face-to-face lecture week in the second year. Sixty topics relevant to poisonings on the African continent [1] are presented through an online platform to ensure easy accessibility. Assessment includes weekly quizzes, assignments, reflections, written examination, as well as case simulations. The course was launched in January 2021 with a group of 20 students from diverse backgrounds, including medical professionals, chemists, stakeholders from the agricultural industry, and academia. Three students were from outside South Africa.
**Methods:** Students were asked to give feedback on the course. Feedback topics included their reasons for taking the course, what worked for them and what did not, and whether they would recommend the course to others.
**Results:** Nineteen students completed the course. Most of the students' motivation was to broaden their knowledge and to improve patient care. Overall, students felt that the content had been diverse, with topics relevant to a wide range of backgrounds. A highlight for students was the contact week, as they felt that they were able to learn from one another as a multidisciplinary group. Some constructive criticism of the course was that assignments and weekly reflections took up too much time. Other students suggested more frequent examinations, for example, one presented after each module. The overall feedback regarding the course was positive, with most students remarking that they would recommend others taking it. One student remarked: "I realized Africa in general has a need for Medical Toxicology to give its people advice, information and to guide them."
**Conclusion:** The course succeeded in its aim to provide training in Medical Toxicology for students from South Africa and other African countries. Its success was gauged through the positive student representation, as well as overwhelmingly positive student feedback.

### Reference

[1] Marks C, Louw A, Couper I. Core competencies required by toxicology graduates in order to function effectively in a Poisons Information Centre: a Delphi study. Afr J Emerg Med. 2020;10:173–180.

## 2. Don't shoot the messenger: an outbreak of lead poisoning at a UK firing range

Aamna Warsi[a], Bryce Clark[a], Christopher Yemm[a], Aleha Khan[b], Nicola Barlow[b], Neelsuraj Patel[a], Mark Pucci[a], Sally M. Bradberry[a] and Muhammad E. M. O. Elamin[a]
[a]West Midlands Poisons Unit, City Hospital, Birmingham, United Kingdom; [b]Trace Elements Laboratory, Black Country Pathology Services, Sandwell General Hospital, Sandwell, United Kingdom

**Objective:** Lead exposure from discharged lead dust is a recognised risk of firearm use, handling ammunition and visiting shooting ranges [1]. We report a lead poisoning outbreak amongst staff and their close contacts at a UK indoor 24 metre shooting range.
**Case series:** In June 2022, a 66-year-old shooting range officer presented to hospital with a 3-month history of fatigue, constipation, and abdominal pains. He was found to have a blood lead concentration (BLC) of 9.94 μmol/L (205.76 μg/dL). Subsequently, a total of 59 patients, aged between 6 months and 78 years, were tested for BLC following exposure at the firing range or via close contacts. The highest BLC at presentation was 11.71 μmol/L (242.40 μg/dL). The median BLC of personnel working at the range ($n = 25$) was 2.40 μmol/L (49.68 μg/dL), and for contacts and service users ($n = 34$) was 0.14 μmol/L (2.90 μg/dL). Of the eighteen patients assessed by a clinical toxicologist, only nine reported symptoms at presentation, none of which included encephalopathy or major neurological deficit. Thirteen patients with BLC more than 2.4 μmol/L (49.68 μg/dL) received lead chelation therapy. Two patients, both aged 17, were treated at lower BLCs of 2.2 μmol/L (45.54 μg/dL) and 2.02 μmol/L (41.81 μg/dL). Of the 15 patients treated with chelation therapy, complete data were obtained for 14. Five patients received oral succimer (dimercaptosuccinic acid, DMSA) 30 mg/kg/day for five days; nine patients received intravenous sodium calcium edetate 75 mg/kg/day for five days and one patient received a split course of oral succimer and sodium calcium edetate due to acute shortage of

chelating agent. Seven patients received a second course of chelation therapy (six received oral succimer and one received sodium calcium edetate). Two patients will require a third chelation round. Optimal treatment of the patients was limited by substantial shortages of chelating agent stock supply.
**Conclusion:** Though previously reported internationally, this is the first recorded lead poisoning outbreak at a UK indoor firing range. This incident highlights the importance of regulation of lead both occupationally and recreationally. It reinforces the importance of considering lead exposure in patients presenting with vague symptoms following work at or use of firing ranges. This case series also reflects the challenges presented by limited drug stocks in management of mass exposure incidents.

## Reference

[1] Laidlaw MA, Filippelli G, Mielke H, et al. Lead exposure at firing ranges-a review. Environ Health. 2017;16:34.

# 3. Inadvertent instillation of electronic cigarette liquid into the eyes

Eleri Thomas[a], Sally M. Bradberry[b], Euan A. Sandilands[c], Ruben H. K. Thanacoody[d] and Laurence A. Gray[a]

[a]National Poisons Information Service, Cardiff, United Kingdom; [b]National Poisons Information Service, Birmingham, United Kingdom; [c]National Poisons Information Service, Edinburgh, United Kingdom; [d]National Poisons Information Service, Newcastle, United Kingdom

**Objective:** Electronic cigarette liquids are used to replenish e-cigarette devices. They are presented in small, 10–15 mL bottles, compromising screw cap lids and dropper style tips for administration into e-cigarette reservoirs. Products typically contain variable nicotine concentrations, up to 20 mg/L, vegetable glycerine and propylene glycol. These products could be administered inadvertently as pharmaceutical eye drops, owing to similarities of design and size.
**Methods:** Enquiries relating to the accidental administration of e-cigarette liquid into the eyes received by the UK NPIS between 1 April 2007 and 31 March 2021 were analysed retrospectively. Enquiries were evaluated to consider trends and patterns of exposure, features and outcomes.
**Results:** The UK NPIS received a total of 139 enquiries involving acute ocular exposure to e-cigarette liquids. The highest number of calls ($n = 77$, 58%) were received between 2015/2016 and 2018/2019. Forty-six percent ($n = 64$) involved ocular administration following product misidentification. Documented reasons for error include ocular dispensation following parental error ($n = 4$), self-administration when the solution was "mistaken for hay fever drops" ($n = 2$) and identification error by visually impaired patients ($n = 2$). Enquiries peaked in June (14%, $n = 19$) and September (12%, $n = 16$), with total average across the year of 8% ($n = 11$). Fourteen percent more female patients ($n = 79$) administered solutions into their eyes compared with males ($n = 60$). The most common age/gender groups were 50–59-year-old females (14%) and 20–29-year-old males (13%). In children and adolescents, 9% of enquiries occurred in those aged 0-9-years, and 6% in 10 to 19-year-olds. In adults, 23% occurred in 20–29-year-old patients. Thirteen percent involved patients aged 30–39 and 40–49-years-old, 19% in 50–59-year-olds, 6% in 60–69-year-olds, 4% in 70–79-year-olds, 3% in 80–89-year-olds; 5% were documented as adults/unknown. Thirty cases (21%) remained asymptomatic. Common reported local features included eye pain (32%), conjunctivitis (23%) and eye irritation (15%). Three enquiries (2%) reported systemic features (headache and vomiting). Seventy-one percent ($n = 100$) exhibited at least one feature of a maximum Poisoning Severity Score (MAXPSS) 1, others presented with multiple MAXPSS1 features. Only 2% ($n = 3$), reported a MAXPSS 2.
**Conclusion:** E-cigarette liquids are available in small, amber coloured dropper bottles that closely mimic other pharmaceutical dispenser vessels, such as hay fever and conjunctivitis therapies. Almost half of all enquiries in this study used e-cigarette liquid inadvertently as therapeutic eye drops. A change of product design, compromising a dissimilar bottle or clearer product label could help to ensure that these products are used as intended.

# 4. Massive follow-up by short message service (SMS) of patients calling the French Poison Control Centers (PCCs): a retrospective bicentric study

Dominique Vodovar[a], Christine Tournoud[b], Inesse Dridi[a], Hervé Laborde-Casterot[a], Marion Evrard[b], Laurine Le Visage[a], Emmanuel Puskarczyk[b] and Jérôme Langrand[a]

[a]Paris Poison Center, Paris, France; [b]Est Poison Center, Nancy, France

**Objective:** To compare follow up between two French PCCs, one using telephone only patient follow-up (Grand-Est PCC, Nancy) and the other using telephone or SMS (Paris PCC) follow-up. To compare the success rate of the different follow-up methods and the overall follow-up rate.
**Methods:** We extracted all exposure cases for which follow-up was allocated to the Paris or Grand-Est PCC in 2021. We included cases eligible for SMS follow-up [1], i.e., asymptomatic cases or cases with minor symptoms at the time of the call and that did not require medical consultation. As the telephone number is personal data and not available after anonymization of the data, we hypothesized that the proportion of patients having a cell phone was similar between the two PCCs in agreement with French national data [2]. We excluded cases with specific follow-up (lead or carbon monoxide exposures, exposures during pregnancy, exposures involving multiple patients). Results are expressed as number and percentage and compared using the Chi-square test.
**Results:** Of the 31,547 cases of exposure eligible for SMS follow-up, 20,137 (63.8%) were followed-up (Table 1). The telephone follow-up success rate did not differ significantly to that of SMS ($p = 0.2$). The overall follow-up rate was greater in the Paris than in the Grand-Est PCC ($p < 0.0001$).
**Conclusion:** Massive follow-up by SMS of eligible patients seems to be an interesting alternative to conventional follow-up by telephone of patients calling the French poison control centers.

## References

[1] Vaucel JA, Enaud N, Paradis C, et al. Poison Control Centres and alternative forms of communication: comparison of response rates between text message and telephone follow-up. Clin Toxicol. 2022;21:1–7.

Table 1. Follow-up and follow-up rate according to the PCC and the method of follow-up used for eligible cases in 2021.

| | Overall | Paris PCC | Grand-Est PCC |
|---|---|---|---|
| Cases eligible for SMS follow-up (*n*) | 31,547 | 19,475 | 12,072 |
| Followed-up (*n*, %) | 20,137 (63.8%) | 15,301 (78.6%) | 4836 (40.1%) |
| Success (*n*, %) | 17,695 (87.9%) | 13,407 (87.6%) | 4288 (88.7%) |
| Followed-up by telephone (*n*, %) | 6940 (22.0%) | 2104 (10.8%) | 4836 (40.1%) |
| Success (*n*, %) | 6072 (87.5%) | 1784 (84.8%) | 4288 (88.7%) |
| Followed-up by SMS (*n*, %) | 13,197 (41.8%) | 13,197 (67.8%) | – |
| Success (*n*, %) | 11,623 (88.1%) | 11,623 (88.1%) | |

[2] Croutte P, Muller J. Digital barometer, 2021 edition [cited 2022 Sep 24] (French). Available from: https://www.credoc.fr/publications/barometre-du-numerique-edition-2021.

## 5. N-acetylcysteine reduces acetaldehyde levels in binge alcohol drinking

Boris Podobnik[a], Lenart Demšar[a], Lucija Šarc[b], Aleš Jerin[c], Joško Osredkar[c], Jurij Trontelj[d], Robert Roškar[d] and Miran Brvar[e]

[a]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; [b]Centre for Clinical Toxicology and Pharmacology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [c]Department of Clinical Biochemistry, Faculty of Pharmacy, Institute of Clinical Chemistry and Biochemistry, University Medical Centre Ljubljana, University of Ljubljana, Ljubljana, Slovenia; [d]Department of Biopharmaceutics and Pharmacokinetics, Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia; [e]Centre for Clinical Toxicology and Pharmacology, University Medical Centre Ljubljana and Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

**Objective:** Alcohol hangover (veisalgia) is a fairly common phenomenon. The pathogenesis of veisalgia is not understood and treatment has not yet been established. The pathogenesis could include ethanol, acetaldehyde, dehydration, inflammation, or oxidative stress. Occasionally, students take N-acetylcysteine (NAC) before binge drinking to alleviate hangover. The aim of the study was to evaluate the effect of ethanol and NAC on serum concentrations of electrolytes, enzymes, acetaldehyde, oxidative stress biomarkers and symptoms of veisalgia.
**Methods:** In this randomised double-blind placebo-controlled study, healthy students who regularly attend drinking parties were randomly assigned into two groups, one receiving NAC (1.2 g before and 1.2 g after drinking alcohol), and the other placebo. Blood samples were taken before drinking, 30 minutes after a 1.5-hour-long drinking session and in the subsequent morning (9 hours after drinking). Serum concentrations of electrolytes, urea, creatinine, muscle and liver enzymes, ethanol, acetaldehyde and biomarkers of oxidative DNA damage (8-hydroxydeoxyguanosine, 8-OHdG) and lipid peroxidation (N-epsilon-hexanoyllysine, HEL) were measured. The participants completed the Acute Hangover Scale (AHS) based on symptoms. Data were analysed using one-way ANOVA with Bonferroni correction and logistic regression.
**Results:** Overall, 40 students (20 male; aged 17–29 years) were included. After drinking, their blood ethanol concentration was 1.4 ± 0.3 g/L and they had elevated serum acetaldehyde concentration (0.43 ± 0.16 mg/L) compared to its concentration before drinking (0.13 ± 0.07 mg/L) and the next morning (0.14 ± 0.10 mg/L) ($p = 0.01$). Serum acetaldehyde concentration after drinking was lower in the NAC group (0.37 ± 0.16 mg/L) than in the control group (0.51 ± 0.14 mg/L) ($p = 0.01$). Serum sodium concentration after drinking (143.1 ± 2.2 mmol/L) was elevated comparing to before drinking and the next morning (140.4 ± 1.9 and 140.8 ± 1.7 mmol/L, respectively) ($p = 0.01$) as well, but NAC had no effect on sodium. Interestingly, students in both groups had decreased serum urea concentration on the second day, probably due to (over)hydration. The oxidative biomarker 8-OHdG concentration was increased after alcohol drinking (48 ± 42 μg/L) ($p < 0.01$) and remained elevated until the next morning (48 ± 40 μg/L) ($p = 1.00$). NAC had no effect on 8-OHdG. Alcohol and NAC also had no effect on creatinine, liver and muscle enzymes and HEL. Veisalgia was reported in both groups, but its severity (NAC 2.6 ± 1.8 versus placebo 3.3 ± 2.7; $p = 0.45$) and AHS score (NAC 2.6 ± 1.3 versus placebo 2.6 ± 1.1; $p = 0.84$) did not differ between the groups.
**Conclusion:** Binge alcohol drinking increases serum sodium, acetaldehyde and 8-OHdG concentrations. NAC prevents serum acetaldehyde increase, but it has no effect on electrolytes, oxidative biomarkers and severity of veisalgia.

## 6. Envenomation from non-indigenous marine species in the Mediterranean Sea: a case series from Pavia Poison Control Center

Valentina Negrini[a], Benedetta Brolli[a], Davide Lonati[b], Lucia Bernasconi[a], Cristina Grazioli[a], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Toxicology Unit, Postgraduate School of Pharmacology and Clinical Toxicology, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, University of Pavia, Pavia, Italy; [b]Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Toxicology Unit, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Non-indigenous species (NIS) are defined as animals (and plants) intentionally or inadvertently brought into a new environment. It is estimated that more than 400 species have come from the Red Sea via the Suez Canal, or from the Oceans into the Mediterranean Sea. Human factors (e.g., travel and transport of goods) and climate change (e.g., alignment of salinity grade and overheating of surface waters) are also involved in the adaptation of alien species to new environments. As a consequence, the settlement of NIS may influence and menace endemic biodiversity and endanger human health, because some species produce toxins.
**Methods:** We retrospectively evaluated the cases of contact with marine NIS coming from the Red Sea or the Oceans, referred to Pavia PCC from January 2007 to August 2022. We considered only the cases of accidents with wild species, excluding aquarium specimens. For every species, contact route, symptoms, latency and therapy were evaluated.

Table 1. Cases of envenomation from non-indigenous marine species reported to the Pavia Poison Control Center.

| | *Hermodice carunculata* (bearded fireworm) | *Pterois miles* (devil firefish, common lionfish) | *Pterois volitans* (red lionfish) | *Plotosus lineatus* (striped eel catfish) |
|---|---|---|---|---|
| Number of cases | 9 | 8 | 7 | 1 |
| Mean time to contact with Poison Center | 1 Hour | 5 Days | 1 Hour | Unknown (hours) |
| Symptoms | Burning pain, oedema, paraesthesia | Burning pain, oedema, erythema, paraesthesia | Burning pain, oedema, erythema, paraesthesia | Local pain, oedema |
| Therapy | Chaetae removal, hot water, non-steroidal anti-inflammatory drugs (NSAIDs) | Hot water, NSAIDs, antibiotics (where needed) | Hot water, NSAIDs, antibiotics (where needed) | Hot water, NSAIDs |
| Imaging | – | X-rays | X-rays | – |
| Outcome | Recovery | Recovery | Recovery | Recovery |

**Results:** The most commonly involved species were *Hermodice carunculata*, *Pterois volitans*, *Pterois miles* and *Plotosus lineatus*. Common clinical features were local pain, oedema and hyperaemia (Table 1). Therapeutic strategies consist in immersing the part of the body in hot water, followed by analgesic support and antibiotics if signs of infection are present. All cases were followed after the accident, because of the risk of retained fragments of stings or chaetae that may cause persistence or resumption of symptomatology; in those cases, X-rays were suggested.
**Conclusion:** Introduction of alien species in a new environment is relevant to human health, because of the risk of contact with natural toxins. Pain and local symptoms are predominant, but long-term sequelae are possible. Knowledge about the toxic mechanism and intervention strategies is crucial to reach a good clinical outcome.

## 7. A randomised controlled trial of antivenom for red-bellied black snake envenoming

Geoffrey K. Isbister[a], Shane Jenkins[a] and Nicholas A. Buckley[b]

[a]Clinical Toxicology Research Group, University of Newcastle, Newcastle, Australia; [b]Clinical Pharmacology & Toxicology Research Group, School of Medical Sciences, University of Sydney, Sydney, Australia

**Objective:** Antivenom is first line treatment for snake envenoming worldwide, despite few placebo controlled clinical trials demonstrating effectiveness. We aimed to investigate whether early antivenom in red-bellied black snake (RBBS; *Pseudechis porphyriacus*) bites would prevent systemic envenoming, including myotoxicity.
**Methods:** We undertook a multicentre randomized placebo-controlled trial of antivenom for RBBS bites, recruited from the Australian Snakebite Project (ASP: July 2014–June 2020). Patients (>2 year) with a definite RBBS bite and early systemic effects were randomized to receive 50% glucose (placebo) or tiger snake antivenom within 6 hours post-bite. The primary outcome was the proportion of patients with myotoxicity defined as a peak creatine kinase (CK) > 1000U/L. Secondary outcomes were the area under the curve (AUC) of the CK rise during hospital admission, presence of free circulating venom 1 hour after antivenom, early adverse reactions and serum sickness.
**Results:** There were 104 RBBS bite presentations over the period, and 15 were recruited to the randomised controlled trial. After treatment, 2/7 patients from the placebo arm had a peak CK >1000 U/L versus 0/8 from the antivenom arm (difference in favour of antivenom; 29%; 95%CI −18% to +70%; $p = 0.2$). The difference in area under the curve (AUC) between placebo and antivenom was 27195 U/L.h (95%CI −4314 to 58705 U/L.h; $p = 0.085$). Nine patients had venom concentrations measured, with three patients from the placebo arm having detectable venom post-administration compared to none of six patients given antivenom. Two patients in the antivenom arm had immediate hypersensitivity reactions, one being severe anaphylaxis, and one patient had serum sickness. Of 87 not randomised with CK measured, 3/29 received antivenom <6 hours and 15/58 did not. Combining randomised and not randomised patients, 17/65 (26%) patients not receiving antivenom <6 hours post-bite had a peak CK >1000 U/L versus 3/37 (8%) given antivenom (difference in favour of antivenom; 19%; 95%CI 0.2–32%; $p = 0.037$).
**Conclusion:** Administration of antivenom in RBBS bites within 6 hours post-bite appeared to decreased the proportion of patients with myotoxicity, but a quarter of patients had adverse reactions.

## 8. What drives the risks of being bitten by a viper? A fine spatial scale study in western France

Gaël Le Roux[a], Mickaël Guillon[b], Lise Bernard[a], Géraldine Meyer[a], Luc De Haro[c], Olivier Lourdais[b] and Alexis D'Escatha[a]

[a]Centre Antipoison Grand Ouest, Angers, France; [b]Centre d'Études Biologiques de Chizé, CNRS, Chizé, France; [c]Centre Antipoison Sud, Marseille, France

**Objective:** Research on viper bites in France has so far focused on clinical consequences of envenomation, efficacy of antivenom and epidemiology of bites [1]. By contrast, we aimed to find patterns of spatial variation in bite incidence at a fine scale, an approach which is rare and relatively new.
**Methods:** The study focuses on viper bites recorded over the last 10 years in 4 regions of western France. We looked for the determinants of bite at the individual level and at the municipality level, considering the risk of at least one bite, and the total number of bites per municipality. We considered the following variables: probability of viper presence [2], viper species, climatic data, tourism function rate, soil artificialization and landscape use.
**Results:** In total 703 bite cases were analysed with significant disparities between regions and between municipalities. Bites occurred mainly in the second and third quarters, with a maximum in July, either during a garden-related activity (339 cases, 51.2%) or during an activity in the countryside (300 cases, 45.3%). Most bites (502 cases, 75.8%) were the result of a chance encounter with the snake. The probability of presence of a viper at the municipality level positively influenced the risk of being

bitten (multiplied by 3 for a variation in probability of 0.25 from 0.5), as well as the mean annual temperature (+1 °C multiplied the risk by 1.83–1.92). Soil artificialization had a positive effect on the risk of bites. In particular, the denser the urban fabric of a municipality, the greater the risk. Finally, a tourism function rate above 50 beds/100 inhabitants was strongly associated with an increase in the risk of occurrence and frequency of bites.
**Conclusion:** Overall, the viper bites recorded in our study are concentrated on the south coastline of the Pays de la Loire region. The coastal towns of the Pays de la Loire and Brittany and the preserved agricultural landscapes are areas of tourist attraction as well as offering favorable habitats for vipers. This convergence of habitats favors human/wildlife encounters and should be taken into account to reconcile human population flows with the protection of habitats favorable to the development of biodiversity.

## References


[1] Jollivet V, Hamel JF, de Haro L, et al. European viper envenomation recorded by French poison control centers: a clinical assessment and management study. Toxicon. 2015;108:97–103.

[2] Guillon M. From physiology to distribution: climatic adaptations and thermal sensitivity in a glacial relict [PhD]. Université de Poitiers; 2012. Available from: https://www.researchgate.net/publication/285589768_DE_LA_PHYSIOLOGIE_A_LA_REPARTITION_ADAPTATIONS_CLIMATIQUES_ET_SENSIBILITE_THERMIQUE_CHEZ_UNE_RELIQUE_GLACIAIRE


# 9. Has the re-scheduling of modified-release paracetamol in Australia affected the frequency of overdoses?


Michaela Ryan, Andis Graudins and Anselm Wong

Department of Medicine, School of Clinical Sciences at Monash Heath, Monash University, Victoria, Australia



**Objective:** Modified-release paracetamol (APAP-MR) may result in prolonged and unpredictable absorption after overdose (OD). Guidelines for immediate-release paracetamol (APAP-IR) OD may not be suitable for APAP-MR. In June 2020, APAP-MR preparations were up-scheduled from schedule-2 (available in pharmacy) to schedule-3 (available by request to a pharmacist only). This study aims to ascertain whether the up-scheduling has affected frequency of APAP-MR overdoses presenting to Monash Health and referrals to the Victorian Poisons Information Centre (VPIC).
**Methods:** This is a retrospective cohort study of two data sets from 1 June 2017 to 31 May 2022. Monash Health data were extracted using diagnosis of paracetamol overdose coding and electronic medical records data. Calls regarding APAP-MR overdoses to VPIC were extracted from the poison centre call database. Both datasets were divided into cohorts before and after 1 June 2020.
**Results:** From Monash Health, 826 paracetamol overdoses presented between June 2017 and June 2020; 12.7% (106) involved APAP-MR. After the legislative change, 723 cases were identified, 10.1% (62) involving APAP-MR. This change was not significant ($p = 0.08$, Chi-squared). The median monthly paracetamol presentations between the two periods increased from 23 (IQR: 20–25.8) to 28 (IQR: 23–31), $p = 0.01$. This was primarily the result of an increase in monthly APAP-IR overdoses from 20 (IQR: 17.3–23.8) to 25 (IQR: 20–27), $p = 0.006$. The monthly presentations of APAP-MR overdose did not change after the legislative change, with 2 (IQR:2–4) before and 2.5 (IQR:2–4) afterwards. VPIC received 19,087 calls regarding paracetamol overdose before June 2020, 5.3% (965) involved APAP-MR. After June 2020, there were 17,611 calls regarding paracetamol, 4.1% (699) involved APAP-MR. This small decrease was statistically significant ($p = 0.0001$, Chi-squared). The monthly number of paracetamol calls did not change significantly after June 2020.
**Conclusion:** The up-scheduling of access to APAP-MR to schedule-3 did not change the proportion of presentations to Monash Health. However, the number of monthly paracetamol overdose presentations increased, mainly due to APAP-IR overdose. There was a minor decrease in proportion of calls to VPIC regarding APAP-MR. Although the absolute number of monthly calls did not change. Further legislative changes may result in a further decrease of APAP-MR overdoses and calls to poisons centres.


# 10. Increase in deliberate self-poisonings by adolescents reported to the National Poisons Information Center during the second year of the COVID-19 pandemic


Arjen Koppen[a], Ilze M. J. Thoonen[a], Agnes G. van Velzen[a], Claudine C. Hunault[a], Dylan W. de Lange[b] and Saskia J. Rietjens[a]

[a]Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht, Netherlands; [b]Intensive Care, Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht, Netherlands



**Objective:** The COVID-19 pandemic has been associated with a decline in the mental health of adolescents and young adults, possibly caused by social isolation due to containment measures. A retrospective study was performed in order to characterize deliberate self-poisonings (DSPs) among adolescents reported to the National Poisons Information Center (NPIC) from 2016 until 2021, covering two years of the COVID-19 pandemic (2020 and 2021).
**Methods:** All inquiries to the NPIC regarding DSPs by adolescents (13–17 years of age) were retrospectively analyzed. A case was labelled as "DSP" where an exposure occurred with the (suspected) intent of self-harm or as a cry for attention. Exposures to drugs of abuse or alcohol with no clear intent of self-harm or as a cry for attention were excluded. DSP characteristics included: age, gender, bodyweight, toxicant, dose, route of exposure and symptoms at the time of NPIC consultation.
**Results:** A total of 6915 DSPs in adolescents were recorded from 2016 up to and including 2021; 84% of the cases involved females. During 2016–2020, no clear increase or decrease in the total annual number of DSPs was observed. However, in 2021 there was a considerable increase of 45% in the number of DSPs compared to 2020 ($n = 1512$ versus $n = 1044$). This increase was most prominent in 13-, 14- and 15-year-old adolescents (increase of 49, 75 and 77%, respectively), and stronger among girls compared to boys (50 versus 20%, respectively). The most commonly involved drugs were paracetamol, ibuprofen, methylphenidate, fluoxetine and quetiapine (42, 17, 7, 6, and 6% of all DSPs, respectively). The number of DSPs with paracetamol increased considerably (62% of all DSPs in 2021 compared to 40% in 2020). Mono-intoxications with paracetamol, methylphenidate and quetiapine required medical examination or hospital observation more often than mono-intoxications with ibuprofen and fluoxetine (56, 69, and 42% of all DSPs with that particular drug versus 22 and 19%, respectively).
**Conclusion:** The strong increase in the number of DSPs during the second year of the COVID-19 pandemic suggests that long-term containment measures such as quarantine, lockdown and school closures may increase self-harm behavior among adolescents. Policy makers should realize that mitigation measures during

pandemics can have adverse effects, for instance on mental well-being. Furthermore, the high frequency of DSPs with paracetamol among adolescents, often requiring medical examination or hospital observation, suggests that further restriction measures for the sale of paracetamol to adolescents may be necessary.

## 11. One-year single hospital study of acute poisonings in Israel

Konstantin Brusin[a], Meital Zikry Deitch[a], Elena Kishenevsky[a], Arkady Shklyar[a], Gennady Bregman[a], Hasan Agbaria[a], Haytham Attoun[a] and Knut Erik Hovda[b]

[a]Kaplan Medical Center, Rehovot, Israel; [b]Department of Acute Medicine, Oslo University Hospital, Oslo, Norway

**Objective:** Acute poisoning contributes to a substantial number of hospital admissions. To reveal the poisoning pattern of different regions is not only interesting, but also important to initiate preventative measures, as well as describe the current practice of treatment. The aims were to determine a pattern, rate, and outcomes of acute poisonings in related area; to evaluate the treatment given, and the rate of complications. Only general epidemiological data are presented in the current work.
**Methods:** A one-year registry cohort study of acute poisonings adults (age 18) admitted to emergency department of the Kaplan Medical Center (18 September 2021 to 17 September 2022). Data were recorded by using case report forms created in Oslo University for previous studies [1,2], with minor changes. Statistical analyses were performed using EXCEL and SPSS 28 (IBM). Results presented as median and [25;75] percentiles. Pearson Chi-Square test was used for difference assessment.
**Results:** Overall, 431 cases were observed with age 30 [21–48] years old, 61.7% were males. One patient died. Pharmaceuticals were considered the cause in 59.2% of cases. The most common agents were ethanol 22.5%, benzodiazepines 18.6% and paracetamol 7.9%. Street drug poisonings were surprisingly scarce (3.7%), while the impact of legal opioids was 5.8%. A total of 172 patients (40%) were admitted to hospital, of whom 25 were admitted to the intensive care unit. The three most common agents of poisoning among the hospitalized patients were benzodiazepines 26.2%, paracetamol 12.2% and ethanol 7.6%. For the patients discharged from the emergency department, ethanol 32.4%, benzodiazepines 13.5% and smoke inhalation 6.6% were most frequently seen. Possible or certain suicide attempt contributed to 80.2% of the hospitalized cases, but only 36.3% among the ones discharged prehospitally ($X^2(1df) = 80.29$ ($p < 0.01$), Phi $=0.432$, $p < 0.01$). Previous or current psychiatric treatment was recorded in 22.1% among the hospitalized cases, and 12% among the non-hospitalized ($X^2(1df) = 7.88$ ($p < 0.05$), Phi 0.135, $p < 0.05$). Drug abuse behavior was reported among 8.7% of the hospitalized patients, versus 14.7% of the non-hospitalized (the difference is not significant).
**Conclusion:** Hospital admission in the present study correlated with suicide intention and psychiatric morbidity.

### References

[1] Lund C, Vallersnes OM, Jacobsen D, et al. Outpatient treatment of acute poisonings in Oslo: Poisoning pattern, factors associated with hospitalization, and mortality. Scand J Trauma Resusc Emerg Med. 2012;20:1.
[2] Krayeva YV, Brusin KM, Bushuev AV, et al. Pre-hospital management and outcome of acute poisonings by ambulances in Yekaterinburg, Russia. Clin Toxicol. 2013;51:752–760.

## 12. The impact of socioeconomic status on toxicological exposures in pregnancy

Will Heise[a], Stephanie Christensen[b] and Laura Mercer[a]

[a]University of Arizona College of Medicine Phoenix, Phoenix, AZ, USA; [b]Kaiser Permanente, San Diego, CA, USA

**Objective:** To assess the relationship between socioeconomic status and its impact on toxicologic exposures in pregnant patients.
**Methods:** This study analyzed a seven-year dataset from the National Poison Data System of all toxicologic exposures in pregnant patients and their medical outcomes to assess for trends based on socioeconomic quartiles as determined by 5-digit ZIP codes. ZIP code data was used to obtain family income data from the Census Bureau, which served as an indicator of socioeconomic status. The cases examined are from across the United States and include pregnant patients in all three trimesters of gestation. Similar datasets have been analyzed to provide information on substances this specific population is at risk of exposure to, but correlation with socioeconomic status has not been published to date.
**Results:** Pregnant individuals from lower income households versus higher income households: younger, $26 \pm 6$ years versus $30 \pm 6$ years; more intentional exposures $n = 3{,}994$ (32%) versus 2,113 (17%); more likely to experience any effect, a major effect or a moderate to major effect $n = 4{,}499$ (36%), 173 (1%), 1,551 (12%) versus 3,008 (24%), 138 (1%), 935 (7%). For different toxins: Higher income patients: plants $n = 234$ (2.4%) versus 92 (1.0%); paints and stripping agents 185 (1.9%) versus 84 (0.9%); heavy metals 149 (1.2%) versus 78 (0.6%); foreign bodies 534 (4.3%) versus 244 (2.0%); vitamins 445 (4.6%) versus 331 (3.4%); electrolytes 250 (2.0%) versus 192 (1.5%); miscellaneous foods/products 271 (2.2%)/733 (5.9%) versus 184 (1.5%)/501 (4.0%); infectious disease 408 (3.3%) versus 303 (2.4%); and fumes and vapors 955 (7.6%) versus 714 (5.7%). Lower income patients: cardiovascular drugs $n = 230$ (1.8%) versus 124 (1.0%); bites and envenomations 645 (5.2%) versus 524 (4.2%); analgesics 1,699 (13.6%) versus 977 (7.8%); anticonvulsants 197 (1.6%) versus 122 (1.0%); miscellaneous drugs 540 (4.3%) versus 407 (3.3%); alcohols 222 (1.8%) versus 183 (1.5%); sedative/hypnotic/antipsychotics 450 (4.6%) versus 231 (2.4%); stimulants or street drugs 262 (2.7%) versus 139 (1.4%).
**Conclusion:** The study suggests an association between socioeconomic status of pregnant patients and toxicologic exposures in pregnancy. Individuals from lower income households show higher rates of intentional exposures, exposure to more serious toxins, and more negative outcomes than those from higher income households.

## 13. Acute paracetamol poisoning in children: a retrospective study

Julia V. Radenkova-Saeva and Miroslava T. Petkova

Toxicology Clinic, University Hospital for Emergency Medicine "NI Pirogov", Sofia, Bulgaria

**Objective:** To analyze a group of pediatric patients admitted in a toxicology department for acute paracetamol (acetaminophen) poisoning.
**Methods:** We performed a 20-month retrospective study that collected data from the medical records of all children, admitted

to a pediatric toxicology department at UHEM "Pirogov" between January 2021 and August 2022 for acute paracetamol poisoning. The patients were characterized according to age, gender, amount of paracetamol ingested, co-ingested substances, time elapsed from ingestion, clinical features, blood test results, including serum paracetamol concentration and treatment received.

**Results:** There were 17 children, hospitalized in the pediatric toxicology department, due to paracetamol poisoning during the study period. The age of the patients varied from 2 to 17 years. Most were female 16 (94.1%) and 1 (5.9%) male; 15 (88.2%) of the girls were between the ages of 12 and 17 years. Fifteen (88.2%) of the patients took a tablet form of paracetamol in a dose of 5–80 tablets (500 mg) and two (11.8%) of them ingested paracetamol syrup. In 11 (64.7%) of the cases, the intoxications were mono-ingestions, and 6 (35.3%) were poly-intoxications. The additional drugs ingested with paracetamol were flu remedies, nonsteroidal anti-inflammatory drugs, antibiotics, antihistamines, vitamins and others. The mean time from ingestion to hospital admission was 4.5 hours and the ingested paracetamol dose was significantly higher in patients who ingested only paracetamol. Fifteen (88.2%) of the patients ingested the medicines as a suicide attempt. During the clinical examination, nausea, vomiting and abdominal pain were found in all patients, headache and dizziness in 8 (47.1%), fatigue and malaise in 7 (41.2%). Hepatotoxicity developed in 6 (35.3%) of the cases. Paracetamol concentrations were measured in all children and were above the therapeutic concentration in 7 (41.2%). The liver enzymes were elevated and the International Normalized Ratio (INR) prolonged in 7 (41.2%) patients. All of the children received antidotal acetylcysteine, decontamination with activated charcoal as well as symptomatic treatment. There were no deaths in this series of children.

**Conclusion:** The study showed a high frequency of cases of paracetamol overdoses, taken in suicidal attempts in girls aged 12–17 years. Implementation of strategies, with emphasis on health education, are needed in order to reduce cases of acute exogenous poisoning in this group.

## 14. Results of a toxicovigilance program in a tertiary hospital of the community of Madrid, from January 2020 to August 2022

Arturo Gómez, Javier Guijarro, Rosario M. Torres, Rosa Mayayo, Lucía Díaz, Alberto M. Borobia, Antonio J. Carcas and Mikel Urroz

La Paz University Hospital, Madrid, Spain

**Objective:** According to the definition by the WHO, toxicovigilance is the active process of identification and evaluation of existing toxic risks in a community, and the study of possible measures aimed at their reduction or elimination [1]. Our center has a validated toxicovigilance search tool (SAT-HULP) [2]. The objective is to examine the epidemiological profile of intoxicated adult patients treated at our hospital.

**Methods:** A descriptive epidemiological analysis was carried out based on the data obtained from consultations for poisoning attending the Adult Emergency Service of La Paz University Hospital from 1 January 2020 to 31 August 2022 through the validated search tool SAT-HULP. The cases were verified manually through the electronic medical record system implemented since 2018 for the collection of additional data. A descriptive statistical analysis was carried out; quantitative variables were expressed as mean and median, while qualitative variables were expressed as absolute frequency and relative percentage.

**Results:** During the 32 month study period, 331,652 patients were treated, of which 3,028 (0.91%) attended due to poisoning (Table 1). The mean and median age was 40 (range 15–101) and 39 years, respectively. The distribution by sex was 50.2% men and 49.8% women.

**Conclusion:** Poisoning in our community continues to be a common reason for emergency room attendance. Study of the variables in this population is an essential tool for preventive measures, as well as to learn the optimal management to improve treatment and the outcome of these patients.

### References

[1] World Health Organization. Chemical Safety and Health Unit [cited 2022 Oct 10]. Available from https://www.who.int/publications/m/item/toxicovigilance.

Table 1. Characteristics of consultations for poisoning presenting over a 32 month period to La Paz University Hospital.

| Characteristic | Category | Percentage (%) |
|---|---|---|
| Intentionality | Abuse | 55 |
| | Suicidal | 34 |
| | Accidental | 10 |
| | Chemical submission | 0.5 |
| Number of substances involved | Polyintoxication | 19.35 |
| | Mono-intoxication | 80.65 |
| Nature of the substances involved | Drugs of abuse | 54 (of which alcohol was present in 91%) |
| | Drugs* | 40 |
| | Household products | 5 |
| | Industrial products | 2 |
| | Gases | 2 |
| Outcome | Medically or voluntarily discharged | 88.6 |
| | Admission required | 11.3 |
| | Death** | 0.06 |
| Days of the week with the highest number of visits due to poisoning | Sunday | 19% |
| | Saturday | 17.5% |
| | Monday | 14.5% |

*Benzodiazepines 85%, antidepressants 7%, antipsychotics 6% and acetaminophen 5%.
**Two cases, both secondary to digoxin.

[2] Muñoz R, Borobia AM, Quintana M, et al. Development and validation of a poisoning surveillance program with automatic case detection in a tertiary care hospital (SAT-HULP). Emergencias. 2013;25:423–429.

## 15. Adolescent poisonings reported to the UK National Poisons Information Service (NPIS): a 6.5 year study

Annie Watt[a], Thomas M. Caparrotta[a], Ruben H. K. Thanacoody[b], Laurence A. Gray[c], Sally M. Bradberry[d], Gillian Jackson[a] and Euan A. Sandilands[a]

[a]National Poisons Information Service, Edinburgh, United Kingdom; [b]National Poisons Information Service, Newcastle, United Kingdom; [c]National Poisons Information Service, Cardiff, United Kingdom; [d]National Poisons Information Service, Birmingham, United Kingdom

**Objective:** Adolescent poisoning is a significant issue. Our objective was to analyse NPIS enquiries regarding adolescent patients to determine epidemiology, severity, and agents involved.
**Methods:** A retrospective analysis of the UK poisons information database (UKPID) to identify enquiries regarding 10–18-year-olds between 1 January 2015 and 30 June 2021.
**Results:** The NPIS received 25,232 enquiries (mean 3805/year) during the study period with no significant variability in the number of enquiries per year. Females accounted for the majority (16,451; 65.2%) with enquiries regarding 15-year-olds accounting for a significantly greater proportion than other age groups ($p < 0.0001$). Most enquiries involved intentional exposures (13,029; 51.6%), followed by accidental (6474; 25.7%), therapeutic error (2778; 11.0%), recreational (1446; 5.7%) and unknown (1505; 6.0%). Pharmaceuticals accounted for the majority of agents (20,873; 82.7%: Table 1). Recreational drugs (3450; 13.7%), household products (3007; 11.9%), vitamins/minerals (1440; 5.7%), and other agents (4180; 16.6%) accounted for the rest. An unknown agent was involved in 358 enquiries (1.4%). Most patients were asymptomatic or had minor symptoms (22,160; 87.8%). Moderate and severe symptoms were recorded in 1786 (7.1%) and 712 (2.8%) enquiries, respectively. In 574 enquiries (2.3%) symptoms were unknown. Thirty-eight deaths (mean 6.3/year) were recorded, with most occurring in 17- and 18-year-olds (21; 55.2%). Common agents included recreational drugs (20; 52.6%), propranolol (5; 13.2%) and colchicine (3; 7.9%). Agents involved in one death each included citalopram, clobazam, diphenhydramine, drotaverine, flecainide, hydroxychloroquine, propafenone and paracetamol. Some deaths involved multiple agents and in three the agent was unknown.
**Conclusion:** Adolescent poisoning remains a common enquiry to the NPIS with a peak age in 15-year-olds. Most enquiries relate to pharmaceutical agents often found in the household. Reassuringly most incidents are associated with low toxicity although deaths do occur, frequently in the context of recreational drug exposure. Continued surveillance is important particularly following the COVID-19 pandemic which is known to have significantly impacted this age group.

Table 1. Enquiries involving pharmaceutical exposure (n = 20,873) in adolescents.

| Pharmaceutical | Number | Percentage |
|---|---|---|
| Paracetamol/paracetamol-containing products | 7234 | 34.7 |
| Non-steroidal anti-inflammatory drugs (NSAIDs) | 2334 | 11.2 |
| Antidepressants | 2284 | 10.9 |
| Iron preparations | 1057 | 5.1 |
| Antihistamines | 1006 | 4.8 |
| Antipsychotics | 745 | 3.6 |
| Benzodiazepines | 673 | 3.2 |
| Opioid analgesics | 657 | 3.1 |
| Antibiotics | 652 | 3.1 |
| Attention deficit hyperactivity disorder (ADHD) drugs | 595 | 2.9 |
| Cardiac drugs | 521 | 2.5 |
| Hormonal/contraceptives | 512 | 2.5 |
| Anticonvulsants | 439 | 2.1 |
| Aspirin/salicylates | 391 | 1.9 |
| Gabapentin/pregabalin | 200 | 1.0 |
| Antiemetic preparations | 163 | 0.8 |
| Insulin | 38 | 0.2 |
| Others | 1372 | 6.6 |

## 16. Increased risk of major adverse cardiovascular events in middle-aged obese patients receiving Chinese herbal medicine: a nationwide cohort study in Taiwan

Yi-Ju Ho[a], Wen-Chieh Yang[b] and Te-I Weng[c]

[a]National Taiwan University Hospital, Taipei, Taiwan; [b]Taipei Veterans General Hospital Hsinchu Branch, Hsinchu, Taiwan; [c]Department of Forensic Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan

**Objective:** In Taiwan many obese patients visit traditional Chinese medicine (TCM) clinics for Chinese herbal medicine (CHM) [1]. In 2013, a news report disclosed ephedra misuse by a local Chinese medicine clinic in Taipei, resulting in out of hospital cardiac arrest [2]. This study aimed to determine the risk of major adverse cardiovascular events (MACE) among adults with obesity diagnosis in Taiwan, with or without CHM.
**Methods:** Obese patients aged between 18 and 50 years were identified from the Taiwanese National Health Insurance Research Database (NHIRD) from 2008 to 2018. We enrolled 67,655 CHM users and 67,655 non-CHM users, randomly selected using propensity score matching from the remaining cases. All patients were followed from the study date until MACE development, death, or the end of 2018. The Cox proportional regression model was used to evaluate hazard ratios of MACE between CHM and non-CHM cohorts.
**Results:** During a median follow-up period of 4.2 years, the incidence rate of MACE was higher in the CHM cohort when compared with the non-CHM control cohort (9.35 versus 8.27 per 1,000 person-years). The risk of MACE was 1.13-fold higher in the CHM group compared with the non-CHM control (adjusted hazard ratio [aHR]: 1.13; 95% confidence interval [CI]: 1.07–1.19), especially in ischemic stroke (aHR: 1.18; 95% CI: 1.07–1.31), arrhythmia (aHR: 1.26; 95% CI: 1.14–1.38), and young people aged 18–29 (aHR: 1.22; 95% CI: 1.05-1.43). Continuous use of CHM for approximately 360 days still had a 1.18-fold higher risk of MACE.
**Conclusion:** Middle-aged obese patients receiving CHM have a 1.13-fold higher risk of MACE than non-CHM users. CHM may be an independent risk factor for MACE in middle-aged obese patients.

## References

[1] Liu JP, Zhang M, Wang WY, et al. Chinese herbal medicines for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2004;2002: CD003642.
[2] Taiwan High Court criminal judgment case No. 107, medical appeal, 3. Taiwan, R.O.C: Taiwan High Court; 2020 (Chinese).

## 17. No laughing matter: trends in nitrous oxide misuse in the United States during the COVID-19 pandemic

Ryan J. Cole, Rita Farah and Nathan P. Charlton
University of Virginia Health, Charlottesville, VA, USA

**Objective:** To determine trends in nitrous oxide misuse before and during the COVID-19 pandemic and evaluate the associated demographic data and outcome data as reported to US Poison Centers (PCs).
**Methods:** We conducted a retrospective review between 1 January 2000 and 31 December 2021 of the National Poison Data System (NPDS), the data warehouse for the 55 US PCs. Medical outcomes are coded as no effect, minor, moderate, or major effect, or death. Data were analyzed using SAS 9.4. All reported cases of intentional exposures to nitrous oxide were included. Trends per 100,000 human exposures were analyzed using Poisson regression methods.
**Results:** A total of 1947 cases of intentional exposure to nitrous oxide were reported to the NPDS from 1 January 2000 to 13 December 2021. Between 2000 and 2021, there was a three-fold increase in intentional nitrous oxide exposures (3.4/100,000 versus 10.74/100,000; 231% increase; $p = 0.04$). Also in 2021, there was a four-fold increase as compared to 2009 (2.5/100,000 versus 10.74/100,000; 328% increase; $p = 0.03$). Compared to pre-pandemic rates (2019), there was a two-fold increase in 2021 (104% increase; $p = 0.04$). Analyzing the distribution by age group, we found that the proportion of intentional exposures among teenagers (13–19 years) has been consistently declining; between 2000 (39.7%) and 2012 (20.9%), we observed a 48% decrease ($p = 0.02$) and between 2000 (39.7%) and 2021 (8%), there was an 80% decrease ($p < 0.001$). In contrast, nitrous oxide intentional exposures in the 30–39 age group has been consistently increasing. Between 2000 (5.9%) and 2010 (21.5%), there was a 3.6 fold increase ($p = 0.005$) and between 2000 (5.9%) and 2021 (24.5%), there was more than a four-fold increase ($p = 0.001$) in this age group. In 2021, 163 cases of single substance nitrous oxide exposure were reported to US PCs. Most of these exposures occurred in the patient's own residence ($n = 146$; 90%). Eighty one exposures (50%) resulted in a serious outcome (1 case of death, 11 cases resulted in major effect, and 69 resulted in moderate effect).
**Conclusion:** Nitrous oxide misuse rose significantly during the COVID-19 pandemic. Further study is required to determine the cause of this rise.

## 18. 2,4-Dinitrophenol use as discussed on social media

Ali Abdelati[a], Stefan Bartell[b] and Michael Chary[b]
[a]Weill Cornell Medicine-Qatar, Doha, Qatar; [b]Weill Cornell Medicine, New York, NY, USA

**Objective:** 2,4-Dinitrophenol (DNP) is an oxidative phosphorylation uncoupler used for weight loss. The USA Food & Drug Administration (FDA) declared DNP too dangerous for human consumption in 1938. Increasing fatalities suggest ongoing use. However, a federal ban and known toxicity raise substantial barriers to experimental study. Our objective was to determine the sublethal dosage, usage, and coingestants of DNP in humans using self-reported usage described on the Internet.
**Methods:** We analyzed Internet posts from 2017 to 2020 from discussion forums dedicated to bodybuilding. Posters were anonymous and consented to re-use their data when they agreed to each website's terms of service. We combined our previously developed natural language processing techniques with a novel ontology to extract doses, effects, and the names of substances used from each post. Each post was tokenized into mentions of substances and effects and mapped to standardized mentions of substances (using RxNorm) and effects using an ontology.
**Results:** We identified 680 posts (634 unique), describing a median dose of 250 mg (25th–75th percentile 200–500 mg), 114 effects and 94 coingestants. The most common side effects reported were sweating (101/634; 16%), feeling hot (82/634; 12.9%), lethargy (57/634; 9.0%), and night sweats (55/634; 8.6%). There were fewer than 5 total mentions of tachycardia, palpitations, or yellow discoloration. The most commonly reported coingestants were androgenic anabolic steroids (AAS) (testosterone 51/634, 8.6%; trenbolone 79, 12.4%) and substances previously reported as used for lipolysis (clenbuterol 37/634, 5.8%; levothyroxine 75/634, 11.8%; ephedrine-caffeine-aspirin [ECA] 29/634, 4.6%). There were fewer than 5 mentions of selective estrogen or androgen receptor modulators.
**Conclusion:** An analysis of Internet discussions on DNP usage found most reported ingested doses between 200 and 500 mg, which were associated with sweating, feelings of warmth, and lethargy, but no palpitations or yellow discoloration. Co-mention of substances known to be used in bodybuilding (AAS, clenbuterol, ECA) support the validity of our method. Our results may be affected by reporting bias and non-authentic posting (trolling). Our approach complements data from Poison Control Centers and Medical Examiners, which may be biased towards more severe poisonings. Our analysis also provides an ontology, a standardized list of terms used to report and describe 2,4-dinitrophenol ingestion that made help future efforts to excavate toxicological information from unstructured text on the Internet.

## 19. Medication errors in the neonatal intensive care unit

Ophir Lavon, Amit Wasserman and Yamit Musai
Carmel Medical Center, Haifa, Israel

**Objective:** To report the characteristics of medication errors in a Neonatal Intensive Care Unit (NICU).
**Methods:** A retrospective review study of the pharmacovigilance registry of voluntary reports of medication errors and near misses in Carmel Medical Center NICU, Haifa, Israel, during the period of January 2015 to May 2022. Data regarding events' circumstances and outcomes were collected and subjected to descriptive statistical analysis.
**Results:** The analysis included 161 reports, 99 errors (61.5%) and 62 near misses (38.5%). Nurses ($n = 145$, 90%) reported most of the events. The main culprit was usually a nurse ($n = 72$, 44.7%) or a physician ($n = 69$, 42.6%). Most of the errors resulted in no or mild clinical manifestations. Only two reports were with moderate to high severity; both involved erroneous caffeine dose administration that resulted in cardiac instability. All cases recovered with no sequelae. The main types of events were wrong dose or administration rate ($n = 39$, 24.2%), wrong medication ($n = 20$, 12.4%), wrong timing or frequency ($n = 20$, 12.4%), expired medication ($n = 14$, 8.7%), wrong patient ($n = 12$, 7.5%), and wrong route ($n = 5$, 3.1%). The main medications involved were antibiotics ($n = 39$, 24.2%), total parenteral nutrition formulations ($n = 24$, 15%), caffeine ($n = 7$, 4.3%), and paracetamol ($n = 6$, 3.7%).
**Conclusion:** While NICU is a site with a high level of supervision, control and awareness to safety, medication errors are still a

reality with similar characteristics to other medical sites. Interventions for mitigation of these adverse events are required.

## 20. Belgian Poison Centre: annual overview 2021

Dominique Vandijck, Jonas Van Baelen, Eline Bekaert, Evelien De Smet, Jonas Moens, Pamela Selway, Régine Pire, Sarah Desmaele, Karolien De Leener and Anne-Marie Descamps
Belgian Poison Centre, Brussels, Belgium

**Objective:** This study gives an overview of the number and type of calls received by the Belgian Poison Centre (BPC) in 2021 and compared potential changes with the COVID-19 year 2020.
**Methods:** Data of all calls to the BPC (1 January – 31 December 2021) were collected and analysed using appropriate statistics (SAS).
**Results:** The BPC received 61,029 calls in 2021 of which 52,497 calls (86%) (involving 47,164 human victims and 6,773 animals) were due to an exposure, and 8,532 (14%) were an information request. This is a 6.6% decrease ($p > 0.05$) as compared to 2020 (65,308 calls), but a 16.1% increase ($p < 0.05$) since 2012 (52,582 calls). In 72.3% the patient or his/her proxy, and in 21.5% a (para)medical professional called the BPC. The reason for consultation was a non-intentional (86.8%) versus intentional exposure (12.3%), $p < 0.05$. Of all human victims, children (age 0–13 years) accounted for 19,765 victims, of which 69.0% were within the age category 1–4 years ($p < 0.05$). Despite a decrease of 5.0% (20,666 in 2020 versus 19,629 in 2021, $p > 0.05$), the vast majority (32.2%) of exposures were drug-related (12,714 adults versus 6,915 children, $p < 0.05$), of which 11.2% ($n = 2,208$) involved paracetamol. The latter is an increase of 17.0% as compared to 2020 ($n = 1,833$, $p < 0.05$). Drugs affecting the nervous system (e.g., antipsychotics, antidepressants, etc.) were most frequently involved (40.0%). There were 10,406 (2021) versus 11,836 exposures (2020) ($p > 0.05$) to chemical household products (6,259 adults versus 4,184 children, $p < 0.05$), of which 39.7% related to cleaning products (excluding biocides). Cosmetic- and food-related exposures accounted for 8,222 calls (3,286 adults versus 4,723 children, $p < 0.05$) in 2021 compared to 9,308 in 2020 ($p < 0.05$), of which food and nutritional-supplements accounted for 39.8% of calls ($n = 3,105$, $p < 0.05$). Incidents due to biocides were responsible for 3,610 exposures in 2021 (1,691 adults versus 1,446 children, $p > 0.05$), of which almost half (48.4%, $n = 1,517$) included calls about alcohol-based hand sanitizers ($p < 0.05$). Finally, in 2021 the BPC received a total of 6,773 calls (12.6%) related to veterinary toxicological incidents. Intoxications among dogs ($n = 5,398$, 79.7%) and cats ($n = 1,001$, 14.8%) were responsible for 94.5% of veterinary calls.
**Conclusion:** Regardless of 2020 (COVID-19 pandemic), in 2021 the BPC received the highest number of calls in its history. Drug-related calls were the most important reason to call the BPC. Animal-related calls are increasing over time.

## 21. Severity and outcome in acutely intoxicated patients with elevated creatine kinase

Aleksandra Babulovska, Daniela Chaparoska, Natasha Simonovska, Zanina Pereska, Niko Bekjarovski, Irena Jurukov, Afrodita Berat-Huseini, Kristin Kostadinoski and Kiril Naumoski
Clinical Centre, Medical Faculty, University Clinic of Toxicology, Sts Cyril and Methodius University in Skopje, Skopje, North Macedonia

**Objective:** Rhabdomyolysis is a clinical entity characterized by the release of intracellular enzymatic content from skeletal muscle into the bloodstream that leads to systemic complications. We determine the causes of mortality in patients with rhabdomyolysis following acute intoxication with psychotropic and chemical substances.
**Methods:** This was a prospective clinical study, which included 140 patients with rhabdomyolysis divided into two groups depending on the substance taken, psychotropic or chemical intoxications. The severity of rhabdomyolysis was assessed according to the Poison Severity Score. Patients were divided into 3 groups a) mild rhabdomyolysis, CPK level from 250 to 1,500 U/L); b) moderate rhabdomyolysis CPK level from 1,500 to 10,000 U/L) and c) severe rhabdomyolysis CPK greater than 10,000 U/L. We included adult patients ages 18 and older with rhabdomyolysis in the study. They had been acutely intoxicated with either psychotropic or chemical substances within 48 hours prior to hospital admission.
**Results:** In the group with psychotropic intoxications, the level of CPK on the first day in patients with a fatal outcome was significantly higher ($p = 0.0242$) compared to survivors. In the chemical intoxication group, the patients with fatal outcomes compared to survivors had lower CPK levels on the first day, but this difference was not significant ($p = 0.2747$ versus $p = 0.5779$). Mortality was registered in a total of 9.3% ($n = 13$) patients with rhabdomyolysis, of which 23.1% ($n = 3$) had psychotropic intoxication and 76.9% ($n = 10$) chemical intoxication. The analysis indicated a significantly lower mortality in psychotropic compared to chemical intoxications ($p = 0.0001$). Mortality in the group of psychotropic intoxications, according to the etiological cause was highest with methadone at 13.3% ($n = 2$), and neuroleptics at 8.3% ($n = 1$). In the chemical intoxication group, the prevalence of mortality according to the etiological cause was highest in patients intoxicated with herbicides 50% ($n = 1$), ethylene glycol 33.3% ($n = 1$), corrosives 33.3% ($n = 4$) and organophosphates 26.7% ($n = 4$).
**Conclusion:** Rhabdomyolysis had no significant effect on the fatal outcome in acutely intoxicated patients with psychotropic and chemical substances. Mortality was significantly lower in patients with rhabdomyolysis intoxicated with psychotropic drugs compared to chemical intoxications. In patients intoxicated with chemical substances, which were mild or moderate rhabdomyolysis, the causes of death were corrosive agents, ethylene glycol, herbicides, and organophosphates. The fatal outcome was due to the toxic effects of these agents and the severe disorders they cause.

## 22. Are nicotine pouches a toxicological problem in Austria?

Susanna Dorner-Schulmeister and Tara Arif
Poisons Information Centre, Vienna, Austria

**Objective:** There are several tobacco and tobacco-free pouches which can be used as an alternative to cigarettes. In toxicological consultations, a differentiation must be made between these products. In Austria, nicotine pouches contain synthetic nicotine in the tobacco-free version and are not subject to the tobacco laws. The aim of this study was to analyse consultations to the

Austrian Poisons Information Centre (PIC) regarding circumstances and symptoms after exposure to nicotine pouches.
**Methods:** A retrospective and descriptive analysis of enquiries to the PIC concerning single exposures to nicotine pouches to humans was conducted from January 2019 to June 2022. Acute exposures were evaluated for age, symptoms, and Poisoning Severity Score (PSS).
**Results:** In total 38 nicotine pouch exposures were extracted from the database, of which 8 were excluded because the amount or circumstance of the exposure was not clear. Thus, 30 cases with confirmed exposures were evaluated. In 10 cases a follow-up was performed. In the paediatric group, 12 children (5 girls, 7 boys; age: 7 months to 14 years) were involved. In 9 cases the intake was accidental and three (aged 13 to 14 years) used this product intentionally. Five children had no symptoms (PSS 0) and seven patients had mild symptoms (PSS 1: vomiting $n = 4$, nausea $n = 4$, dizziness $n = 3$, vertigo $n = 2$, tachycardia $n = 1$, hypertension $n = 1$). In the 18 adults (15 males, 3 females; 16–32 years of age) the consumption was always intentional. However, in 17 cases the product was swallowed accidentally and in one case buccal use caused symptoms. In 10 cases there were no symptoms (PSS 0) and 8 patients had mild symptoms (PSS 1: restlessness $n = 2$, nausea $n = 4$, vomiting $n = 4$, diarrhoea $n = 2$, mucous membrane irritation $n = 1$, dizziness $n = 2$, sweating $n = 1$). In 8 cases the exact time of onset and duration of symptoms could be determined. Symptoms appeared 5 minutes to 5 hours after exposure and usually disappeared after 7 hours. Only in one case light dizziness persisted for one day.
**Conclusion:** Nicotine pouches are not a major toxicological problem in Austria. In the age group of 16 to 32 years more men were affected. Only mild symptoms occurred, which resolved within 7 hours in most cases.

## 23. National reports of e-liquid poisoning received by French Poison Control Centers from July 2019 to December 2020

Fanny Pelissier[a], Juliette Bloch[b], Cécilia Solal[b] and Nicolas Franchitto[c]

[a]Centre Antipoison et Toxicovigilance Occitanie, Centre Hospitalier et Universitaire de Toulouse-Purpan, Toulouse, France; [b]ANSES, Maisons-Alfort, France; [c]Service d'Addictologie Universitaire, Centre Hospitalier de Toulouse-Purpan, Toulouse, France

**Objective:** E-liquids are of particular concern as a growing body of literature suggests an increased risk of exposure incidents related to e-cigarette use and misuse. Exposure to e-cigarette liquids, whether intentional or accidental, may lead to adverse events. This study aims to describe the prevalence and characteristics of exposures to e-liquids reported to French Poison Control Centers.
**Methods:** All e-liquid exposure cases reported to French Poison Control Centers from 1 July 2019 to 31 December 2020, were reviewed. The distributions of exposures by demographic and clinical factors were determined. The overall severity was defined according to the Poison Severity Score [1]. Chi-square tests and multivariable logistic regression analysis were used to test associations.
**Results:** During the study period, a total of 919 cases of exposure to e-liquids were reported. The highest number of exposures (50.7%) concerned infants (0–5 years), 3.1% children (5–12 years), 5.9% adolescents (12–18 years), and 40.1% of cases concerned adults. Most of the patients were male (55.7%). The majority of cases were accidental (95.0%) and concerned infants (53.8%). Intentional exposures (4.9%) were mainly observed in patients older than 12 years of age ($p < 0.001$). The method of exposure was ingestion in 73.7% of the cases. Symptoms were noted in 464 out of 919 (50.4%) patients in the study. The most common symptoms reported were nausea/vomiting (31.6%), followed by ocular burns (28.2%), abdominal pain (15.7%), and headaches (3.8%). A total of 455 exposures resulted in null severity, while 437 were coded with minor poisoning. No death was recorded.
**Conclusion:** Involuntary exposures to e-liquids occurred more often in children under the age of five, mainly by ingestion. Severe exposures were uncommon when unintentional compared to intentional ingestions. These results indicate that surveillance of such exposures by the toxicovigilance network should continue to prevent these exposures and injuries and to focus on the regulation of these products.

### 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.

## 24. How does rhetorical stance affect the content of online discussions about DNP use?

Stefan Bartell and Michael Chary

Weill Cornell Medicine, New York, NY, USA

**Objective:** 2,4-Dinitrophenol (DNP) is an uncoupler of oxidative phosphorylation touted for weight loss. Its consumption was banned in America by the Food and Drug Administration in 1938. Since 2000, calls to Poison Control Centers involving DNP use and fatalities, have increased, suggesting a change in the perceived safety of DNP. Social media narratives may provide data on user perception of prohibited substances when experimental data are not available. Our objective was to investigate whether the content of online posts differed for posts that advocated for DNP use, against its use, or did not explicitly advocate.
**Methods:** We scraped online discussion forums dedicated to bodybuilding, weight loss, and steroid use for publicly available discussion threads mentioning DNP or related keywords (e.g., 2,4-DNP). In each comment we counted the overall number of substances mentioned, times DNP was mentioned, and mentions of alternative substances (e.g., caffeine, ephedra, clenbuterol). Two reviewers rated each comment as explicitly solely endorsing DNP use, explicitly solely condemning DNP use, or neither (neutral). To be rated a comment had to explicitly mention DNP and use language only explicitly endorsing or condemning its use, for example "use DNP it's great" or "don't use DNP it's lethal". Comments that expressed mixed opinions or did not explicitly mention DNP were classified as neutral.
**Results:** We obtained 4,130 unique comments from 5 online discussion forums between 2018 and 2022. Of those comments, 1,339 explicitly mentioned DNP, 46/1339 (3.4%) explicitly advocated for DNP use ("pro-DNP"), 88/1339 (6.6%) explicitly condemned ("anti-DNP"), and the rest, 1204/1399 (90%), "neutral". The two raters were in 100% agreement. The 46 pro-DNP comments mentioned 1.39 [1.2–1.48] substances besides DNP and 0.56 [0.48–0.68] alternative substances per comment, expressed as median (interquartile range). The 88 anti-DNP comments mentioned 1.38 [1.2–1.51] substances besides DNP and 0.375 [0.3–0.42] alternatives per comment. Neutral comments mentioned 0.94 [0.8–1.0] substances per comment besides DNP and 0.21 [0.1–0.28] alternatives per comment. Pro-DNP comments

mentioned statistically significantly more alternative substances than anti-DNP comments ($p < 0.005$; chi-square test). Neutral comments mentioned fewer substances overall and alternatives than pro- or anti-DNP comments did ($p < 0.03$; chi-square test followed by Tukey's *post-hoc* test).
**Conclusion:** In an analysis of posts about DNP use in forums dedicated to bodybuilding, most comments did not mention DNP use. Of those that did, most did not explicitly advocate for or against it. Comments with an explicit stance mentioned more substances and alternatives than neutral comments. Pro-DNP comments mentioned approximately 60% more alternative substances than anti-DNP comments. Our study did not consider indirect rhetorical stances, for example, mentioning the ineffectiveness of DNP. We did not consider that mentions of alternative substances could be suggesting combining those substances with DNP rather than replacing.

## 25. Characterization of exposures in preschoolers reported to a Chilean Poison Control Center in 2020

Antonia Sateler[a], Marli Bettini[b], Lorena Silva[b], Patricio Medel-Jara[a,b,c], Pablo Iturra[a], Francisco Figueroa[b], Lisette Irarrázabal[c] and Juan Carlos Ríos[a,b,d]

[a]Programa de Farmacología y Toxicología, Pontificia Universidad Católica de Chile, Santiago, Chile; [b]Centro de Información Toxicológica, Pontificia Universidad Católica de Chile (CITUC), Santiago, Chile; [c]Escuela de Enfermería, Pontificia Universidad Católica de Chile, Santiago, Chile; [d]Departamento de Laboratorios Clínicos, Pontificia Universidad Católica de Chile, Santiago, Chile

**Objective:** Exposure cases in pediatric patients constitute a public health problem [1]. Despite preventive measures, emergency services continue to manage pediatric patients with poisoning [2]. The goal of this study is to characterize exposures in preschool children, according to the reports received by a poison center in Chile in 2020.
**Methods:** A retrospective study of the reports received by the Centro de Información Toxicológica de la Pontificia Universidad Católica (CITUC) was conducted through the call registration system CITUC SRL, to identify cases of human exposure in patients between 2 and 6 years of age, between 1 January and 31 December 2020.
**Results:** A total of 7,204 cases corresponding to the category of preschoolers were reported, equivalent to 23.2% of all reports. Two-year-old children accounted for 12.8% of the reports. Regarding gender, 52.3% of all exposed children were male; 55.4% of reports were from home, and 43.9% were made from healthcare centers where the preschooler was admitted. Regarding the caller, in most reports it was a family member of the exposed child (53.3%). Analyzing the toxic agents, pharmaceutical products were the most prominent (63.5%), followed by cleaning products (14.0%) and chemical products (9.1%). Analyzing agents individually, acetaminophen was the most common agent (4.8%), followed by household bleach (4.8%), chlorphenamine (2.0%) and clonazepam (1.8%). Most exposures happened at the child's house (99.5%), through ingestion (92.2%). At the time of calling the poison center, 76.5% of preschoolers were asymptomatic.
**Conclusion:** Despite most exposures occurring at home, a significant percentage of incoming calls were made from healthcare centers, which means that caretakers attend directly to a healthcare center before calling a poison center. Preschoolers are exposed mainly to pharmaceutical products, acetaminophen being the most frequent and accessible in homes, therefore it should be prevented [3]. It is crucial to educate caretakers about exposures, and the existence of poison centers and the ways caretakers can contact their local poison center for advice.

### References

[1] Gkentzi D, Sinopidis X, Gourdoupi D, et al. Acute poisoning: an old-time classic issue in pediatrics. World J Pediatr 2019;15:622–623.
[2] Glenn L. Pick your poison: what's new in poison control for the preschooler. J Pediatr Nurs. 2015;30:395–401.
[3] Hines, E. Pediatric poisonings: the risk of over-the-counter pharmaceuticals. Pediatr Ann. 2017;46:454–58.

## 26. Impact of COVID-19 pandemic in rising suicide attempts through intentional acute poisoning in teenagers in Chile. Analysis of the major Chilean Poison Control Center data

Patricio Medel-Jara[a,b,c], Lorena Silva[d], Marli Bettini[d], Claudio Retamal[d], Francisco Figueroa[d], Sandra Solari[b,d,e] and Juan Carlos Ríos[b,d,e]

[a]Centro de Información Toxicológica, Pontificia Universidad Católica de Chile (CITUC), Santiago, Chile; [b]Programa de Farmacología y Toxicología, Pontificia Universidad Católica de Chile, Santiago, Chile; [c]Escuela de Enfermería, Pontificia Universidad Católica de Chile, Santiago, Chile; [d]Facultad de Medicina, Centro de Información Toxicológica y de Medicamentos (CITUC), Pontificia Universidad Católica de Chile, Santiago, Chile; [e]Departamento de Laboratorios Clínicos, Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

**Objective:** The incidence of suicide attempts among young people has nearly doubled after the COVID-19 pandemic across the globe [1]. It is hypothesized that suicide attempts through intentional acute poisoning of teenagers has also increased in Chile after COVID-19. The objective of this work is to assess the impact of the COVID-19 pandemic on acute intentional poisoning in teenagers in Chile.
**Methods:** Analysis of 2019-2021 data on poisonings in teenagers (between 12 and 17 years of age) recorded by Chile's Poison Control Center (CITUC) was conducted, comparing the main characteristics before and after the pandemic started in Chile (3 March 2020), including the number of cases, age, sex, and exposure circumstances. Statistical testing used chi-square and significance was considered with a $p < 0.05$.
**Results:** CITUC recorded 15,682 poisoning cases in the study group, 8578 in the pre-pandemic period, and 7104 in the pandemic period. Teenagers accounted for 6590 of the suicide attempts in the pandemic period, representing 84.8% (95% CI 83.96–85.63) of the total cases in that age group, compared to 76.8% (95%CI 75.95–77.71) pre-pandemic. The 8.0% rise in the proportion of suicide attempts after the pandemic started is statistically significant, with a chi-squared value of 157.6, and a *p*-value $<0.0000001$. Stratified by sex, the rise in suicide attempts were 5.5% (95%CI 4.29–6.64) in females and 8.5% (5.07–11.84) in males. The overall odds ratio of suicide attempts comparing the pandemic versus pre-pandemic period is 1.68 (95%CI 1.55–1.83), adjusted by sex. The stratified analysis shows that in females, the OR was 1.64 (95% CI 1.47–1.82), and in males, 1.42 (95%CI 1.23–1.63). The ORs between males and females are statistically

significant, with a Mantel-Haenszel chi-squared value of 101.8, and a $p$-value $<0.0000001$.
**Conclusion:** The proportion of suicide attempts among teenagers increased above 8% after the pandemic started in Chile, along with a rise of 68% in the risk of suicide attempts in the study group (OR $=1.68$). The risk is higher in females but, interestingly, male teenagers showed a greater increase in the proportion of suicide attempts compared with females, although this last group remains at the highest risk. It is important to study the effects of the COVID-19 pandemic, which can be much more profound than imagined.

## Reference

[1] Goto R, Okubo Y, Skokauskas N. Reasons and trends in youth's suicide rates during the COVID-19 pandemic. Lancet Reg Health West Pac. 2022;27:100567.

# 27. Proportion of poisoned patients at the emergency department with QTc prolongation, based on different correction formulas

Irma S van den Hengel-Koot, Saskia J Rietjens, Douwe Dekker, Dylan W de Lange and Laura Hondebrink

University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands

**Objective:** A proportion of intoxicated patients at the Emergency Department (ED) are admitted due to QT interval prolongation, because this is a risk factor for developing arrhythmias. Since the QT interval varies with heart rate (HR), the corrected QT (QTc) is determined, usually automatically by the electrocardiogram (ECG) device, which uses Bazett's formula. In this study, we compare the proportion of patients classified with prolonged QTc interval, when using Bazett and other correction formulas.
**Methods:** All intoxicated patients with ECG data who were presented at our ED between January 2015 and June 2016 were included. ECG data were collected from electronic patient files. QTc intervals were determined with 5 different correction formulas: Bazett, Hodges, Fredericia, Framingham, Rautaharju and the Isbister nomogram. QTc interval was considered prolonged at $\geq$450 ms or when above the Isbister nomogram line. Patients were stratified by HR: normal (60–100 bpm), high ($>$100 bpm), or low ($<$60 bpm).
**Results:** We included 251 intoxicated patients with a median age of 41 years (IQR 27–51 years) and equal gender distribution. Compared to Bazett's formula, all formulas resulted in less patients classified with QTc prolongation at normal and especially at high HR, while at low HR, all formulas resulted in more patients classified with QTc prolongation (Table 1).
**Conclusion:** Compared to other correction formulas, Bazett overestimates the QTc interval at high and normal HR, possibly leading to unnecessary admission of patients for observation for development of arrhythmias. This is especially important for poisoned patients with tachycardia, as the largest differences in the proportion of patients with a prolonged QTc were observed in that group. However, at low HR, Bazett underestimates the QTc interval, possibly leading to patient discharge, when observation is warranted. When using QTc interval as a diagnostic tool, selecting the right correction formula is important.

# 28. Electronic clinical files of patients in the emergency department. Usefulness as tools for toxicosurveillance

Francisco J Ruiz-Ruiz[a], Mario Angulo-Artal[b], Ana Serrano-Ferrer[c], Rafael Marron-Tundidor[d] and Ana Ferrer-Dufol[e]

[a]Emergency Department, Unit of Clinical Toxicology, Hospital Clinico Universitario, Zaragoza, Spain; [b]Universidad de Zaragoza, Zaragoza, Spain; [c]Hospital Clínico Universitario, Zaragoza, Spain; [d]Servicio Aragones de Salud, Zaragoza, Spain; [e]Unit of Clinical Toxicology, Hospital Clinico Universitario, Zaragoza, Spain

**Objective:** Since 2009, patient care data at the emergency departments (EDs) of public hospitals of the Aragon Region (Spain) are collected using electronic software (PCH). Several updates have improved the analysis of data collected in various circumstances such as sepsis or COVID-19 cases. The aim of this study is to explore the potential of this software and possible improvements to use it as an effective tool for obtaining an automated register of acute poisoning treated in our EDs.
**Methods:** An extraction of all cases obtained from the PCH Database was carried out covering the 11 hospitals with EDs in Aragon during the years 2019 and 2020. The cases related to acute poisoning were selected among all the obtained diagnoses, according to the ICD-9 classification. Each case was categorized according to the causative agent of the poisoning and the data that could be extracted from the program were analysed.
**Results:** During the study period, 610,426 care visits were carried out in 2019 and 438,143 in 2020 in the EDs of Aragon. The percentage of acute poisoning cases treated were 0.58% (3,536) and 0.63% (2,760) in 2019 and 2020, respectively. The variables that could be obtained automatically were: hospital, affiliation data, date, type of attention, reason for consultation, priority in care, age, sex, length of stay in the emergency department, tests performed, need for treatment, diagnosis and destination of the patient. The median age of cases was $38.7 \pm 19.7$ years; 55.3% (3480) of the patients were male. In half of the cases, the priority of care assigned to the patient in triage was intermediate (level 3). The most frequent agent group were drugs of abuse, with alcohol being implicated, followed by drugs, where the most frequent were benzodiazepines. In this period, 924 cases (14.7%)

Table 1. Proportion of patients with QTc $\geq$450 ms.

| Correction method | All ($N=251$) | Normal heart rate $N=169$ (67%) | Heart rate $>$100 bpm $N=62$ (25%) | Heart rate $<$60 bpm $N=20$ (8%) |
|---|---|---|---|---|
| Bazett | 119 (47%) | 68 (40%) | 45 (73%) | 6 (30%) |
| Fredericia | 43 (17%) | 26 (15%) | 7 (11%) | 10 (50%) |
| Framingham | 35 (14%) | 25 (15%) | 2 (3%) | 8 (40%) |
| Hodges | 43 (17%) | 21 (12%) | 11 (18%) | 11 (55%) |
| Rautaharju | 65 (26%) | 36 (21%) | 19 (31%) | 10 (50%) |
| Isbister | 30 (12%) | 9 (5%) | 13 (21%) | 8 (40%) |

required hospitalisation and 78 cases (1.2%) were admitted to the ICU. Only one patient died in the ED. Data concerning signs and symptoms related to poisoning could not be obtained from this data nor the evolution of the hospitalized patients.
**Conclusion:** The evaluated PCH software is a useful tool for toxicosurveillance in the EDs. To improve the quality of the obtained data, some changes are required, including a specific section for poisonings which will allow a thorough analysis of clinical data and treatment. These are feasible changes as they have already been incorporated for other pathologies.

## 29. The rise in edible marijuana related calls following cannabis decriminalization: one poison center's experience

Rita Farah, Will R. Goodrich, Ryan J. Cole and Christopher P. Holstege

Department of Emergency Medicine, Division of Medical Toxicology, University of Virginia School of Medicine, Charlottesville, VA, USA

**Objective:** To describe the epidemiology of exposures to marijuana edibles as reported to a poison center (PC) following cannabis decriminalization.
**Methods:** We conducted a retrospective review of calls to a PC between 1 June 2020 and 30 September 2022 following cannabis decriminalization. All inquiries about exposures to marijuana edible preparations were analyzed for reasons of exposure, clinical effects, medical care and outcome.
**Results:** Between June 2020 and September 2022, the PC received 228 calls regarding exposure to marijuana edible preparations in comparison to 17 calls prior to June 2020. More than half of the exposures ($n = 128$, 56%) occurred among children and adolescents (<20 years) and 29% ($n = 65$) occurred among children aged <7 years. All exposures ($n = 72$) among children aged <7 years and 23/26 exposures among those aged 7–12 years were unintentional, while exposures were mostly intentional in age group 13–19 years (24/30) and 20 years and above (87/100). Most exposures were reported directly by healthcare providers (n = 127, 56%). The majority of exposures were reported as single substance exposures ($n = 211$, 93%). Among calls reporting multiple substance exposures, the most commonly reported substances were heroin, hallucinogenic mushrooms and ethanol. Most exposures required emergency department evaluation ($n = 160$, 70%); 46 (20%) required hospital admission, of which 14 (6%) required admission to a critical care unit. Medical outcomes were reported as major for 16 exposures (7%) and moderate for 130 exposures (57%). Descriptive analysis of clinical effects in isolated marijuana edible exposures ($n = 211$) revealed that 78% ($n = 177$) experienced at least one neurological symptom including moderate central nervous system (CNS) depression ($n = 41$, 18%), mild CNS depression ($n = 25$, 11%), dizziness ($n = 32$, 14%), agitation ($n = 30$, 13%), confusion ($n = 27$, 12%), tremors ($n = 18$, 8%), hallucination ($n = 12$, 5%), and seizure ($n = 9$, 4%). At least one cardiovascular symptom was reported in 100 cases (44%); the most frequently reported symptoms were tachycardia ($n = 100$, 44%), hypertension ($n = 25$, 11%) and QRS prolongation ($n = 7$, 3%). Gastrointestinal symptoms were reported in 25% of cases ($n = 57$) and included nausea, vomiting, diarrhea and abdominal pain.
**Conclusion:** While the dose required to achieve clinical effects is unclear, the reported medical outcomes and health effects suggest that exposure to marijuana edible preparations is an emerging public health concern following cannabis decriminalization. Due to lack of state regulation regarding the marketing of marijuana edibles, products are widely available in stores, packaged in colorful containers, sweetly flavored, and candy-themed which makes them attractive to children.

## 30. Shortages of medications for alcohol withdrawal treatment in the US and Europe: a five year analysis

Christopher J. Counts and Jennifer S. Love

Mount Sinai Hospital Department of Emergency Medicine, New York City, NY, USA

**Objective:** To summarize and compare United States (US) and European medication shortages for acute alcohol withdrawal treatment in the last five years.
**Methods:** We completed a retrospective analysis of chlordiazepoxide, lorazepam, diazepam, phenobarbital, ketamine, propofol, and dexmedetomidine shortages from September 2017 to September 2022 using the American Society of Health-System Pharmacists, Federal Drug Administration, European Medicines Agency (EMA), and national drug shortage databases. Data collected included number of shortages, duration, reason, current status, and number of manufacturers. Statistical analyses were performed using SAS for Academics.
**Results:** All medications included in the analysis had one or more shortages in the US and Europe. In the US, we identified 10 shortages with a mean duration of 26.2 months (1.5–59.5 months). The most common reasons were manufacturing delays, increased demand, and manufacturer discontinuation. The mean number of manufacturers per medication was five. Chlordiazepoxide and phenobarbital have the fewest current manufacturers ($N = 2$), while dexmedetomidine has the largest number of manufacturers ($N = 14$). Linear regression modeling revealed that the number of drug manufacturers positively predicted the number of drug shortages ($p = 0.0409$). In Europe, reported drug shortage data varied by country. Four EU nations did not have publicly available registries. Although multiple countries were affected by shortages, none of the medications are currently assessed in the EMA shortage catalog. Chlordiazepoxide and phenobarbital were the least commonly reported shortages (4.3% of countries), while propofol, lorazepam, and ketamine were the most commonly reported (reported by 52.2, 21.7, and 21.7% of countries, respectively).
**Conclusion:** The US and the EU experienced shortages of seven medications used for acute alcohol withdrawal treatment during the study period. US data demonstrated prolonged shortage durations and variability in the number of manufacturers of each agent. The number of manufacturers was a positive predictor of the number US drug shortages for acute ethanol withdrawal. In the EU, shortages were reported nationally with variable data reported. Propofol was the most commonly reported shortage. Standardization of shortage reporting across the US and EU may improve national and international responses to shortages [1]. Importantly, the impact of these shortages on clinical outcomes of patients with acute alcohol withdrawal remains an important area of study.

### Reference

[1] Ravela R, Lyles A, Airaksinen M. National and transnational drug shortages: a quantitative descriptive study of public registers in Europe and the USA. BMC Health Serv Res. 2022;22:940.

## 31. The diagnosis and treatment of cannabinoid hyperemesis syndrome

Arón Misa García[a], Álvaro Medina Guerrero[b], Marina Fages Pérez[c], Yolanda Ibáñez Borau[d], Beatriz Calderón Hernanz[b], Montserrat Vilanova Boltó[b] and Miguel Agudo García[d]

[a]Hospital Pharmacy Department, Hospital Universitario de Ourense, Ourense, Spain; [b]Hospital Pharmacy Department, Hospital Universitario Son Llàtzer, Palma de Mallorca, Spain; [c]Hospital Pharmacy Department, Hospital de la Línea, Cádiz, Spain; [d]Emergency Department, Hospital Universitario Son Llàtzer, Palma de Mallorca, Spain

**Objective:** To collect diagnostic orientation criteria for cannabinoid hyperemesis syndrome (CHS) and reflect on the prevalence of this syndrome and current treatments used in the emergency department.
**Methods:** Retrospective observational study including patients diagnosed with CHS from October 2018 to June 2022. For diagnosis of CHS, the following criteria were established: abdominal pain, severe vomiting, urine positive for tetrahydrocannabinol (THC) and normal results of complementary tests. Data were obtained from the digital medical record (HCIS®) and laboratory database (Gestlab®). Variables collected were: sex, age, number of visits to emergency department caused by symptoms of the syndrome (before and after diagnosis), length of stay in the emergency room, positive drug tests and concentration of THC in urine and type of pharmacological treatment received during admission.
**Results:** Nineteen patients with normal complementary tests were included. Nine (47.4%) were women. Average age was 35 years. All of them fulfilled the criteria for diagnosis of CHS. The number of emergency department visits caused by symptoms of the syndrome were 121 (6.37 per patient). Ten patients (8.3%) required hospital admission and on 23 occasions (19%) the patient returned to the emergency department in less than 72 hours. The average time spent in the emergency department was 12.3 hours. The average urine THC concentration was 650 ng/mL (>500 ng/mL indicates chronic use). Pharmacological treatments received in the emergency admissions were: classic antiemetics (metoclopramide and/or ondansetron) in 84.3%, antipsychotics (haloperidol) 5%, benzodiazepines (diazepam) 37.2%, antacids (omeprazole and/or ranitidine) 55.4% and analgesics (paracetamol, metamizole, dexketoprofen and/or tramadol) 75.2%.
**Conclusion:** CHS is highly prevalent and entails a large number of admissions associated with extra healthcare costs. A good interview, well recorded in digital medical software is crucial for a quick and accurate diagnosis at emergency department. Therefore, Simonetto et al. [1] established new major criteria to guide diagnosis: severe vomiting, improvement with abstinence from cannabis, relief of symptoms with hot water, and epigastric pain. Variability of current treatments and the high number of relapses highlight the need to use suitable therapeutic targets. Recent studies have shown good results in the treatment of CHS with topical capsaicin [2].

### References

[1] Simonetto DA, Oxentenko AS, Herman ML, et al. Cannabinoid hyperemesis: a case series of 98 patients. Mayo Clin Proc. 2012; 87:114–119.
[2] Burillo-Putze G, Trujillo-Burillo D, García-Hernandez JC, et al. Cannabis hyperemesis syndrome: Incidence and treatment with topical capsaicin. Medicina Clínica. 2022;159:183–186.

## 32. Aetiology and clinical severity of carbon monoxide poisoning in Germany

Nina Glaser, Michael Reuser and Kathrin Begemann

German Federal Institute for Risk Assessment, Berlin, Germany

**Objective:** In Germany, all poisonings must be notified to the German Federal Institute for Risk Assessment (BfR) by the attending physicians or the responsible statutory accident insurances on a legal basis. All cases notified to BfR are validated and registered in a standardised manner in BfR's national poisoning database. Severity is assessed according to the Poisoning Severity Score (PSS). For this study, the BfR evaluated reports of carbon monoxide poisoning.
**Methods:** All cases reported to the BfR from 2002 to 2021 with carbon monoxide as the most toxicologically relevant noxa were evaluated according to exposure location, aetiology and severity. The aetiology of the fatal cases was compared with data from the Information System of the Federal Health Monitoring in Germany [1].
**Results:** From 2002 to 2021, 747 poisonings with carbon monoxide were reported to the BfR. The proportion of reports on carbon monoxide in relation to all reports increased six-fold in the period under review. The proportion of occupational exposures was 54%. The sources of carbon monoxide and clinical signs differentiated by occupational or private exposure are illustrated in Table 1 (other and unknown exposure sites not shown). In total 238 moderate and severe poisonings were reported (32% of all cases), including 26 fatalities. Most deaths were of accidental origin (80%), while 62% of all fatal cases in the Information System of the Federal Health Monitoring were suicides (5084 of 7969 cases; 2002–2020).

Table 1. Source and severity of carbon monoxide poisoning in cases reported to the German Federal Institute for Risk Assessment (BfR) 2000–2021.

| | | Exposure site | | |
|---|---|---|---|---|
| | | Occupational | Private | Total |
| Reported sources of carbon monoxide (selection) | Charcoal grills (including 18 suicide attempts) | 1 | 112 | 113 |
| | Heating | 47 | 65 | 112 |
| | Vehicles and devices with combustion engines | 76 | 13 | 89 |
| | Fires | 27 | 48 | 75 |
| | Shisha | 0 | 36 | 36 |
| Poison Severity Score (PSS) | Asymptomatic | 51 | 18 | 69 |
| | Minor | 256 | 102 | 358 |
| | Moderate | 61 | 110 | 171 |
| | Severe | 6 | 61 | 67 |
| | Cannot be assessed | 35 | 34 | 69 |
| | Total | 409 | 325 | 734 |

**Conclusion:** The study presented here shows the differences in occupational and private exposure with carbon monoxide regarding sources and severity of symptoms. The large number of severe poisonings shows that carbon monoxide is still the noxa with the most serious poisoning potential in Germany and underlines the importance of continuous public education.

## Reference

[1] The Federal Health Reporting Information System [cited 2022 Oct 10]. Available from; https://www.gbe-bund.de/gbe/.

# 33. Analysis of suicide attempts by chemicals in the years 2017–2021 gathered in the Spanish Toxicosurveillance Program

Ana Serrano-Ferrer[a], Francisco Ruiz[b] and Ana Ferrer-Dufol[c]

[a]Psiquiatría Hospital Clinico Universitario, Zaragoza, Spain; [b]Urgencias, Zaragoza, Spain; [c]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza University, Zaragoza, Spain

**Objective:** The Spanish Toxicosurveillance Program prospectively collects, on a daily basis, data of poisoning cases produced by chemicals in patients attending emergency departments of 20 hospitals. Nearly 30,000 cases have been collected over 26 years. Contrary to what happens when the cases produced by medicines and drugs of abuse are considered, the cases related to chemicals are mostly accidental. Here we present the etiology, clinical evolution of the cases produced as a suicide attempt with a chemical agent in the last 5 years of the Program.
**Methods:** The cases are incorporated by means of an online encrypted form downloaded in a database describing demographic data, case chronology, intentionality, agent, toxicological analysis, clinical data, treatment and evolution. We analyse the characteristics of the self-inflicted cases.
**Results:** From 2017 to 2021, 5638 cases were registered and 526 (9%) were suicide attempts. Of these cases 53 (10%) were minors (17 or less years old), 359 were between 18 and 60 years old and 108 were older than 60 years. The age distribution shows a significant difference with the general group where 22% were minors. The patients were evenly distributed by gender: 259 were male and 260 were female. The most used substances by far were caustics (271 cases, 52%) followed by pesticides (61 cases, 12%), solvents (58 cases, 11%) and toxic gases (47 cases, 9%). Among the caustics the most frequently involved agent is bleach (175 cases, 33%). The most frequent route of entry was oral (451 cases, 86%) followed by the respiratory route (66 cases, 13%). Overall, 404 patients developed symptoms, 296 digestive (56%), 116 neurologic (22%), 73 respiratory (14%) and 47 cardiovascular effects (9%). Some form of treatment was used in 480 cases (91%), mainly symptomatic care. Admission to the intensive care unit (ICU) occurred in 25 cases and there were 26 deaths (5%) which is significantly higher than the lethality in the general chemical cases which is 0.8%
**Conclusion:** Suicide attempts using chemical products are a group with some relevant differences compared to the general chemical group and represent a higher risk group, which are sentinels to establish preventive measures addressing restricting availability of the most dangerous products. The Spanish Toxicosurveillance Program is a useful tool to maintain an updated profile of these type of events.

# 34. Pandemic and post-pandemic intoxications in the intensive care unit (ICU) of a general public hospital

Clara Serrano-Ferrer[a], Laura Sanchez[b], Sara Gomez[c], Elena Lacruz[b], Ana Serrano-Ferrer[c], Ana Ferrer-Dufol[d] and Begoña Zalba[b]

[a]Intensive Care Unit, "Principe de Asturias" Hospital, Alcalá de Henares, Spain; [b]Intensive Care Unit, Clinical University Hospital, Zaragoza, Spain; [c]Psychiatric Unit, Clinic University Hospital, Zaragoza, Spain; [d]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza, Spain

**Objective:** To describe the epidemiology and profile of acute poisoning among patients admitted to the intensive care unit (ICU) in the context of the COVID-19 pandemic.
**Methods:** Observational, descriptive study, of 26 patients admitted to the ICU in a general public hospital covering a population of 300,000 inhabitants due to acute poisoning from 2020 January to 2022 September.
**Results:** The mean age was 49.9 years old (SD 21.5), with a majority of women (57.7%). The yearly admission distribution was 3 patients in 2020, 16 patients in 2021, and 7 in 2022. Psychiatric disorders were present in 18 patients (65.4%), of which 17 were diagnosed with anxious depressive disorder. Alcohol abuse was present at 19.2% of cases, and opioid abuse in 7.7%. The reason for ICU admission was low consciousness level in 17 patients (65.4%), indication of monitoring in 6 patients, digestive injury in 2 patients, and severe agitation in 1 case. Drug overdose was the most common cause of poisoning (22, 84.6%). There were caustic ingestions in 2 patients, one mushroom poisoning and one polyethylene glycol ingestion. The most frequent cases involved multiple psychotropic drugs. In three cases, the involved drug was a benzodiazepine; in three cases a neuroleptic drug, and two more were overdoses of colchicine and insulin. Three cases were due to toxicity caused by metformin, and three were due to lithium toxicity. The circumstance of poisoning was suicidal in 17 patients, overconcentration of a prescribed drug in 6 patients, and accidental in 3 cases. Intubation was necessary for 14 patients with a mean length of mechanical ventilation of 4 days. Vasoactive drugs were needed in 8 patients, and continuous hemodiafiltration was needed in 5 patients. The mean length of stay was 6 days. In 6 cases, there were complications, and 2 patients died.
**Conclusion:** Acute severe poisoning requiring ICU admission in our hospital occurs more frequently in women with psychiatric antecedents and due to suicidal overdoses of their psychotropic prescribed drugs. Relevant numbers of overconcentration of therapeutic drugs (metformin and lithium) are also present. More than half of the patients need mechanical ventilation, and a third required vasoactive drugs. The low number of admissions in the year 2020 can be attributed to the overload of COVID patients that produced a limitation of ICU admission for not-so-severe cases that were diverted to other hospital wards.

## 35. Hospital-treated deliberate self-poisoning in Azerbaijan: epidemiological features and clinical outcomes

Ismayil Afandiyev[a] and Jamil Afandiyev[b]

[a]Clinical Toxicology, Department of Internal Diseases, Azerbaijan Medical University, Baku, Azerbaijan; [b]Department of Psychiatry, Azerbaijan Medical University, Baku, Azerbaijan

**Objective:** Suicide attempts by poisoning is a global public health problem. The aim of this study was to analyze the epidemiological features and clinical outcomes of deliberate self-poisoning in Azerbaijan.
**Methods:** A retrospective analysis of all intentional in-patient poisoning cases with suicidal intent presenting to the National Clinical Toxicology Center, Baku, 1 January 2016 to 31 December 2020.
**Results:** There were 3993 patients with suicidal self-poisoning attempts (1272 males, 2721 females). The youngest was eight, the oldest, 103 years old; 56 (1.4%) patients were 0–14 years old. The mean age was 31.6 ± 13.0 years in women and 37.1 ± 14.5 years in men. Over a third of cases (35.7%) occurred in 20–29 year olds. The main causes of a suicide attempt referred to problems in the family (48.1%), economic problems (22.4%), problem/stress at work or in school/university (10.5%) and health problems (8.7%); 119 (3.0%) patients had a previous history of intentional poisoning; 9.2% had history of psychiatric disorder. Most patients were unemployed (56.6%). The peak of these hospitalizations occurred in the summer months (June-August, 29.6%). According to ICD-10, among the pharmaceutical poisoning cases ($n = 2460$) the highest number involved sedatives, anticonvulsants and psychotropic drugs (T42/T43), with 1435 patients or 58.3% of all patients in this group. The main substances used in the group were amitriptyline ($n = 278$; 19.4%), carbamazepine ($n = 145$; 10.1%) and phenazepam ($n = 125$; 8.7%). Suicidal self-poisoning attempts by non-opioid analgesic, antipyretic and antirheumatic drugs (T39) were the second largest group among pharmaceutical poisoning cases (361 patients, 14.7%). The main substances used in this group were metamizole ($n = 110$; 30.5%), paracetamol ($n = 89$; 24.7%) and acetylsalicylic acid ($n = 79$; 21.9%). Among non-medical intentional intoxications (T51–T65; $n = 1520$), the main agent was concentrated acetic acid ($n = 1009$; 66.4%). Other significant chemical xenobiotics were pesticides (organophosphates $n = 139$; 9.1%, rodenticides $n = 139$; 9.1%). Lethal outcomes occurred in 4.5% of cases ($n = 177$). Most fatal poisonings were due to concentrated acetic acid (i = 127; 71.8%). Self-poisoning among elderly patients (≥60 years) was associated with poorer outcomes ($n = 53/229$; lethality 23.1%) than in younger adults 20–50 years ($n = 122/3293$; lethality 3.7%).
**Conclusion:** Deliberate self-poisoning is a significant healthcare problem in Azerbaijan. Despite the prevalence of pharmaceutical self-poisoning, deliberate intoxications by concentrated acetic acid in our study had the highest hospital mortality rate. Banning the sale of concentrated acetic acid in grocery shops and supermarkets should be considered by State bodies. The Healthcare Authorities should organize educational courses on the prevention of intentional poisoning among vulnerable groups.

## 36. Intentional ingestions in children and adolescents as a worldwide phenomenon

Anna A. Celentano[a], Alvin A. Bronstein[b], Marcello M. Ferruzzi[a], Fabrizio F. Sesana[a], Giovanni M. Milanesi[a] and Francesco F. Scaglione[a]

[a]Milan Poison Control Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [b]Emergency Medical Services & Injury Prevention System Branch Hawaii State Department of Health Leahi Hospital-Honolulu, Honolulu, HI, USA

**Objective:** Intentional ingestions in adolescents is a public health event. The pandemic waves and online social media trends have influenced the spread of experimenting with medications and some other substances in children and adolescent populations as a worldwide phenomenon.
**Methods:** We analyzed intentional ingestions in children and adolescents from an Italian Poison Control Centre from 1 January 2016 to 31 August 2022 by sex, age, agent name, category distribution, clinical effects and severity of symptoms.
**Results:** Over the study period, a total of 3072 cases were collected. Of them, 2559 were female and 498 were male and 15 were unknown. The age distribution was as follows: 9 cases 5–9 years, 833 cases 10–14 years, 2220 cases 15–17 years. Medications and household products were the categories most involved. The most frequently reported clinical effects were pharyngodynia, vomiting, nausea, abdominal pain, heartburn, diarrhea, slowdown, and drowsiness. Clinical cases have doubled from 2020 ($n = 308$) to 2021 ($n = 623$) and 531 cases in 2022. The age class 15–17 years showed an increase in medication ingestion from 2021 with 634 medications involved and 706 medications involved in 2022. The age class 10–14 years also showed an increase in medication ingestion, 86 during 2020, 257 in 2021 and 227 in 2022 (Table 1). In 15–17 year olds the most frequently involved drugs were: pain medications (21.3% in 2021; 30.8% in 2022) and benzodiazepines (17.8% in 2021; 19.3% in 2022) as shown in American Poison Control data. Household products are less involved but are more hazardous and often require more significant medical management.

Table 1. Intentional ingestions in children and adolescents 2016–2022, the experience of an Italian Poison Control Centre.

| | | Medications involved | | | Household products involved | | |
|---|---|---|---|---|---|---|---|
| Year | Cases | 5–9 years | 10–14 years | 15–17 years | 5–9 years | 10–14 years | 15–17 years |
| 2016 | 426 | | 126 | 357 | | 31 | 79 |
| 2017 | 404 | 3 | 125 | 339 | 3 | 22 | 53 |
| 2018 | 419 | 2 | 133 | 381 | | 26 | 42 |
| 2019 | 361 | 1 | 99 | 297 | | 30 | 48 |
| 2020 | 308 | 1 | 86 | 285 | 2 | 13 | 31 |
| 2021 | 623 | 1 | 257 | 634 | | 29 | 69 |
| 2022 (till August) | 531 | 2 | 227 | 706 | | 23 | 81 |
| Total | 3072 | 10 | 1053 | 2999 | 5 | 174 | 403 |

**Conclusion:** This study showed an increase in intentional ingestion of medications in adolescents aged 15-17 years. It is essential that parents monitor the medications in the home, and understand the risks to their children. Poison Centres and other healthcare professionals should undertake education programs for this population.

## 37. Marijuana exposures reported to the US Poison Centers

Saumitra Rege, Will R. Goodrich and Christopher P. Holstege

University of Virginia, Charlottesville, VA, USA;

**Objective:** Marijuana is the most commonly used federally illegal drug in the United States; according to the Centers for Disease Control and Prevention (CDC), 48.2 million people in the US used it at least once in 2019. Long-term or frequent marijuana use has been linked to increased risk of psychosis or schizophrenia in some users. The present study sought to evaluate the recent trends in marijuana exposures reported to the US poison centers (PCs).
**Methods:** The National Poison Data System (NPDS) was queried for marijuana exposures that were reported to the US PCs from 2017 to 2021. We identified and descriptively assessed the relevant demographic and clinical characteristics. Poisson regression models were used to evaluate the trends in the number and rates (per 100,000 human exposures) of marijuana. Percent changes from the first year of the study (2017) were reported with the corresponding 95% confidence intervals (95% CI).
**Results:** Overall, there were 74,070 marijuana-related cases resulting reported to the US PCs during the study period. Single substance marijuana exposures accounted for 59.1% marijuana exposures, with this proportion increasing significantly during the study period (49–66.8%). The proportion of cases from acute care hospitals decreased during the study period (68.6 versus 53.6%). Among cases, ages between 13 and 19 years (24.7%) constituted the most common age group. The proportion of such cases (27.9–20.1%) decreased during the study period. Males accounted for 55.4% cases. Most exposures occurred in a residence. The most frequently co-occurring substances observed with the cases were alcohol (9.7%) and benzodiazepines (8.7%). Intentional abuse (35.1%) and suspected suicides (15%) were the most common reasons for exposure. Among the sample, approximately 12% of the cases were admitted to the critical care unit with majority of the patients being treated, evaluated and released. Serious (major and moderate) effects were seen in 38.6% of cases with the case fatality rate being 1.1%. Fluids/IV was the most common therapy with naloxone used in 5.1% of cases, mostly without prior PC recommendation. Agitation, drowsiness/lethargy and tachycardia were the commonly seen clinical effects. The frequency of marijuana exposures increased by 104.2% (95% CI: 93.6%, 115.3%, $p < 0.001$) while the rate increased by 107.6% (95% CI: 91.2%, 123.3%, $p < 0.001$).
**Conclusion:** The number of marijuana exposure cases handled by the PCs increased significantly. The younger population was most affected by such toxic exposures. PCs can play a key role in the management of such exposures.

## 38. Exposures and suspected intoxications in children aged 0–14 years: real-world data from an Italian reference Poison Control Centre before and during the COVID-19 pandemic

Valentina Brilli[a], Giada Crescioli[a], Francesco Gambassi[b], Andrea Missanelli[b], Alessandra Ieri[b], Cecilia Lanzi[b], Alessandra Pistelli[b], Arianna Totti[b], Alfredo Vannacci[a], Guido Mannaioni[a] and Niccolò Lombardi[a]

[a]Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, University of Florence, Florence, Italy; [b]Medical Toxicology Unit and Poison Control Center, Careggi University Hospital, Florence, Italy

**Objective:** This study describes clinical characteristics of exposures and suspected intoxications in children (0–14 years) managed by an Italian reference Poison Control Centre (PCC).
**Methods:** A 7-year retrospective study was performed on medical records collected in the electronic registry of the Toxicology Unit and PCC, Careggi University Hospital, Florence (Italy). A multivariate logistic regression was used to estimate the odds ratios (ORs) of emergency department (ED) visit or hospitalisation according to the children's demographic and clinical covariates.
**Results:** During the study period (2015–2021) a total of 27,212 phone consultation were managed by the PCC, of which 11,996 (44%) involved subjects aged 0–14 years. Most of the cases occurred in males (54%) aged 1–5 years (73.8%), mainly at home (97.4%), with an oral route of intoxication (93%). Cases were mainly accidental. Consultations were generally requested by caregivers, however, in the age group 12–14 years, 70% of them were requested by healthcare professionals, due to voluntary intoxications. Cleaners (19.4%) and other household products (10.9%), toys (9.3%), cosmetics (8.3%), and plants (7.2%) were the most represented suspected agents. Pharmacological agents accounted for 28.8% of total exposures. Main covariates associated with a higher risk of an ED visit or hospitalisation were voluntary intoxication (OR 29.18 [11.76–72.38]), inhalation route (OR 1.87 [1.09–3.23]), and pharmacological agents (OR 1.34 [1.23–1.46]), particularly central nervous system medications.
**Conclusion:** In most cases, consultations do not burden national and regional healthcare facilities, placing the activity of PCCs as a strategic role in reducing public health spending, even during the COVID-19 pandemic.

## 39. Drug poisoning: data analysis from the Poison Control Center in Florence, Italy (2018–2020)

Francesco Gambassi[a], Guido Mannaioni[b], Cecilia Lanzi[a], Alessandra Pistelli[a], Simone Sartori[b], Andrea Burgalassi[b], Brunella Occupati[b] and Alessandra Ieri[b]

[a]Medical Toxicology Unit and Poison Center, Careggi University Hospital, Florence, Italy; [b]NEUROFARBA Department, Pharmacology and Toxicology Section, University of Florence, Florence, Italy

**Objective:** Poisonings represent a major health problem, as they are an important cause of hospitalization and death and acute

drug intoxications represent an important portion of the total poisoning burden. According to the Annual Reports of the American Association of Poison Control Centers, five classes of drugs rank in the first ten most involved categories in human exposures and account for about 46% of the substances involved in human exposures, with significant increases in the last ten years. Out of these, analgesics (11.0%) represents the top category followed by antidepressants (5.3%), miscellaneous sedative/hypnotics/antipsychotics (5.2%), cardiovascular drugs (4.6%) and antihistamines (4.4%). Drugs occupy eight places in the top ten categories related to intoxication mortality with miscellaneous sedative/hypnotics/antipsychotics (9.7%) ranking first among the causes of fatalities, followed by pharmaceutical and illegal opioid preparations (9.2%), acetaminophen alone (6.3%), calcium antagonists (4.8%) and beta blockers (3.3%). Drug poisonings are increasingly involved in acute intoxications, representing about 40% of the total of involved agents.
**Methods:** The present study analyzed the cases of drug poisonings from the Italian PCC in Florence from 2018 to 2021. The analysis focused on age groups, place and circumstances of exposure, route, symptom severity using the Poison Severity Score (PSS) and the poisoning outcome emerged from the follow-up.
**Results:** Data analysis confirmed the preponderance of drug poisonings (45% of the total). The age classes commonly involved were <1 year (5%), >1–5 years (19%) and 20–50 years (29.9%). Almost all the exposures (86%) occurred at home and by means of the oral route. The modality was voluntary in 38.2% and accidental in 60.9%. Exposure assessment resulted in no symptom (PSS 0) in 53.5%, minor (PSS 1) in 24.5%, moderate (PSS 2) in 14.9%, severe (PSS 3) in 4.7%, and undetermined in 2.3%. Death occurred in 0.19% (11 cases). According to Anatomical Therapeutic Chemical (ATC) classification, the most represented pharmaceutical classes were central nervous system agents in 65%, cardiovascular system agents in 8%, and muscular-skeletal system in 5% of the total.
**Conclusion:** Drug-associated deaths were rare amounting for 11 cases (0.19%), and occurred due to adverse drug reaction in most cases. As regards single drugs, there was a high number of calls related to the use of paracetamol, for which the ages involved and the type of exposure were highlighted. Alprazolam, lorazepam and quetiapine, valproic acid and clonazepam were also greatly involved.

## 40. Self-reported xylazine exposure and experiences: a mixed methods study of Reddit users

Anthony Spadaro[a], Jeanmarie Perrone[a], Lakamana Sahithi[b], Karen O'Connor[a], Rachel Wightman[c], Jennifer Love[d] and Abeed Sarker[b]

[a]University of Pennsylvania, Philadelphia, PA, USA; [b]Emory University, Atlanta, GA, USA; [c]Brown University, Providence, RI, USA; [d]Mount Sinai Health System, New York City, NY, USA

**Objective:** Xylazine is an alpha-2 agonist utilized as a veterinary sedative and increasingly prevalent in the illicit drug supply [1]. The anonymity of the Reddit social media forum provides a hub for the open discussion of substance use experiences [2]. Our objectives were to curate information about xylazine through social media from People Who Use Drugs (PWUDs). Specifically, we queried to answer the following: (1) what are the demographics of Reddit users exposed to xylazine? (2) is xylazine a desired additive? and (3) what effects of xylazine are PWUDs experiencing?
**Methods:** Natural Language Processing (NLP) was used to retrieve mentions of "xylazine" from posts by Reddit subscribers who also posted on opioid-related subreddits. Posts were qualitatively evaluated for xylazine-related themes. A survey was developed to gather demographic information, use patterns of other drugs, and experiences with xylazine. This survey was posted on subreddits that were identified by NLP to contain xylazine-related discussions from March 2022 to October 2022 to recruit subscribers to participate via a survey link. This study was exempted from Institutional Review Board review by the authors' institution.
**Results:** NLP was utilized to extract 76 posts mentioning xylazine from 765,616 posts by 16,131 Reddit users (January 2018 to August 2021). Redditors described xylazine as an unwanted adulterant in their opioid supply. Overall, 58 participants completed the survey. Of those that disclosed their location, 22/43 (51%) participants reported locations in the Northeastern United States. The most common patterns of xylazine use were via intranasal administration (36%) and mixed with other drugs intravenously (30%). Of participants who responded 29/56 (51%) reported experiencing xylazine withdrawal; common withdrawal symptoms included anxiety, depression and insomnia. Frequent adverse events reported were prolonged sedation (45%) and increased skin wounds (24%).
**Conclusion:** Among respondents on these Reddit forums, xylazine appears to be an unwanted adulterant. PWUDs may be experiencing negative side effects such as prolonged sedation and xylazine withdrawal characterized by anxiety and insomnia. This appeared to be a more common problem in the Northeast and among people who self-report fentanyl use.

### References

[1] Kariisa M, Patel P, Smith H, et al. Notes from the field: xylazine detection and involvement in drug overdose deaths – United States, 2019. MMWR Morb Mortal Wkly Rep. 2021;70:1300–1302.
[2] Spadaro A, Sarker A, Hogg-Bremer W, et al. Reddit discussions about buprenorphine associated precipitated withdrawal in the era of fentanyl. Clin Toxicol. 2022;60:694–701.

## 41. Circumstances of acute occupational exposure to acids and alkalis reported to the Dutch Poisons Information Center

Anja P. G. Wijnands[a], Irma de Vries[a], Tim Verbruggen[a], Maxim Carlier[a], Dylan W. de Lange[a,b] and Saskia J. Rietjens[a,b]

[a]Dutch Poisons Information Center, University Medical Center Utrecht, University Utrecht, Utrecht, The Netherlands; [b]Department of Intensive Care Medicine, University Medical Center Utrecht, University Utrecht, Utrecht, The Netherlands

**Objective:** Hazardous substances at the workplace can cause a wide variety of occupational incidents. Acids and alkalis are often involved in acute occupational exposures. Insight into the circumstances of workplace incidents is important for occupational health and safety management.
**Methods:** From 1 September 2020 to 31 August 2021 a prospective study on acute occupational exposure to acids and alkalis reported to the Dutch Poisons Information Center was performed. Data on the circumstances and causes of the incident, the exposure(s), clinical course and treatment, were

collected by a telephone survey with victims, using a standardized questionnaire.
**Results:** We interviewed 108 patients (65% male, 35% female, median age 33 years, range 16–63 years). Patients were often exposed via multiple routes. Dermal contact was the most common route of exposure (42%), followed by ocular contact (37%) and inhalation (25%). Overall, 56 patients were exposed to an acid and 52 to an alkali. Acids most often involved were nitric acid ($n = 11$), hydrochloric acid ($n = 8$), hydrogen fluoride ($n = 7$) and sulphuric acid ($n = 7$). Alkalis most often involved were sodium hydroxide ($n = 31$) and potassium hydroxide ($n = 13$). After dermal contact, redness (24%) and pain (23%) were often reported. The most commonly reported symptoms after eye contact were pain in the eyes (27%), irritation (21%) and (temporary) loss of vision (15%). Inhalation most commonly resulted in pain in mouth and/or throat (12%) or dyspnea (10%). The majority of the patients reported mild to moderate health effects that recovered quickly (75% within one week), which can possibly be explained by prompt decontamination as a first-aid measure. Most incidents occurred in the business classes industry (31%), accommodation, provision of meal and drinks (13%) and agriculture (12%). Exposure often occurred during cleaning activities (51%). The main root causes of these incidents were technical factors such as damaged packaging (28%) and defective apparatus (10%), organizational factors such as lack of work instructions (42%) and poor communication or planning (32%), and personal factors such as disregarding work instructions (12%), not (adequately) using personal protective equipment (19%) and personal circumstances (59%) such as inaccuracy, time pressure or fatigue.
**Conclusion:** Poison Control Center data are valuable for the identification of risk factors in acute occupational exposure. Insight into the technical, organizational and personal factors leading to exposure, can be helpful in developing risk mitigation measures to reduce the risk of occupational exposure in the future.

## 42. Reports on occupational poisoning cases with detergents and cleaning agents to the German Federal Institute for Risk Assessment from 2012 to 2021

Kathrin Begemann, Nina Glaser, Michael Reuser and Herbert Desel

German Federal Institute for Risk Assessment, Berlin, Germany

**Objective:** Under the national Chemicals Act, the German Federal Institute for Risk Assessment (BfR) receives reports on poisonings with chemical substances or products from physicians and statutory accident insurances and employer's liability insurances. All cases notified to the BfR are validated and registered in a standardised manner in BfR's national poisonings database. Severity is assessed according to the Poisoning Severity Score (PSS) and a product category recorded according to the TKS category system of the German Society for Clinical Toxicology or the European Product Categorisation System (EuPCS) is assigned to all agents.
**Methods:** All cases with detergents and cleaning agents registered between 2012 and 2021 were analysed for patient data, categories of products involved, route of exposure and the clinical course.
**Results:** In the years 2012–2021, BfR received a total of 57,414 notifications of poisoning. In 11,192 (19.5%) of these cases, detergents and cleaning agents were the cause of the poisoning; 10,996 of the 11,192 reports received from the statutory accident insurances and employer's liability insurances describing occupational accidents. Of these 159 cases (1.4%) were medically treated because of a poisoning concern but no symptoms were reported. The majority of the patients suffered minor symptoms only (9,206; 83.7%). The proportion that developed poisoning (PSS moderate in 904 cases and PSS severe in 14 cases) was 8.3%. In 713 (6.5%) cases the severity could not be assessed. In terms of poisonings with detergents and cleaning agents the proportions of eye exposures and dermal exposures were particularly high at 6,987 (63.5%) and 3,347 (30.4%), respectively. Inhalation (618; 5.6%) and oral (239, 2.2%) exposures to detergents and cleaning agents tend to play a subordinate role in the notifications to BfR. In 16 cases the route of exposure was not reported. Multiple entries are possible. In 3,739 cases (34.0%) the cleaning agent could not be determined in detail, followed by 2,404 cases (21.9%) with cleaning agents for special types of dirt such as limescale or rust remover, label removal, etc. In 1,108 cases (10.1%), there was an exposure to cleaning agents for the kitchen, closely followed by bathroom and sanitary cleaning agents (1,104, 10.0%).
**Conclusion:** It is already known that poisoning with detergents and cleaning agents are very common in the home. The data from BfR show that occupational poisonings are also common with this product group. The majority of cases progress with only minor health problems.

## 43. A protracted, low dose dermal exposure and a short-lasting, high dose dermal exposure to aniline caused methaemoglobinaemia in two workplace accidents at the same facility

Anja J. Huusom[a], Kristian Andersen[b], Steen K. Barnung[b] and Lotte C. G. Høgberg[c]

[a]Department of Occupational and Environmental Medicine, Danish Poisons Information Centre, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [b]Department of Anaesthesiology, Centre of Head and Orthopaedics, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark; [c]Department of Anaesthesia and Intensive Care, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** Aniline is a highly toxic compound used in the production of plastics, dyes, and pharmaceuticals. Dose-response data on aniline-induced methaemoglobinaemia following inhalation, ingestion or dermal exposure are sparse.
**Case series:** Case 1. At 9–10 am a 24-year-old male technician replaced a heat-exchanger mounted on a tank containing aniline (100%) and nitrogen. He wore chemical resistant protective suit and gloves, and a light filter mask. At 12.15 pm, a colleague noticed his cyanotic appearance. On hospital arrival at 1 pm, he was awake/aware, blood pressure 120/60 mmHg, heart rate 60/min, respiratory rate 25/min, oxygen saturation 98% (oxygen supply 15L/min); a $2 \times 5$cm skin lesion between glove and suit was observed, and decontamination was performed. Initial arterial blood gas showed methaemoglobinaemia, 31%, 3–4 hours post-exposure (Table 1). Intravenous methylene blue, 2 mg/kg, immediately reduced the methaemoglobin to 22%. Case 2. At 4 pm a 44-year-old male technician performed a routine check on a tank-level monitor in a supposedly empty aniline tank; he did not wear a chemical resistant protective suit. The pressure from the partially filled aniline tank caused 1–2 L aniline (100%) to

Table 1. Time-line and relevant arterial blood gas data in two patients with aniline exposure at the same workplace.

| | | Case 1 (exposed 9–10 am) | | | Case 2 (exposed 4 pm) | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Reference | 1.01 pm | 1.47 pm | 4.27 pm | 6.11 pm | 6.55 pm | 8.26 pm | 10.15 pm |
| Haemoglobin | 8.3–10.5 mmol/L | 8.8 | 8.2 | Not measured | 9.1 | 8.9 | 8.7 | 8.7 |
| Methaemoglobin | <0.02 | 0.308 | 0.223 | 0.04 | 0.13 | 0.15 | 0.13 | 0.09 |
| Oxyhaemoglobin (Fe, total arterial blood) | 0.92–0.99 | 0.69 | 0.78 | Not measured | 0.84 | 0.85 | 0.86 | 0.90 |
| Oxygen saturation, (Hb, POC) | 0.92–0.99 | 0.98 | 0.99 | Not measured | 0.97 | 0.99 | 0.99 | 0.99 |
| $pO_2$ | 9.6–13.7 kPa | 44.8 | Report not possible | Not measured | 12.9 | 30.8 | Not measured | Not measured |
| Base excess | −1.5 to 3.0 | 0.0 | −0.7 | Not measured | −0.7 | −0.4 | 1.6 | 2.0 |
| Lactate | 0.7–2.1 mol/L | 0.6 | 0.5 | Not measured | 0.5 | 0.6 | 0.7 | 0.5 |
| pH | 7.37–7.45 | 7.41 | 7.46 | Not measured | 7.42 | 7.39 | 7.41 | 7.40 |

contaminate his left forearm, his bare neck and chin. The estimated total exposure time was 25 seconds until he was fully decontaminated under a newly installed showerhead close by. On arrival, his lips and fingers were cyanotic. Initial arterial gas showed methaemoglobin 13% which peaked at 15% at 7 pm. Treatment was oxygen 10L/min, and he was discharged at 11 pm.

**Conclusion:** Aniline is readily absorbed via dermal exposure; small but protracted exposures or large, short-term exposures can lead to a significant methaemoglobinaemia. The importance of prompt decontamination was emphasised. Although the first case increased the awareness of dermal absorption and the time to decontamination in the subsequent case was significantly reduced, further risk reduction management may reduce future accidental aniline exposures.

## 44. Why does this gas keep killing??? Rotten egg smell does not protect you!

Paula E. C. Hammer[a] and Lotte C. G. Høgberg[b]

[a]Department of Occupational and Environmental Medicine, Danish Poison Information Centre, Copenhagen, Denmark; [b]Department of Anaesthesia and Intensive Care, Danish Poison Information Centre, Copenhagen, Denmark

**Objective:** Biological degradation of sulfur-containing products produces hydrogen sulfide ($H_2S$, also known as "sewer gas"), a colorless gas, denser than air, and highly toxic. It is characterized by its rotten egg odor (corresponding to air concentrations of 0.02–0.15 ppm). Concentrations around 20–50 ppm cause local irritation of mucous membranes in the eyes and nose, but when the air concentration reaches 100–150 ppm, the olfactory nerve is paralyzed and the ability to smell the gas is eliminated. The objective of this study is to identify preventable cases of $H_2S$ poisoning at workplaces through data from the Danish Working Environment Authority (DWEA) and the Danish Poison Information Center (DPIC).

**Methods:** Review of cases of serious work safety issues and workplace accidents involving $H_2S$ registered by the DWEA between 2017 and 2022 and contacts to the DPIC regarding $H_2S$ poisoning between 2011 and 2022.

**Results:** We identified 39 contacts to the DPIC regarding moderate/severe $H_2S$ poisoning ($n = 41$ exposed workers) and 14 contacts regarding life-threatening $H_2S$ poisoning ($n = 24$ exposed workers), resulting in 4 lethal cases of $H_2S$ poisoning. DWEA inspections identified 52 cases of serious work safety issues in workplaces, where workers were at risk of being exposed to toxic levels of $H_2S$, and 9 cases of life-threatening $H_2S$ poisoning (3 of these cases overlapped with contacts to DPIC). Most of the cases involved men aged 30–50 years old and occurred primarily in swine farms and the fishing industry. Based on the information available on the circumstances of the poisoning episodes (from DWEA reports or the DPIC database) most of the workers involved in the accidents were aware of the potential risk of $H_2S$ poisoning prior to the work task. In many cases the workers thought that they would be able to avoid poisoning by smelling rotten egg odor or noticing the occurrence of red eyes.

**Conclusion:** Despite being known as a deadly toxin since the 17th century [1] $H_2S$ is still the cause of lethal poisoning at Danish workplaces. This indicates an urgent need for preventive measures, especially because these accidents may be prevented by relatively simple safety measures as the use of a $H_2S$-alarm and a face mask with a fresh air supply. Future potential preventive measures and collaboration with authorities and relevant labour organizations in Denmark may add further to risk reduction of this "old fashioned" poisoning.

### Reference

[1] Szabo C. A timeline of hydrogen sulfide ($H_2S$) research: from environmental toxin to biological mediator. Biochem Pharmacol. 2018;149:5–19.

## 45. Isolated nicotinic toxicity and urinary discoloration following unintentional pediatric carbaryl ingestion

Marlis Gnirke[a], Joshua Bloom[a], Ramya J. Sivasubramanian[a], David Sardar[a], Anna Mai[b], Samara Soghoian[a], Robert S. Hoffman[a] and Sage W. Wiener[c]

[a]Ronald O. Perelman Department of Emergency Medicine, Division of Medical Toxicology, NYU Grossman School of Medicine, New York City, NY, USA; [b]Department of Pediatrics, SUNY Downstate Health Sciences University, New York, NY, USA; [c]Department of Emergency Medicine, SUNY Downstate Health Sciences University, New York, NY, USA

**Objective:** Carbaryl is a carbamate pesticide. Carbamylation of acetylcholinesterase leads to accumulation of acetylcholine in synapses and typical clinical manifestations result from excessive stimulation of muscarinic and nicotinic cholinergic receptors. We report a case of unintentional pediatric carbaryl ingestion resulting in clinical signs of nicotinic excess in the absence of signs of muscarinic excess.

**Case report:** A 5-year-old girl was unintentionally served cereal mixed with an initially unidentified "rodenticide." The patient developed abdominal pain approximately one hour later,

followed by diffuse tremors over the next few hours. On arrival to the emergency department approximately 10 hours following ingestion, vital signs were remarkable for tachycardia (heart rate 168/minute) and physical examination was remarkable for fasciculations of the tongue, chest and abdominal walls, and extremities. There were no muscarinic signs or symptoms. Approximately 20 hours following ingestion the "rodenticide" was identified to be "Sev7en®," a powdered pesticide composed of 85% carbaryl. By this time the patient's abdominal pain and fasciculations had resolved without intervention. One day post-ingestion the patient's urine was noted to be a dark green/brown. Urinary discoloration resolved with subsequent voids and the patient was discharged at her neurologic baseline. Subsequent quantitative serum analysis confirmed exposure with a carbaryl concentration of 31 ng/mL and 1-naphthol concentration of 940 ng/mL.

**Conclusion:** We report an unusual presentation of isolated nicotinic toxicity following carbaryl ingestion. Prior to identification of the ingested "rodenticide," acetylcholinesterase inhibitor poisoning was considered unlikely in this patient given the absence of muscarinic signs. Upon subsequent product identification, the patient's presenting tachycardia and fasciculations are consistent with expected nicotinic excess, however she never displayed any signs or symptoms of muscarinic excess. We note the green/brown urinary discoloration as a second interesting clinical finding in this case. Similar urinary discoloration has been reported following carbofuran ingestion and was believed to be due to phenolic metabolites [1]. 1-Naphthol is a major urinary metabolite in carbaryl metabolism and is a possible cause for the urinary discoloration observed in this case [2].

## References

[1] Viswanathan S, John A. Common poison, uncommon urine. Nephrology. 2011;16:617–618.

[2] Best EM Jr, Murray BL. Observations on workers exposed to Sevin insecticide: a preliminary report. J Occup Med. 1962;4:507–517.

# 46. Evaluation of biocidal product enquiries to the Austrian Poisons Information Centre, 2020

Tara Arif and Dieter Genser

Poisons Information Centre, Vienna, Austria

**Objective:** Biocidal products are substances or mixtures 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. There are 4 main groups of biocidal products: disinfectants, preservatives, pest control and other biocidal products. We reviewed enquiries received by our Poison Centre in 2020.

**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 2020.

**Results:** In 2020 the Austrian PIC received 28,229 telephone enquiries in total. Regarding biocidal product exposure the PIC was contacted in 1335 cases: 626 patients (46.9%) were under the age of 15, and 709 (53.1%) persons aged from 15 years and above. In 1144 cases, a poisoning could be excluded due to minor exposure. In 52 cases the risk of intoxication could not be estimated as there was not sufficient information available at the time of the consultation. In 115 cases intoxication was suspected and medical observation was recommended. In only 24 patients (including one child) intoxication was diagnosed based on the severity of the symptoms. The causative substances were chemical disinfectants ($n = 14$), chlorine gas ($n = 4$), industrial chemicals ($n = 3$) and various other chemicals ($n = 3$). No deaths were reported to the local PIC.

**Conclusion:** In relation to the total number of calls, enquiries regarding biocidal products are relatively rare. The number of human intoxications seems to be small; severe symptoms occurred in only 24 cases, which had to be treated medically.

# 47. Impact of plasma concentrations of glyphosate, its metabolite and polyethoxylated tallow amine surfactants on clinical outcomes following glyphosate poisoning

Shuping Qiang[a,b], Fahim Mohamed[c,d], Nicholas A. Buckley[e], Lorraine Mackenzie[a,b] and Michael S. Roberts[a,f]

[a]University of South Australia Clinical and Health Sciences, University of South Australia, Adelaide, Australia; [b]Therapeutics Research Centre, Basil Hetzel Institute for Translational Health Research, The Queen Elizabeth Hospital, Adelaide, Australia; [c]South Asian Clinical Toxicology Research Collaboration, University of Peradeniya, Peradeniya, Sri Lanka; [d]Department of Pharmacology, Faculty of Medicine and Health, Sydney Pharmacy School, University of Sydney, Sydney, Australia; [e]Faculty of Medicine and Health, Translational Australian Clinical Toxicology (TACT) Research Group, Biomedical Informatics and Digital Health, The University of Sydney, Sydney, Australia; [f]Therapeutics Research Centre, The University of Queensland Diamantina Institute, The University of Queensland, Brisbane, Australia

**Objective:** Common major co-formulants in glyphosate-based herbicides, polyethoxylated tallow amine (POEA) surfactants, initially thought to be inert, are contributing to glyphosate toxicity in humans. However, there is limited information about the utility of plasma concentrations of POEAs for predicting clinical outcomes. POEAs are not present in glyphosate products in Europe due to ongoing concerns about their potential toxicity, but they are still commonly used in many glyphosate-based herbicides globally. Our objective was to investigate if plasma concentrations of glyphosate, its metabolites and POEAs are predictive of severe acute kidney injury (AKI) and mortality following acute glyphosate poisoning.

**Methods:** Overall 151 patients (median age 30 years, IQR 23–40) with acute glyphosate poisoning providing multiple samples between October 2010 and January 2013 were enrolled. Severity of poisoning was graded based on clinical staging. More than 500 plasma samples were analysed for concentrations of glyphosate, its metabolite aminomethylphosphonic acid (AMPA) and POEAs using liquid chromatography-tandem mass spectrometry (LC-MS/MS). A subset of 67 patients were enrolled in a nephrotoxicity study. AKI was defined using the Kidney Disease: Improving Global Outcomes (KDIGO) classification. Associations between plasma concentrations and severity of poisoning were examined. These samples were part of an on-going large biobank exploring different research hypotheses in pesticide poisoning. The results regarding mortality were based on 151 patients, and the results regarding AKI were based on the renal biomarker cohort ($n = 67$).

**Results:** Admission plasma concentrations of glyphosate and AMPA displayed excellent performance in predicting AKI $\geq 2$ with an area under the curve (AUC)-receiver operating characteristic

(ROC) of 0.88 (95% CI 0.77–0.98) and 0.93 (95% CI 0.83–1.00), respectively. POEAs with unsaturated (u) tallow moieties are good indicators for predicting AKI ≥2 (AUC ≥0.7), among which $C_{18}u(EO)_{11}$ yielded the highest AUC-ROC of 0.94 (95% CI 0.77–1.00). There was a trend that the tallow moieties having smaller numbers of repeating ethoxylate (EO) units being a stronger association with AKI ≥2 than those with longer EO chains although only $C_{18}u(EO)_{11}$ gave significantly elevated odds ($C_{18}u(EO)_{10}$: OR 1.439, 95% CI 0.9591–2.978; $C_{18}s(EO)_{10}$: OR 1.532, 95% CI 0.4357–6.019; $C_{18}u(EO)_{11}$: OR 1.222, 95% CI 1.009–1.848; $C_{18}u(EO)_{12}$: OR 1.185, 95% CI 0.9864–1.722; $C_{18}u(EO)_{14}$: OR 1.103, 95% CI 0.9481–1.387). Glyphosate and AMPA were excellent predictors of mortality with an AUC-ROC of 0.99 (95% CI 0.98–1.00) and 0.92 (95% CI 0.83–1.00), respectively. POEAs were only detected in one out of four fatal cases, with concentrations ranging from 8.5 ng/mL for $C_{18s}(EO)_{10}$ to 49.2 ng/mL for $C_{18}u(EO)_{11}$, which were higher than those in survivors.
**Conclusion:** Glyphosate and AMPA concentrations were excellent predictors of both AKI ≥2 and mortality following glyphosate poisoning. One of the POEA surfactants, $C_{18}u(EO)_{11}$, was predictive of the development of AKI ≥2. More research with larger samples sizes is required to better understand POEA-related glyphosate toxicity and guide treatment.

## 48. Death of two infants due to misuse of a pesticide product

Esther Feistkorn, Nina Glaser, Michael Reuser and Kathrin Begemann

German Federal Institute for Risk Assessment, Berlin, Germany

**Objective:** Some metal phosphides are used as rodenticides, such as aluminium phosphide, magnesium phosphide or zinc phosphide. The metal phosphides react by hydrolysis to phosphine ($PH_3$). Phosphine is acutely toxic and inhalation or ingestion can cause severe intoxication. Poisoning occurs mostly by inhalation. The German Federal Institute for Risk Assessment (BfR) maintains a case database for intoxications reported by physicians. Poisoning data reported to BfR is used to fulfill the European reporting obligations for poisonings with biocides [(EU) No 528/2012] and plant protection products [2009/128/EG]. An incident involving two children was selected to illustrate poisonings with phosphine due to misuse of a pesticide product.
**Case reports:** Two infants were found lying lifeless in their beds in the early morning. The brother of the two siblings called the emergency services. The emergency doctor could only determine the death of the two infants. Phosphine was detected during measurements carried out in the house. The father stated that he had previously applied aluminium phosphide-containing rodenticide to several mouse holes in the flat. This work resulted in a chemical reaction in the form of the release of phosphine as a result of possible misuse. Already during the night, an emergency doctor had been called because of the children's nausea, vomiting and diarrhoea. Appropriate medication had been prescribed. The results of the autopsy report support the suspicion of intoxication with phosphine.
**Conclusion:** For good reason, pesticides containing metal phosphide are only sold to competent professional users and only to be used by trained specialists or under their supervision and in strict compliance with country-specific regulations. The application of these products is only permitted outdoors. In the case reports described, misuse of the product occurred in the way it was used and applied. Infants and young children are known to be more susceptible than adults to the toxic effects of pesticides. The cases are passed on in accordance with the international reporting obligations and thus support the chemical evaluation of the EU.

## 49. Paraquat poisoning exposures: a South African Poisons Information Helpline experience

Catharina E. Du Plessis[a], Carine J. Marks[a] and Cindy R. Stephen[b]

[a]Stellenbosch University, Cape Town, South Africa; [b]University of Cape Town, Cape Town, South Africa;

**Objective:** Paraquat, a non-selective herbicide, is highly toxic to humans. Although the lungs are the main target organ, ingestion of 20–30 mL can cause multi-organ failure within 24 hours. Currently, no effective treatment is available, resulting in a high mortality rate [1]. Agricultural pesticide poisonings play a major role in the global burden of suicide [2]; however, literature on the incidence of paraquat exposures on the African continent is limited. Therefore, the aim of this study is to describe the incidence of paraquat poisoning exposures as received by the Poison Information Helpline, Western Cape (PIHWC), South Africa.
**Methods:** We conducted a retrospective review of calls to the PIHWC related to paraquat exposures during a six-year period (January 2016 – December 2021). All human-related paraquat poisoning exposure data collected were extracted from the database, excluding repeat calls concerning the same case. Key variables included patient demographics, circumstances of exposure, clinical presentation, severity of clinical features according to the Poisoning Severity Score (PSS) and outcomes.
**Results:** There were 117 human-related paraquat exposures received by the PIHWC. The majority of the exposures were received from state hospitals, 98 patients (83.8%), involving 94 adults (80.3%), and 81 male patients (69.2%). Overall, almost two-thirds (61.5%) of the ingestions were intentional, including 15 (88.2%) adolescent exposures. Vomiting was the symptom most often recorded, in 53 (45.3%) cases. Other symptoms included oesophageal discomfort (40; 34.2%), oral lesions (14; 12.0%), renal impairment (16; 13.7%) and respiratory compromise (17; 14.5%). At the time of the calls, most patients (61; 51.3%) had mild resolving symptoms (PSS1) with 15 patients (12.8%) having severe or life-threatening symptoms and signs (PSS3). Four deaths were recorded, including one child.
**Conclusion:** Paraquat poisoning cases were seldom followed up, which might have resulted in an underestimation of the true mortality rate of this study. Also, all poisoning cases are not reported to the PIHWC, therefore the incidence of paraquat poisoning in South Africa may be much higher than the study indicated. Improved safety measures across several regulatory authorities should be put in place, to limit exposures and prevent self-harm.

## References

[1] Gawarammana IB, Buckley NA. Medical management of paraquat ingestion. Br J Clin Pharmacol. 2011;72:745–57.
[2] Mew EJ, Padmanathan P, Konradsen F, et al. The global burden of fatal self-poisoning with pesticides 2006–15: systematic review. J Affect Disord. 2017;2:93–104.

## 50. Consultations regarding plant protection products 2019 – 2021 to the Austrian Poisons Information Centre

Tara Arif and Helmut Schiel

Poisons Information Centre, Vienna, Austria

**Objective:** Plant protection products (PPP) are pesticides and weed killers used to protect crops. According to the Plant Protection Products Act, plant protection products are only approved if there are no direct or indirect harmful effects on human or animal health, no unacceptable effects on the environment and the plants and plant products to be protected. The aim of this study was to analyse the Austrian Poisons Information Centre (PIC) consultations regarding circumstances and symptoms after PPP exposure.
**Methods:** A retrospective and descriptive analysis of enquiries to the PIC concerning PPP exposures in humans 2019–2021 was conducted. Cases of acute exposures were analysed according to the age of the affected persons, symptoms, course of the events, and Poisoning Severity Score (PSS) at the time of PIC consultation.
**Results:** In total, 129 PPP exposures were extracted from the database. Twelve animal and 6 human cases were excluded because there was no correlation between exposure and symptoms and one patient was additionally exposed to a grill cleaner. Thus, 110 cases could be evaluated. The distribution across years was homogeneous (2019 $n = 35$, 2020 $n = 35$, 2021 $n = 40$). In the paediatric group 42 children (5 months to 9 years of age, one unknown) were involved. In all cases, the exposures were accidental. Exposures involved mainly dermal ($n = 6$) and oral contact ($n = 35$, including one patient with oral and dermal contact). Additionally, there was one ocular contact and one inhalation. In total 39 children had no symptoms (PSS 0) and three patients had mild symptoms (PSS 1: vomiting $n = 2$, skin rash $n = 1$). In 68 adults (17–91 years of age, 17 unknown) the exposure was unintentional ($n = 59$), suicidal ($n = 5$) or had other reasons ($n = 4$). Exposures involved inhalation ($n = 32$), oral ($n = 19$), dermal ($n = 17$), and ocular ($n = 11$) contact. Few adults ($n = 11$) had multiple routes of exposure. There were no symptoms in 25 cases. Symptoms were mild in 39 cases with the following symptoms: dysgeusia, numbness of the tongue, gastralgia, mucous membrane irritation, nausea, dizziness, vomiting, diarrhoea, paraesthesia, muscle fasciculation, headache, dyspnoea, hypersalivation and eye irritation. There were only two moderate cases, caused by zinc phosphide and dimethoate. The only severe case was caused by an automatic fogger with pyrethroid.
**Conclusion:** In total there are few enquiries regarding plant protection products to the Austrian PIC. Evaluation from 2019 to 2021 shows that there is no significant fluctuation. Moderate and severe cases are rare.

## 51. Bromoxynil and 2-methyl-4-chlorophenoxyacetic acid (MCPA) poisoning resulting in death

Pramod Chandru and Dushan Jayaweera

Department of Clinical Pharmacology & Toxicology, Western Sydney Health, Sydney, Australia

**Objective:** Deaths due to combination of bromoxynil and MCPA have been noted with increasing frequency. Uncoupling of oxidative phosphorylation leads to hyperthermia, increased carbon dioxide ($CO_2$) production and acidosis [1]. As the underlying process of poisoning cannot be reversed treatment options include interventions aimed at cooling by intubation and paralysis together with enhanced elimination with urinary alkalinisation and dialysis [2]. Both intubation with paralysis and urinary alkalinisation could lead to increasing $CO_2$ levels with worsening acidosis and contribute to mortality. We present a fatal case of poisoning with these herbicides.
**Case report:** A 62-year-old male ingested 150 mL of a weed killer containing bromoxynil 200 g/L, MCPA 220 g/L and a solvent hydrocarbon 343 g/L. He presented to the emergency department (ED) 2 hours post overdose with Glasgow Coma Score 15, temperature 36.9 °C, heart rate 75 bpm, blood pressure 171/89 mmHg, respiratory rate 18/min and diaphoresis. A venous blood gas taken 3.5 hours post ingestion showed a pH 7.43, $pCO_2$ 34 mmHg, bicarbonate 21 mmol/L, base excess −1, and lactate 3.2 mmol/L. Urinary alkalinisation was commenced in the ED and the patient transferred to the intensive care unit for urgent haemodialysis. Six hours following the overdose, post insertion of vascular access for dialysis, he complained of feeling hot and became agitated needing intubation and ventilation. Rapid sequence induction was used with propofol 100 mg, fentanyl 100 mcg and rocuronium 100 mg. The ventilator mode was set to Synchronized Intermittent Mandatory Ventilation (SIMV), $FiO_2$ 100%, pressure support 10 mmHg, post end expiratory pressure 10 mmHg, tidal volume 500 mL, respiratory rate 12/min with minute ventilation 7 L/min. Sustained low-efficiency dialysis (SLED) was commenced after intubation. Around 45 minutes following intubation he had an asystolic cardiac arrest with a peri-arrest end tidal $CO_2$ of 151 mmHg. Resuscitation was unsuccessful.
**Conclusion:** Ventilatory adjustment to match increased $CO_2$ production is an important consideration in intubated and paralysed patients with bromoxynil and MCPA poisoning.

### References

[1] Berling I, Buckley NA, Mostafa A, et al. 2-Methyl-4-chlorophenoxyacetic acid and bromoxynil herbicide death. Clin Toxicol. 2015;53:486–488.
[2] Chiew AL, Page CB, Clancy D, et al. 2-Methyl-4-chlorophenoxyacetic acid (MCPA) and bromoxynil herbicide ingestion. Clin Toxicol. 2018;56:377–380.

## 52. Case series of acute 4,6-dinitro-o-cresol (DNOC) self-poisoning

Gordana Vukovic Ercegovic, Natasa Perkovic Vukcevic, Olivera Potrebic, Jasmina Jovic Stosic, Dragana Djordjevic, Milica Zlatkovic and Slavica Vucinic

National Poison Control Center, Military Medical Academy, Belgrade, Serbia

**Objective:** 4,6-Dinitro-o-cresol (DNOC), a yellowish crystalline solid used as a pesticide, is highly toxic to humans. It is banned in many countries, including Serbia. Despite that, sporadic cases of acute poisonings indicate that quantities of unused substances exist, especially in rural households. The mechanism of toxicity for DNOC is based on uncoupling of oxidative phosphorylation reducing adenosine triphosphate (ATP) and increasing heat production leading to the characteristic clinical manifestations. We present six patients with acute DNOC poisoning admitted in the

Table 1. Clinical overview in six patients with acute DNOC intoxication.

| Case | Age, sex | Time to presentation (h) | On admission | Vital signs | Blood DNOC on admission (mg/L) | Management | Outcome |
|---|---|---|---|---|---|---|---|
| 1 | 53, M | 6 | Confused, agitated | Tachycardia (115/min), tachypnea, hyperthermia (39 °C) | 8.43 | Full resuscitation including cooling | Died 1 h after presentation |
| 2 | 65, F | 4 | Somnolent | Tachycardia (120/min), hypotension (70/45 mmHg), 37.8 °C | 41.0 | Full resuscitation | Died 7h after presentation |
| 3 | 31, F | 4 | Confused, agitated, flushed | Tachycardia (140/min), tachypnea, extreme hyperthermia (41 °C) | 6.28 | Full resuscitation including cooling | Died 5 h after presentation |
| 4 | 28, M | 4 | Asymptomatic | Within normal limits | 3.5 | Gastric lavage, IV fluids, observation | No signs of toxicity |
| 5 | 43, M | 3 | Nausea | Within normal limits | 20.1 | IV fluids, observation | Self-discharged without signs of toxicity 24 h after admission |
| 6 | 46, F | 3 | Vomiting | Within normal limits | 40.5 | IV fluids, hemodialysis, observation | Full recovery |

Department of Clinical Toxicology in Belgrade, over a 10 year period.

**Case series:** Six patients, all from suburban and rural areas, were presented with a clear history of DNOC ingestion in a suicide attempt within 6 hours (Table 1). Ingested doses could not be determined. Although characteristic yellow discoloration of skin was noted in all cases, in patients with lethal outcome it was quite marked. DNOC in blood was confirmed in all cases using high-performance liquid chromatography/photodiode array detector (HPLC-PDA), but concentrations ranged widely and did not appear related to clinical course, symptom severity or outcome. Rapid course, unresponsiveness to therapy and cardiopulmonary resuscitation (CPR) with early onset of rigor mortis were recorded in deceased patients. Hemodialysis was performed in one patient (Case 6) that fully recovered. In other cases, especially those with significant manifestations it could not be performed due to unavailability or rapid deterioration and lethal outcome (Case 1).

**Conclusion:** The fact that DNOC is still available and the findings of this limited case series that blood concentration was not clearly related to survival, suggest a need for defining indications for potential efficient use of extracorporeal treatments.

## 53. Hydrogen cyanamide exposure: a case series study from Italy

Monica Carnovale[a], Lucia Bernaconi[a], Davide Lonati[b], Azzurra Schicchi[b], Valeria M. Petrolini[b], Benedetta Brolli[a], Valentina Negrini[a], Olha Maystrova[b], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS. Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Hydrogen cyanamide (HC), a plant regulator used to promote budding from dormant plants, was introduced in Italy (as DORMEX®) in 2000, but was removed from the Italian market in April 2008 [1] because of its toxicity; it remains available elsewhere. HC inhalation/dermal exposure may cause severe irritation/caustic burns and severe clinical manifestations when ingested. It inhibits aldehyde dehydrogenase, carrying the risk of a disulfiram-like reaction with concomitant alcohol. We studied the epidemiology of HC exposure in Italy.

**Methods:** We retrospectively evaluated all HC exposures, referred to our Poison Control Centre (PCC) (January 2007–December 2021). For each case: age, sex, exposure route/year, geographical location, intent of exposure, alcohol co-ingestion, Poisoning Severity Score (PSS) at emergency department admission, symptoms, treatment, outcome were analyzed.

**Results:** Twenty-four subjects (95.8% males; median age 47.6 years) were included; 41.6% of patients also co-ingested alcohol. All exposures were unintentional and occurred at work; 92% of cases occurred in Sicily ($n = 22$). On average there was 1 case/year (1–4) with 79.2% of cases after market withdrawal. Mean PSS at presentation was 1.54, ingestion was associated with more severe PSS (3 in the 66.6% of ingestion cases). Clinical symptoms (Table 1), depended on exposure route and alcohol co-ingestion. All patients were treated symptomatically and fully recovered.

**Conclusion:** Despite market withdrawal, HC is still used in parts of Italy and efforts should be made by local authorities to prevent its illegal use. PCCs have a crucial role in surveillance of exposure to hazardous agricultural products. HC exposure can lead to severe health effects both with acute exposure or due to an interaction with alcohol interaction. Awareness of the risk should be increased in countries which still use HC to improve safety measures.

### Reference

[1] The Official Gazette of the Italian Republic. Revocation of the plant protection product Dormex, registered under No. 10247. GU Serie Generale n.84 09/04/2008. Available from: https://www.gazzettaufficiale.it/eli/gu/2008/04/09/84/sg/pdf (Italian).

## 54. Status epilepticus in a child intoxicated by *Psilocybe mexicana* and *Cannabis sativa*

Natanael del Ángel González, Yaneli A. González Chávez, Jorge G. Pérez Tuñón, Mayré I. Bautista Albíter and Arturo G. Ponce de León

Centro Toxicológico Hospital Ángeles Lomas, Huixquilucan, Mexico

Table 1. Clinical features of 24 patients exposed to hydrogen cyanamide.

| Routes of exposure | Number of cases | Clinical manifestation |
|---|---|---|
| Ingestion | 3 | Nausea/vomiting ($n = 2$), oral caustic burns ($n = 1$), corrosive esophagitis/gastritis ($n = 1$), pancreatitis ($n = 2$) and hepatic necrosis ($n = 1$), confusion/drowsiness ($n = 3$), agitation ($n = 3$), coma ($n = 2$), hallucinations ($n = 1$), and hemiparesis ($n = 1$). |
| Dermal | 5 | Hyperemia ($n = 4$); oedema ($n = 2$), III-degree burn ($n = 1$), pruritus ($n = 1$), burning sensation ($n = 1$) and pharyngodynia ($n = 1$) |
| Dermal/inhalation | 3 | Hyperemia ($n = 3$), headache ($n = 1$), nausea ($n = 2$), abdominal pain ($n = 1$) and tachycardia ($n = 1$). |
| Dermal/ocular | 1 | II-degree burn ($n = 1$) ocular oedema ($n = 1$) |
| Inhalation | 2 | Weakness ($n = 1$), nausea ($n = 1$) and vomiting ($n = 1$) |
| Inhalation/dermal - alcohol consumption | 10 | Flushing ($n = 10$), dyspnea ($n = 6$), pharyngodynia ($n = 2$), hypotension ($n = 1$), confusion/drowsiness ($n = 1$), II-degree burn ($n = 1$), cutaneous wheals (n = 1) |

**Objective:** *Psilocybe mexicana* is a macromycete used recreationally as a hallucinogen. Its components, psilocybin and psilocin are substituted tryptamine alkaloids that act as 5-hydroxytryptamine 2A receptor agonists on the central nervous system [1]. *Cannabis sativa* is commonly used as a euphoric agent and to inhibit nausea and vomiting that can be produced by natural psychoactive substances such as *P. mexicana* [2]. Seizures have been described in psilocybe intoxication probably related to the agonism of the 5-hydroxytryptamine 2A, which increases cortical response and glutamate activity. In contrast, anticonvulsant properties have been described for cannabinoid agonists. Additionally, in a systematic review of 3582 children with accidental cannabis ingestion, none presented with hallucinations or seizures. However, tetrahydrocannabinol (THC) acts through the CB1 receptor, causing an increase in the release of 5-HT, which could enhance the effects of other agonists such as psilocybin and psilocin [1,2]. We present a case of a child with ingestion of both psilocybin and cannabis.
**Case report:** A 5-year-old male ingested a preparation containing both *P. mexicana* and *C. sativa*, which his parents had prepared to sell. During his transfer to the hospital he presented hallucinations, impaired consciousness and a seizure that persisted for approximately 15 minutes, until intramuscular midazolam was administered, followed by an intravenous dose of diazepam in the emergency department. His physical examination revealed an unresponsive patient, with blood pressure 105/70 mmHg, heart rate 100 bpm, respiratory rate 12 rpm, temperature 38 °C, oxygen saturations 95%, capillary glycemia 159 mg/dL, 5 mm pupils, increased peristalsis, spastic limbs and loss of urinary sphincter control. After a few minutes a new seizure occurred, so he was sedated, intubated and transferred to the pediatric intensive care unit. Subsequently, coma was induced with thiopental and gastric lavage was performed, obtaining remains of the ingested product. Cyproheptadine and a single dose of activated charcoal were administered. He was extubated 48 hours later and transferred to the pediatric ward. During his hospitalization no sequelae were observed and he was discharged after 5 days.
**Conclusion:** The addition of THC to the psilocybin preparation could have favored the development of hallucinations and seizures in this case, although it would be necessary to carry out experimental studies to establish this correlation.

## References

[1] Jann WM. Psilocybin revisited: the science behind the drug and its surprising, therapeutic potential. Psychiatric Times. 2021;38:39–43.
[2] Richards JR, Smith NE, Moulin AK. Unintentional cannabis ingestion in children: a systematic review. J Pediatr. 2017;190:142–152.

# 55. Root-rhythmia: tejocote (*Crataegus mexicana*) ingestion associated dysrhythmia

Stephen Petrou[a,b], John Keller[a,b] and Craig G. Smollin[a,b]
[a]University of California San Francisco, San Francisco, CA, USA; [b]California Poison Control System – San Francisco Division, San Francisco, CA, USA

**Objective:** Tejocote (*Crataegus mexicana)* is native to Mexico and Guatemala. Marketed as a weight loss supplement in the form of dried root, it is easily accessible online. Although hawthorn is known to produce cardiovascular effects, to our knowledge there are only two case reports of tejocote-induced cardiotoxicity [1,2]. Similar to digoxin and cardiac glycosides, hawthorn is postulated to increase myocardial contractility through inhibition of the sodium-potassium-ATPase and increased intracellular calcium. We describe a case of tejocote root causing bradycardia with atrial bigeminy in an otherwise healthy adult male.
**Case report:** A 23-year-old male with no past medical history presented to the emergency department (ED) with emesis, weakness, palpitations, and visual disturbances described as "flashes of light" after ingesting 10 pieces of tejocote root he obtained and intended for use as a weight loss supplement. He had bradycardia (HR 40–50 bpm) and an electrocardiogram (ECG) showing atrial bigeminy. Laboratory work and electrolytes were unremarkable, and he was placed in the cardiac intensive care unit (ICU) for monitoring. Digoxin concentration was undetectable. He received 10 vials (400 mg) of digoxin immune fab (DIGIFab) and clinically improved over the course of 2 days with resolution of symptoms and ECG changes.
**Conclusion:** While tejocote has been found to cross-react with digoxin assays, in this case digoxin was undetectable. This is believed to be due to structural similarities between flavonoids, found in hawthorn, and digoxin [1]. Unique to hawthorn is its ability to prolong the action potential and refractory period through nitric oxide mediated mechanisms [3]. This may explain its poor clinical response to DIGIFab administration. Tejocote is readily available and sold as a weight loss supplement. To our knowledge, there has only been two documented cases of tejocote (*Crataegus mexicana*)-induced cardiotoxicity. Physicians should be aware of the consequences of unregulated weight loss supplements including tejocote and its ability to produce cardiotoxicity in otherwise healthy individuals.

## References


[1] Palmer KG, Lebin JA, Cronin MT, et al. *Crataegus mexicana* (Tejocote) exposure associated with cardiotoxicity and a falsely elevated digoxin level. J Med Toxicol. 2019;15:295–298.

[2] Mudan A, Livshits Z, Lebin J. Revisiting supplement safety: a near fatal overdose with novel supplement tejocote. Clin Toxicol. 2021;59:531–532.

[3] Holubarsch CJF, Colucci WS, Eha J. Benefit-risk assessment of crataegus extract WS 1442: an evidence-based review. Am J Cardiovasc Drugs. 2018;18:25–36.


# 56. Suicidal *Digitalis purpurea* poisoning in an adult


Anna-Mariia Termälä and Riikka Palo

Poison Information Center, University of Helsinki and Department of Emergency Medicine and Services, Helsinki University Hospital, Helsinki, Finland


**Objective:** Digoxin usage has reduced by half in Finland during the last ten years, which can make it more challenging to identify digitalis poisoning [1].
**Case report:** An elderly person with hypertonia, hypercholesterolemia, hypothyroidism and long-term psychiatric history had chest pain, shortness of breath and vomiting. Paramedics found him nauseous with squeezing chest pain and pale, cool skin. An electrocardiogram (ECG) showed global ischemia, bradycardia (pulse 29–34/min) and total block. On hospital admission he was agonized with chest pain. ECG showed slow atrial fibrillation and ST changes. Routine laboratory tests were normal including potassium (4.2 mmol/L) and creatinine (66 μmol/L). Only lactate (3.3 mmol/L) was not within normal limits. Morphine 2 mg IV was given for pain with minimal response. There was a suspicion of an ischemic cardiac event, and isoprenaline infusion was started which increased the heart rate to 50/min. Norepinephrine was started to increase the blood pressure. A coronary angiogram was normal; a temporary pacemaker inserted and prophylactic antibiotics started. Echo was normal, and the ejection fraction (EF) was over 60%. Aortic computerised tomography (CT) scan was normal (no aortic dissection). On the next day laboratory values showed troponin T (TnT) had increased from the admission value of 13.7–736 ng/L. On day three he admitted eating two handfuls of *Digitalis purpurea* leaves to commit suicide. Serum digoxin was measured (2.6 nmol/L). The Poison Information Center was contacted, and digoxin antidote was recommended (DIGIFab 80 mg). Plant-derived cardiac glycosides have a longer half-life compared to digoxin [2]. Potassium value was monitored. Sinus rhythm returned and the pacemaker was removed on day four. He was hospitalized for eight days. During the hospital stay he had flutter episodes and preventive anticoagulative medication was started. He had had previous palpitations.
**Conclusion:** Our patient had severe intoxication with chest pain, vomiting and severe bradycardia with ST changes. A single dose of antidote returned adequate hemodynamics allowing withdrawal of a temporary pacemaker. Isoprenaline and cardiac pacing were used successfully without complications even though contraindicated in digoxin intoxication.

## References


[1] Finnish Medicines Agency. Drug sales register 2010–2020 [cited 2022 Oct 6]. Available from: https://www.fimea.fi/web/en/databases_and_registeries/consumption.

[2] Maes KR, Depuydt P, Vermassen J, et al. Foxglove poisoning: diagnostic and therapeutic differences with medicinal digitalis glycosides overdose. Acta Clin Belg. 2020;4:1–7.


# 57. Detectable serum digoxin concentration following exploratory lily of the valley ingestion in an asymptomatic child


Marlis Gnirke[a], Nicholas Otts[b], Mary Ann Howland[c] and Mark K. Su[d]

[a]Division of Medical Toxicology, Ronald O. Perelman Department of Emergency Medicine, NYU Grossman School of Medicine, New York City, NY, USA; [b]Division of Pediatric Emergency Medicine, Westchester Medical Center, Valhalla, NY, USA; [c]St. John's University College of Pharmacy and Health Sciences, New York, NY, USA; [d]New York City Poison Control Center, New York City, NY, USA


**Objective:** Lily of the valley (*Convallaria majalis*) is a plant containing convallatoxin, a cardioactive steroid known to cause digitalis-like effects by inhibition of the sodium-potassium ATPase. Confirmed ingestion of *Convallaria majalis* and resulting toxicity is rarely reported. We report an exploratory pediatric *Convallaria majalis* berry ingestion with a detectable serum digoxin concentration that had a benign clinical course.
**Case report:** An 18-month-old boy bit into a berry from a plant identified by an unspecified smartphone application as "lily of the valley." On arrival to the hospital approximately 90 minutes later, the patient was asymptomatic with normal vital signs and physical examination, normal electrocardiogram without signs of ectopy, and a serum potassium of 4.2 mmol/L. A serum digoxin concentration measured by Elecsys electrochemiluminescence immunoassay (ECLIA) on the Roche Cobas e601 analyzer was 0.4 ng/mL (lower limit of detection 0.2 ng/mL). The patient received activated charcoal and was transferred to a hospital with pediatric intensive care capabilities. On arrival to the receiving hospital six hours post-exposure, he remained asymptomatic with normal vital signs and electrocardiogram. Upon consultation at this time, we recommended repeat serum digoxin concentration measurement. Digoxin was undetectable (<0.1 ng/mL) by particle-enhanced turbidimetric inhibition immunoassay (PETINIA) on the ci8200 Abbott Architect analyzer used at the receiving hospital. No digoxin-specific antibody fragments were administered because the child never developed any clinical signs or symptoms of cardioactive steroid toxicity. The patient remained asymptomatic throughout 24 hours of observation and was discharged home the next day.
**Conclusion:** This is, to our knowledge, one of few laboratory confirmed *Convallaria majalis* ingestions. Based on previously published *in vitro* data for the Roche ECLIA assay used at the first hospital [1], an apparent serum digoxin concentration of 0.4 ng/mL roughly corresponds to 4 mcg/mL of convallatoxin. Convallatoxin pharmacokinetics are largely unknown; assuming they are similar to digoxin, a serum concentration 90 minutes post-ingestion likely represents a pre-distribution concentration. There is no published information regarding cross-reactivity of the Abbott PETINIA assay for convallatoxin; it is unknown whether the repeat serum digoxin concentration represents a decrease in serum convallatoxin concentration or lack of cross-reactivity with this assay. This case report contributes to the scarce literature on confirmed *Convallaria majalis* ingestions and suggests that a single *Convallaria majalis* berry from exploratory pediatric ingestions is likely benign.

## Reference

[1] Fink SL, Robey TE, Tarabar AF, et al. Rapid detection of convallatoxin using five digoxin immunoassays. Clin Toxicol. 2014;52:659–663.


## 58. Poisoning with cardiac glycoside-containing plants reported to the UK National Poisons Information Service: a 7-year study


Victoria A. Eagling[a], Ruben H. K. Thanacoody[b], Laurence A. Gray[c], Sally M. Bradberry[d] and Euan A. Sandilands[a]

[a]National Poisons Information Service, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; [b]National Poisons Information Service, Newcastle, United Kingdom; [c]National Poisons Information Service, Cardiff, United Kingdom; [d]National Poisons Information Service, Birmingham, United Kingdom



**Objective:** Cardiac glycosides are found in a diverse group of plants including species native to the UK, non-native ornamental plants and plant material purchased online. Our objective was to evaluate telephone enquiries related to the ingestion of cardiac glycoside-containing plants reported to the UK National Poisons Information Service (NPIS).

**Methods:** A retrospective search of the UK Poisons Information Database identified relevant enquiries 1 January 2015 to 31 December 2021.

**Results:** During the 7-year-period, there were 137 enquiries (122 patients). The majority related to *Digitalis* (90, 73.8%), followed by lily of the valley (16, 13.1%), oleander (7, 5.7%), yew (5, 2.5%), *Cerbera odollam* (3, 2.5%) and other species (6, 4.9%). Most cases involved children (<5 years: 47 (38.5%); 5-14 years: 17 (13.9%); 15-49 years: 39 (32.0%); >49 years: 17 (13.9%); unknown: 2 (1.6%)). Accidental exposures accounted for 86 cases (70.5%); in 30 cases (24.6%), exposure was intentional; in 6 cases (4.9%) the reason was unclear. Following accidental exposure, Poisoning Severity Scores (PSS) [1] were as follows: 62 asymptomatic (72.1%); 16 minor PSS (18.6%); 6 moderate PSS (7.0%); 1 severe PSS (1.2%) and 1 unknown (1.2%). A greater proportion of patients presented with moderate or severe features following intentional exposures: 10 asymptomatic (33.3%); 8 minor PSS (26.7%); 8 moderate PSS (20.0%); 8 severe PSS (20.0%). One death was recorded (deliberate ingestion of *Digitalis*). Common features included nausea/vomiting (21; 43.8%); electrocardiogram (ECG) abnormalities (e.g., AV block, bundle branch block) (19, 39.6%); and bradycardia (13; 27.1%). DIGIFab® was administered to 10 patients (8.2%); 7 cases following discussion with the NPIS (3 cases prior). Where known, the median (range) number of vials administered was 9 (1–15). Nine patients made a full recovery. One patient died despite administration of DIGIFab® (10 vials).

**Conclusion:** Cases of cardiac glycoside plant toxicity were rare (<2/month). Most were in children and accidental in nature. Reassuringly, following accidental exposure over 90% of patients were asymptomatic or presented with minor symptoms. A significantly greater proportion of intentional exposures resulted in severe toxicity compared to accidental exposures (20.0 versus 1.2%, $p < 0.0001$). The median number of DIGIFab® vials administered was 9 compared to 2 vials for the treatment of poisoning with digoxin [2].



## References

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

[2] Jackson G, Eagling VA, Thanacoody RH, et al. The use of antidote in the management of digoxin poisoning. Poster presented at Society for Toxicology, 61st Meeting, San Diego; 2022.


## 59. Modern day shamanism: a case of repeated ayahuasca consumption in metropolitan France documented by hair and nails analysis


Gaël Le Roux[a], Jérémy Lecot[a], Chloé Bruneau[a], Florian Hakim[b], Alexandr Gish[b] and Jean-Michel Gaulier[a]

[a]Centre Antipoison Grand Ouest, Angers, France; [b]Unité fonctionnelle de Toxicologie, Lille, France



**Objective:** To report a rare case of repeated ayahuasca consumption in France, documented by identification of the substances of interest in nails and hair.

**Case report:** A 44-year-old female, with a history of cured alcoholism and cannabidiol (CBD) use, was referred to the emergency room for mutism and incoherent speech. She presented abulia, bradykinesia, bradyphasic as well as auditory and cenesthetic (but not visual) hallucinations. Biological tests on admission were unremarkable. The brain scan showed a fusiform aneurysm of the M2–M3 junction of the right middle cerebral artery, which did not explain the symptoms. The questioning of her relatives revealed that she had gone to shamanic ceremonies on three occasions (the last one having taken place the previous week) during which she had consumed ayahuasca. The patient was finally hospitalized in a psychiatric service. To verify the use and document the history of its consumption, blood, urine, black hair (30 cm long) and fingernail samples were analysed using both liquid chromatography-tandem mass spectrometry (LC-MS/MS) and liquid chromatography-tandem mass spectrometry (LC-HRMS) previously reported methods [1]. The hair sample was analyzed after segmentation (S1 to S9): 2 cm long hair segments, except for S9 (16 cm from root to tip). Harmine, harmaline together with 5-OH-*N*,*N*-dimethyltryptamine (5-OH-DMT) were identified in blood, urine, hair [S1–S9] and fingernails, *N*,*N*-dimethyltryptamine (DMT) was only detected in urine, hair [S1–S9] and fingernails, *N*-methyltryptamine (NMT) was only detected in urine and fingernails. These results support (i) a hypothesis of a recent consumption of ayahuasca and (ii) a repeated consumption of ayahuasca by this patient for the past 18 months. In addition, hair and nails analysis revealed (1) regular cocaine use up to the last 6 months, and (2) alprazolam use for the last 3 months.

**Conclusion:** Ayahuasca is a traditional psychoactive infusion of the Amazonian natives composed mainly of mixture of *Psychoteria viridis* or related species (containing DMT, 5-OH-DMT and NMT) together with *Banisteriopsis caapi* (containing harmine and harmaline). The anxiolytic, antidepressant and hallucinogenic properties of ayahuasca have made the use of this infusion widespread throughout the world. In this situation, combined blood and urine analysis with hair and nail analysis confirmed recent and repeated use of ayahuasca with a determination of the main alkaloids of two plants.

## Reference

[1] Wiart JF, Hakim F, Andry A, et al. Pitfalls of toxicological investigations in hair, bones, and nails in extensively decomposed bodies: illustration with two cases. Int J Legal Med. 2020;134:1339–1344.

# 60. Surprising lack of symptoms after potentially dangerous colchicine poisoning from *Gloriosa superba* (glory lily) tea

Erik Borski[a], Michael Deters[a], Katja Schulz[b], Joerg Pietsch[c] and Anne Stürzebecher[a]

[a]Poisons Information Centre Erfurt, Erfurt, Germany; [b]Technische Universität Dresden, Dresden, Germany; [c]Technische Universität Dresden, Erfurt, Germany

**Objective:** *Gloriosa superba*, a popular flowering plant in gardens all over Europe, is in the Colchicaceae family and hence contains colchicine (0.6–1% in the tuber). Toxicity of colchicine is well known, and formulations of this substance, as well as ingestion of colchicine-containing plants regularly lead to severe intoxications and even deaths. We report a case of accidental ingestion of *Gloriosa superba* "tea" where potentially (very) toxic blood concentration were detected, but the patient fortunately failed to develop any severe symptoms.
**Case report:** A young man felt slightly ill and wanted to brew some ginger tea. He used a ginger-like-looking tuber from the garden, cutting it up and infusing it with hot water. He then drank a relatively large cup of this infusion, before he became aware of his mistake and contacted the poisons information centre. Due to the known severe toxicity of colchicine, prompt referral to hospital was recommended, and about two hours after ingestion he arrived in the emergency department. Activated charcoal was given immediately plus repeated doses every 4 hours were recommended, and he was transferred to intensive care unit (ICU) for observation. The plasma colchicine concentration was 20 ng/mL (sampled 2 hours post ingestion), which is described as potentially lethal [1]. Continuation of repeated charcoal for at least 24 hours was advised, as well as repeated measurements of plasma concentrations. In ICU, the patient merely developed some minor gastrointestinal disturbances such as nausea, abdominal pain, and discomfort, but no cardiac symptoms or organ toxicity occurred. Within 36 hours, the colchicine plasma concentration dropped to 3.2 ng/mL, and repeated measurements for the next 7 days were all below 2 ng/mL. The patient developed no further symptoms and was discharged without sequelae.
**Conclusion:** Therapeutic and toxic levels of colchicine are well known. Plasma levels of 10–66 ng/mL are given as comatose-fatal [1], however no sampling times are stated. Our patient's initial plasma concentration therefore led to an assumed severe toxicity – that fortunately did not occur. We conclude that the patient vastly benefited from the prompt and repeated dosing with charcoal, reducing colchicine toxicity as previously described *in vitro* [2].

## References

[1] Schulz M, Iwersen-Bergmann S, Andresen H, et al. Therapeutic and toxic blood concentrations of nearly 1,000 drugs and other xenobiotics. Crit Care. 2012;16:R136.

[2] Zawahir S, Gawarammana I, Dargan PI, et al. Activated charcoal significantly reduces the amount of colchicine released from *Gloriosa superba* in simulated gastric and intestinal media. Clin Toxicol. 2017;55:914–918.

# 61. Another victim of omelettes: a case of severe mushroom intoxication with muscarine detection

Chloé Bruneau, Jérémy Lecot, Rebecca Vinas, Marie Deguigne, Estelle Flament and Gaël Le Roux

Centre Antipoison Grand Ouest, Angers, France

**Objective:** To describe a case of severe muscarinic mushroom poisoning confirmed by a muscarine assay.
**Case report:** We report a case of mushroom poisoning in an 81-year-old woman with a medical history of dyslipidaemia, hypertension and hypothyroidism treated with levothyroxine, lisinopril and pravastatin. This patient thought she had ingested a kind of mushroom called "mousserons" (*Marasmius oreades*) at around 8 pm. She had collected the mushrooms in her garden and prepared as an omelette afterwards. Two hours after the meal, she had vomiting, diarrhoea, tremors and diffuse pain. At the emergency department, the patient was conscious (Glasgow Coma Score 14/15), hypothermic (32.3 °C), with low blood pressure (85/46 mmHg), bradycardia (29/min), hypoxia (saturation 91% in room air, respiratory rate 18/min), with profuse sweating, miosis, abdominal pain, hypersalivation and diarrhoea. She immediately received 0.5 mg of atropine and volume repletion (1 L). In intensive care, her haemodynamic constants stabilised (blood pressure 150/110), but she had persistent miosis and slight oedema of the lower limbs, but no mottling or desaturation. The clinical evolution of the patient was marked by a rapid improvement of the digestive disorders and a normalisation of the biological balance concomitant with an increase in troponin level (from 24 to 3681 pg/mL) without chest pain or electrocardiogram (ECG) changes. The abnormalities resolved on day 2, allowing the patient to return home. Blood tests showed dehydration (sodium 146 mmol/L, urea 9.27 mmol/L, protein 89 g/L) and acute renal failure (creatinine 128 µmol/L) with hyperlactatemia at 5.69 mmol/L. Toxin investigation was performed on plasma using a validated method in liquid chromatography with high-resolution mass spectrometry detection. Muscarine was measured at 18 ng/mL and 5.6 ng/mL, respectively, at 8.25 and 19 hours after ingestion.
**Conclusion:** This case shows the potential seriousness of muscarinic mushroom poisoning with a rare analytical confirmation by an appropriate quantitative assay [1]. This analysis allowed us to objectify the misidentification of the mushrooms (probable confusion between *Inocybe*/*Clitocybe* and *Marasmius oreades*).

## Reference

[1] Flament E, Guitton J, Gaulier JM, et al. Human poisoning from poisonous higher fungi: focus on analytical toxicology and case reports in forensic toxicology. Pharmaceuticals. 2020;13:454.

## 62. *Crataegus mexicana* (tejocote) exposure in a 23 month-old, with signs of cardiotoxicity, with normalization of their ECG after administration of digoxin immune Fab

Noah G. Berland[a], Molly Kaminsky[b], Trevor Cerbini[a], Cynthia Santos[a], Diane Calello[a], Howard Greller[a], Christopher Meaden[a] and Lewis Nelson[a]

[a]Rutgers NJMS – NJPIES, Newark, NJ, USA; [b]Morristown Medical Center, Morristown, NJ, USA

**Objective:** *Crataegus mexicana* (tejocote) supplements have been noted in the literature to cause cardiotoxicity similar to digoxin with some digoxin immunoassays showing cross-reactivity [1,2]. However, digoxin immune Fab's utility in managing these patients is unclear [2]. We report on the first known published case of ECG normalization after the administration of digoxin immune Fab in a suspected exposure to tejocote.
**Case report:** A 23 month-old female was found chewing on a piece of a supplement purported to contain tejocote extract used by the mother for weight loss. One hour later the patient developed nausea and vomiting, prompting presentation to an Emergency Department. On evaluation the child was bradycardic for her age at a rate of 93 beats per minute and poison control was consulted. Poison control recommended obtaining an electrocardiogram (ECG) and a serum digoxin concentration, and administering activated charcoal. The ECG revealed sinus bradycardia with a rate of 66 beats per minute and frequent premature ventricular contractions (PVCs). The serum potassium concentration was 4.4 mEq/L and the serum digoxin concentration was 0.5 ng/L (0.65 nmol/L). Poison control recommended administering a single vial of digoxin immune Fab and admission for telemetry monitoring and serial ECGs. The patient's ECG 5 hours post-administration was unremarkable but at 12 hours post-administration, a repeat ECG showed what was believed to be a 2nd degree AV block, bradycardia, and frequent PVCs. A second vial of digoxin immune Fab was administered with normalization of the ECG. Ten hours post-administration of the second vial, the patient was found to have an increasing number of PVCs, without AV block or bradycardia. No additional vials of digoxin immune Fab were administered. She was discharged on hospital day 3 with a normal ECG.
**Conclusion:** Patients presenting with a suspected exposure to tejocote, or other *Crataegus* species, with evidence of cardiac toxicity, should empirically have digoxin immune Fab administered. Further study is needed to understand the causative xenobiotic and digoxin immune Fab's effectiveness as antidotal therapy.

### References

[1] Dasgupta A, Kidd L, Poindexter BJ, et al. Interference of hawthorn on serum digoxin measurements by immunoassays and pharmacodynamic interaction with digoxin. Arch Pathol Lab Med. 2010; 134:1188–1192.

[2] Palmer KG, Lebin JA, Cronin MT, et al. *Crataegus mexicana* (Tejocote) exposure associated with cardiotoxicity and a falsely elevated digoxin level. J Med Toxicol. 2019;15:295–298

## 63. Ceylon leadwort (*Plumbago zeylanica*) induced contact dermatitis and skin erosions

Yaopan Liao

Chang-Hua Hospital, Chang-Hua County, Taiwan

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

## 64. Metabolic acidosis from ingestion of plant roots mimicking cyanide poisoning: a case report of acute *Dioscorea hispida* poisoning

Kai-Wen Cheng

Department of Clinical Toxicology & Occupational Medicine, Taipei Veterans General Hospital, Taipei City, Taiwan

**Objective:** Patients who present with acute change of consciousness and metabolic acidosis after ingestion of root tubers may appear to have poisoning from cyanogenic glycosides in the emergency department. We present a case of acute *Dioscorea hispida* Dennst. poisoning, which mimics cyanide intoxication based on pattern recognition [1].
**Case report:** A 69-year-old female suffered from dizziness, nausea, and non-bilious vomiting after ingesting a few mouthfuls of yam soup at home in western Taiwan. About two hours later, she was brought to a community hospital emergency department due to a change of consciousness (Glasgow Coma Score (GCS) E2V3M4). Given possible cyanide poisoning, sodium nitrite 300 mg and sodium thiosulfate 12.5 g were administered during resuscitation. Arterial blood gas immediately after intubation revealed metabolic acidosis (pH 7.135; $PCO_2$ 50.3 mmHg; $PO_2$ 459.9 mmHg; bicarbonate 16.5 mmol/L). The patient could obey orders at about 8 hours post-ingestion. However, serial arterial blood gas revealed persistent metabolic acidosis (bicarbonate ranged from 14.7 to 17.3 mmol/L) without severe lactatemia (2.4 mmol/L). Bicarbonate concentration was not been above 20 mmol/L until about 35.5 hours post-ingestion. This patient was discharged uneventfully on the sixth-day post-ingestion. Cyanide in a whole blood specimen obtained during resuscitation was undetectable (<0.2 μg/mL). The patient was visited and the wild

yams she harvested for the soup collected. Thin layer chromatography analysis of the 95% ethanol extracts were compatible with *Dioscorea hispida* Dennst (Indian three-leaved yam).
**Conclusion:** The mechanism of *Dioscorea hispida* Dennst. intoxication is not well studied currently. A possible xenobiotic might be dioscorine [2]. It is challenging to differentiate acute *Dioscorea hispida* Dennst. poisoning-induced metabolic acidosis from cyanogenic glycoside intoxication associated with the ingestion of cassava roots.

## References

[1] Heneghan C, Glasziou P, Thompson M, et al. Diagnostic strategies used in primary care. BMJ. 2009;338:b946.
[2] Cahyaningtyas A, Aryanto S, Hidayati T. Food poisoning outbreak caused *Dioscorea hispida* Dennst. in Gading 10 Village, Gunung Kidul, Yogyakarta August 2020: a case report study. BKM Public Health and Community Medicine 2021 [cited 2022 Oct 10]. Available from: https://journal.ugm.ac.id/v3/BKM/article/view/1627.

# 65. Aflatoxicosis at the intersection of modern agriculture and public health

Shahnaz Sonya Rashid[a] and S. Eliza Dunn[b]
[a]Toxikon Consortium, Chicago, IL. USA; [b]Bayer Crop Science, St. Louis, MO, USA

**Objective:** Aflatoxins are a family of mycotoxins that have devastating effects on human and animal health. They can cause hepatocellular carcinomas [1], growth restriction in children and are associated with the development of protein calorie malnutrition otherwise known as kwashiorkor. There are many cost-effective strategies to control aflatoxins [2,3]. We reviewed the importance of aflatoxin control and how it benefits global food production and human health.
**Methods:** We reviewed the literature covering the public health impacts of aflatoxin exposure.
**Results:** Acute exposures of aflatoxins can cause liver failure and hepatitis. The main toxigenic strains of Aspergillus are *Aspergillus flavus* and *Aspergillus parasticus*. These fungi flourish in hot humid climates, which promote fungal growth and the elaboration of mycotoxins that contaminate feed and food. A toxigenic strain of *Aspergillus* was first reported in 1960 in the United Kingdom with Turkey-X-disease, where 100,000 turkeys died from contamination with *A. flavus*. Maize is a staple crop in Kenya and is particularly prone to infection. Multiple outbreaks of aflatoxicosis have been reported in Kenya over the last twenty years. In 2004, there were 317 cases and 125 deaths after people ate food contaminated with aflatoxin B50. Reported levels were 5000 ng/g higher than the allowed limit of 5 g/g per European regulations [4]. Kenya had a similar outbreak in 1982, however the 2004 outbreak was deadlier. These outbreaks cause acute illness and significantly contribute to the burden of hepatocellular carcinoma in the world. Between 25,000 and 155,000 aflatoxin related liver cancers occur per year [1].
**Conclusion:** Control of aflatoxin in agriculture is critical for global public health as trace exposures have significant health impacts on vulnerable populations.

## References

[1] Liu Y, Wu F. Global burden of aflatoxin-induced hepatocellular carcinoma: a risk assessment. Environ Health Perspect. 2010;118:818–824.
[2] Mamo FT, Shang B, Selvaraj JN, et al. Biocontrol efficacy of atoxigenic *Aspergillus flavus* strains against aflatoxin contamination in peanut field in Guangdong province, South China. Mycology. 2021;13:143–152.
[3] Pretari A, Hoffmann V, Tian L. Post-harvest practices for aflatoxin control: evidence from Kenya. J Stored Prod Res. 2019;82:31–39.
[4] Tan K. Aflatoxin and its toxic tragedies in Kenya. J Young Investigators. 2020;38:10–12.

# 66. Acute cyanide poisoning due to ingestion of seeds containing amygdalin in Slovenia, 2019–2021

Ana Mavrič[a], Gašper Razinger[a], Lucija Šarc[a] and Miran Brvar[b]
[a]Centre of Clinical Toxicology and Pharmacology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [b]Faculty of Medicine, Centre of Clinical Toxicology and Pharmacology, University Medical Centre Ljubljana and Centre for Clinical Physiology, University of Ljubljana, Ljubljana, Slovenia

**Objective:** Amygdalin is a cyanogenic glycoside. It is promoted as an alternative anti-cancer agent, often under the misnomer vitamin B547. It is one of the major pharmacological components found in almonds and widely available in the seeds of some plants in the family Rosaceae, such as peaches, apples and plums. When metabolised in the digestive system amygdalin degrades into highly poisonous hydrogen cyanide [1]. The aim of this retrospective study was to evaluate poisonings with fruit seeds of Rosaceae plants in Slovenia.
**Case series:** In the last three years, the Poison Control Centre (PCC) Ljubljana received 6698 calls from physicians about poisonings (1100 calls per million population annually). Of these, 702 consultations were about plant exposures (10.4%) and only 5 adult patients intentionally ingested fruit seeds of Rosaceae plants. Four patients intentionally ingested from 50 to 100 apricot kernels. The most frequent clinical features after apricot kernels ingestion were: dizziness (3/4), vomiting (2/4), headache (2/4), tachycardia (2/4), hypotension 1/4) and weakness (1/4). No patient had lactic acidosis. One patient, a 37-year-old female ingested 426 apple seeds in a suicide attempt. The seeds were collected by the patient and thoroughly chewed upon ingestion. On the arrival at the Emergency Department 3 hours after ingestion she was somnolent with supine blood pressure 140/100 mmHg. The initial laboratory tests showed elevated serum lactate concentration (4.55 mmol/L) and compensated metabolic acidosis. Blood ethanol concentration was 1.1 g/L. She received activated charcoal. The estimated ingested dose of amygdalin was 10–50 mg which was presumably metabolised to 0.8–3 mg of hydrogen cyanide. The lethal dose of hydrogen cyanide is 1.5 mg/kg orally. The patient was treated without antidote, and she was discharged two days after admission without any residual signs of intoxication.
**Conclusion:** The ingestion of apricot kernels resulted in transient signs and symptoms, even if ingested in significant amounts. Ingestion of amygdalin in apple seeds most likely resulted in lactic metabolic acidosis, since significant elevations of blood lactate in acute ethanol intoxication are rare [2]. Intoxication with amygdalin from natural sources with subsequent signs of cyanide poisoning are rare, but large amounts of ingested seeds can result in elevated blood lactate concentration.

## References

[1] He XY, Wu LJ, Wang WX, et al. Amygdalin – a pharmacological and toxicological review. J Ethnopharmacol. 2020;254:112717.

[2] MacDonald L, Kruse JA, Levy DB, et al. Lactic acidosis and acute ethanol intoxication. Am J Emerg Med. 1994;12:32–35.


## 67. Anticholinergic syndrome due to mushroom poisoning: a case series


Benedetta Brolli[a], Cristina Grazioli[a], Valentina Negrini[a], Azzurra Schicchi[b], Valeria M. Petrolini[b], Davide Lonati[b], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy



**Objective:** Mushroom poisoning can be responsible for anticholinergic syndrome (AS). Physostigmine is the antidote in case of central anticholinergic syndrome (CAS) but there is no data about its use in mushroom-induced CAS. The objective of our study was to evaluate clinical characteristics, management and potential role of physostigmine to treat CAS due to mushroom ingestion.

**Methods:** We performed a retrospective observational study including all cases of CAS due to mushroom poisoning managed by our PCC (2011–2022). Inclusion criteria were: (I) history of mushroom ingestion, (II) presence of CAS. For all included patients we collected data about: age, clinical manifestations at hospital admission and during hospitalisation, mycological recognition, treatment and outcome.

**Results:** Ninety-four patients were included, F:36/M:58, median age 60 [47.75] years; 10/94 (10.6%) declared intentional ingestion to obtain an hallucinogenic effect, 84/94 (89.4%) ingested the mushrooms thinking they were edible. For 51/94 cases (54%) mycological recognition was possible and identified as *Amanita pantherina* in 21/51 (55%) and *Amanita muscaria* in 30/51 (45%). The median time between ingestion and clinical manifestations was 2 hours [1,3 hours]. Clinical manifestations were: vomiting 41.5%, hallucinations 33%, seizures 32%, tachycardia 30%, confusion 28.7%, mydriasis 9.6%, xerostomia 6%, coma 6%, and drowsiness 4.5%. Treatment included: gastrointestinal decontamination 100%, benzodiazepines 25.5%, orotracheal intubation 10.6%. Physostigmine was suggested in 30/94 (32%) cases because of severe CAS with hallucinations and/or seizures and/or coma. Of the 30 patients for which physostigmine was suggested, it was available and administered only in 7/30 (23%) cases at the median dose of 1 mg [1,2 mg] without adverse reaction and with prompt resolution of CAS. The median length of hospitalisation was 24 hours [24.72]. All patients fully recovered.

**Conclusion:** *Amanita muscaria* and *Amanita pantherina* represents the most common mushrooms causing AS in our case series. Patients treated with physostigmine presented rapid resolution of symptoms with no adverse events. According to the literature our data suggest that physostigmine is a safe antidote and diagnostic tool but it is important to improve its hospital storage. A prospective study is necessary to evaluate if physostigmine administration could reduce the length of hospital stay of patients with CAS due to mushroom poisoning.


## 68. Activation code of severe acute intoxication (CodiTox): a protocol for detection, prioritisation and treatment of the seriously intoxicated patient


Maria Àngels Gispert-Ametller[a], Juliana González-Londoño[b], Raquel Aguilar-Salmerón[c], Miguel Galicia-Paredes[d], Santiago Nogué-Xarau[e], Lídia Martínez-Sánchez[f], Albert Obiols-González[g] and August Supervía-Caparrós[h]

[a]Emergency Department, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [b]Intensive Care Unit, Hospital Santa Caterina, Girona, Spain; [c]Pharmacy Service, Hospital Universitari Doctor Josep Trueta, Girona, Spain; [d]Emergency Department, Hospital Clínic, Barcelona, Spain; [e]Fundación Española de Toxicología Clínica, Barcelona, Spain; [f]Emergency Department, Hospital Sant Joan de Déu, Barcelona, Spain; [g]Sistema d'Emergències Mèdiques, Barcelona, Spain; [h]Emergency Department, Hospital del Mar, Barcelona, Spain



**Objective:** To describe the criteria for CodiTox activation at pre-hospital level, as well as the referral circuit for intoxicated patients according to their severity.

**Methods:** The Toxicology Working Group of the Catalan Society of Emergency Medicine designed a protocol for the pre-hospital care of the seriously intoxicated patient. This protocol includes initial assessment, treatment, and referral to the most suitable hospital for further treatment. The protocol described two main groups of severely poisoned patients, those who present clinical instability with impaired vital signs, and clinically stable patients with suspected potentially severe poisoning. According to this classification, we distinguished two priorities for activating the code: Priority Zero for unstable patients, who require a referral center with Intensive Care Unit (ICU) facilities, and Priority One for those patients with potentially serious poisoning who require treatment in an Emergency Department (ED). The staff of the Emergency Medical System (EMS) must activate the CodiTox and choose the type of priority. For this activation, it is necessary to evaluate the clinical manifestations, and transmit a set of data to the Coordinating Center, which is in charge of notifying the receiving center of the patient's arrival.

**Results:** In June 2018, CodiTox was approved [1]. This protocol describes activation priorities, as well as decontamination and antidote treatments, according to the toxin involved and the clinical manifestations of the patient. We considered it was necessary to carry out a pilot test of CodiTox in the Girona Health Region. Due to the Covid-19 pandemic, the pilot test was delayed until May 2022. The application of CodiTox in Girona describes the referral circuit for patients with priority zero directly to the ICU of the Santa Caterina Hospital, and for patients with priority one to the ED of the local hospital. Up to October 2022, the EMS has referred 17 zero-priority patients directly to the ICU after pre-hospital care; 53% of them were women, with an average age of 50.7 years and 4.4 days of stay in the ICU. There have been no reported deaths.

**Conclusion:** Assistance to the intoxicated patient frequently begins during pre-hospital care. Having rapid and agile consultation protocols allows a more efficient evaluation and treatment of the intoxicated patient. Referring the intoxicated patient to the most appropriate hospital in the first instance, should improve the prognosis and survival of these patients.

## Reference

[1] Galicia M, Gispert MA, Nogué S, et al. Activation code for acute general poisoning (CodiTox); 2018 [cited 2022 Oct 10]. Available from: http://www.socmue.cat/docs/gr_treball/socmueTox/CodiTOX.pdf (Spanish).


# 69. *In vivo* evaluation of novel target pathways for the development of delayed cardiovascular dysfunction after sulfur mustard exposure


Jacqueline S. Rioux, Carly A. Johnson, Julie W. Harral, Mohamed S. Basiouny, Leslie A. Bloomquist, Shenali R. Uragoda, Denver Armstrong, Jasmine Martinez, Carl W. White and Livia A. Veress

Department of Pediatrics, University of Colorado, Denver, CO, USA



**Objective:** Sulfur mustard (SM) inhalation is known to cause chronic cardiovascular disease in survivors after sublethal exposures [1]. Up to 42% of Iranian veterans exposed to SM had echocardiographic evidence of delayed pulmonary hypertension (PH), with 18% also having right ventricular (RV) dysfunction. The purpose of this study was to elucidate novel mechanisms for the development of delayed cardiovascular injury in a relevant translational animal model of SM inhalation exposure.
**Methods:** This was an *in vivo* research study. Male Sprague-Dawley rats were exposed to an $LD_{50}$ dose of inhaled SM (1.2 mg/kg) as previously described [2] and monitored for 29 days. Steady-state hemodynamics and cardiac function analysis were evaluated at 29 days via diaphragmatic approach and pressure-volume catheter. Weekly transthoracic echocardiography was conducted. Proteomic analysis was performed using liquid chromatography-mass spectrometry (LC-MS) on homogenized lung tissue and interpreted against the rat proteome database.
**Results:** Mean pulmonary artery pressure (mPAP) was elevated at 27 mmHg in SM-exposed versus 20 mmHg in naïve rats (CI: 5.74–6.82, $p < 0.0001$). RV end systolic pressures were elevated at 33 mmHg in SM-exposed versus 23 in naïve rats (CI: 6.19–13.34, $p < 0.0001$). Echocardiography showed that cardiac output was decreased to 72 mL/min in SM-exposed versus 106 mL/min in naïve (CI: 12.1–25.4, $p = 0.02$). Proteomics data showed significant upregulation of several endothelial cell (EC) and cardio/myocyte injury pathways after SM, including: (1) general EC dysfunction (MGP, Slmap, Hspb7, Apobr, Hmox1), (2) EC dysfunction with Hif-regulated changes (HK3), (3) vascular permeability changes (Pacsin3, Ceacam), (4) EC remodeling (Filip1l, Lox), and (5) cardio/myocyte expansion pathways (Hspb, Pdlim5).
**Conclusion:** We showed that our rat model of SM inhalation produced human-relevant cardiovascular dysfunction 29 days after acute exposure, inclusive of development of PH, elevated RV pressures and depressed cardiac output. Moreover, we found that several EC dysfunction and cardio/myocyte injury pathways were upregulated on proteomics analysis, leading to more extensive pathway delineation studies in future research. Development of therapies targeting these aberrantly enhanced pathways may help prevent or improve outcome from chronic cardiovascular disease after SM inhalation.



## References

[1] Mohammadzadeh Shabestari M, Alizadeh L, Moshiri M, et al. Late cardiac complications of sulfur mustard poisoning in 38 Iranian veterans. Cardiovasc Toxicol. 2019;19:220–228.

[2] McGraw MD, Dysart MM, Hendry-Hofer TB, et al. Bronchiolitis obliterans and pulmonary fibrosis after sulfur mustard inhalation in rats. Am J Respir Cell Mol Biol. 2018;58:696–705.


# 70. Viper envenomation in Greece – experience from the Greek Poison Information Center during the year 2022


Vasiliki Mougiou, Myrto Bonataki, Vasiliki Kotsira, Ioanna-Maria Sykara, Vasiliki Papathanasiou, Eleni Basanou and Angeliki Kalostou

Greek Poison Information Center, Pan. and Aglaia Kyriakou Children's Hospital, Athens, Greece



**Objective:** Snake venom poisoning caused by species of the Viperidae family is a common medical emergency in several Greek regions especially during their main season of activity, between early spring and late autumn. *Vipera ammodytes* accounts for the majority of envenomation, yet several other species like *Vipera xanthina*, *Macrovipera lebetinus* (*Vipera lebetina*) and *Vipera berus* can be found in specific areas [1]. The aim of this study was to review the epidemiological, clinical and laboratory findings, as well as the treatment and outcome of snakebite poisoning in Greece as documented retrospectively by the Poison Information Center (PIC).
**Methods:** Data regarding snakebites during the period May 2022 to September 2022 were analyzed from the PIC database and the medical records kept in the corresponding hospitals.
**Results:** A total of 83 snakebites was reported with a predominance of the male gender (72%) and a mean age of 45 years among patients. The most usual anatomical locations for the bites were upper and lower extremities. Overall, 85.5% of all patients developed envenomation characterized mainly by local edema and 45.8% showed rapidly progressive and extensive swelling. Other common complications included erythema, ecchymoses, coagulopathy, gastrointestinal symptoms and thrombocytopenia. A mere 3.6% presented with hypotension while 1 case of elevated cardiac enzymes was documented and other complications like rhabdomyolysis, hemolysis, lymphadenitis and neurological signs (1 ptosis) were rare. All patients received supportive and symptomatic treatment including tetanus prophylaxis, antibiotics, analgesics and IV fluids. Antivenom treatment was administered in 51.8% of all cases, with a range of interval between snakebite and antivenom administration of 2–68 hours, mainly due to patients' delayed presentation at the emergency department. During this period, 2 different types of venom antiserum were available, administered either IV or IM, and they were used equally. In 44.2% of all cases were antivenom was given, a second or even a third dose was needed to control the symptoms. In all other cases, antivenom therapy resulted in prompt clinical improvement and only one case of urticaria was noted as an adverse effect. No deaths occurred in this series.
**Conclusion:** Viper envenomation is a medical emergency that requires hospitalization and close monitoring. Most cases can be treated successfully with either conservative methods or antivenom treatment which is highly effective and very safe.



## Reference

[1] Frangides CY, Koulouras V, Kouni SN, et al. Snake venom poisoning in Greece. Experiences with 147 cases. Eur J Intern Med. 2006;17:24–27.

## 71. An Australian regional review of the use and location of snake antivenom

Amy Thomson and Jared A. Brown
NSW Poisons Information Centre, Sydney, Australia

**Objective:** To reduce waste and improve management of patients with snakebites in Australia's most populous region, New South Wales (NSW) and the Australian Capital Territory (ACT) by providing a statewide approach to snake antivenom stocking.
**Methods:** A retrospective observational study assessing the current location of snake antivenom vials and comparing this to the number of vials used for snake envenomations in humans and the geographical distance from the bite site to the hospital that stocks the antivenom vials. Participants included adults and children who have been previously recruited to the Australian Snakebite Project with a confirmed or suspected snakebite. Main outcome measures included: geographical location of the bite, distance to the hospital, quantity of antivenom used by each hospital and quantity of antivenom stock on hand.
**Results:** A total of 772 snakebite cases were reviewed, of these 361 were envenomed. In total 306 patients received antivenom (254 envenomed patients received antivenom, 52 non-envenomed patients also received antivenom). The median distance by road from geographical snakebite site to the facility that administered antivenom is 28.5 km or 28 minutes transit time (IQR 45.8 km, 35 minutes).
**Conclusion:** Based on historical data many hospitals can safely reduce the quantity of antivenom on hand. Analysis of historical snakebite data can inform a statewide approach to optimal stock levels. There is a need to regularly review antivenom location and stock levels in NSW and the ACT. A statewide approach is needed to reduce waste and increase patient access to antivenom in a timely manner.

## 72. Viper bite: a case report

Victoria Lobo Antuña[a], Celia Piñero[a], Marta Lobo Antuña[b] and Benjamin Climent[a]
[a]Consorcio Hospital General Universitario de Valencia, Valencia, Spain; [b]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

**Objective:** Viper bite is a rare but potentially fatal emergency. Prompt treatment is crucial for a favourable evolution, therefore this type of emergency must be promptly addressed by a trained healthcare professional.
**Case report:** A 44-year-old woman consulted for a snakebite on her right foot while walking in a rural area of south-eastern Spain around 8:00 p.m. on a summer evening. She reported immediate pain and swelling of the limb 30 minutes later. The description of the snake indicated that it was a viper (triangular head, vertical pupils and small scales). Upon her arrival, she was hemodynamically stable but with pain, ecchymosis and ascending edema on the right foot, with pulses present. There were two punctate incisions 2 cm apart in the medial region of the first toe. Compartment syndrome was excluded. Laboratory tests revealed mild leukocytosis with neutrophilia and thrombocytopenia; coagulation and the creatine kinase activity were within normal ranges. Classified as moderate poisoning, antivenom was administered along with analgesia and prophylactic antibiotic therapy. Partial improvement was observed and the patient was discharged 5 days later, but she returned 48 hours later for worsening of the pain. Physical examination revealed erythema and increased local temperature on the back of her right foot, as well as a hematoma following the path of the saphenous vein. D-dimer was elevated and an echo-Doppler of the lower limb showed thrombophlebitis of the superficial veins. Anticoagulant treatment was started but tenderness persisted. After 6 months of treatment the pain resolved but paresthesias remained as a sequela of post-thrombotic syndrome.
**Conclusion:** The incidence of viper bites in Spain is low and in the Iberian Peninsula there are 3 species of vipers [1]. The species *Vipera latastei* inhabits the south-east. This type of emergency occurs predominantly in summer, more frequently among men and the bite is usually located on the upper extremity. The identification of the reptile is of great importance and the geographical location, time of day, characteristics of the reptile and its bite morphology need to be considered. Once the diagnosis has been made and the snake identified, it is essential to determine the severity of the lesion, since the administration of antivenom is only recommended in moderate and severe cases. Viper bites are a rare but serious entity and an adequate approach is decisive in the evolution of these patients.

### Reference

[1] Martín-Sierra C, Nogué-Xarau S, Pinillos Echeverría MÁ, et al. Snakebite poisoning in Spain. Emergencias. 2018;30:126–132.

## 73. The utility of hyperbaric oxygen therapy in severe necrotizing infection secondary to suspected spider bite: a case report

Anna A. Celentano[a], Giovanni G. Sesana[b], Carmela C. Graci[b], Paolo P. Pantini[c], Marcello M. Ferruzzi[a] and Francesco F. Scaglione[a]
[a]Milan Poison Control Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [b]Hyperbaric Medicine Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [c]Civic Museum of Natural Sciences "E. Caffi", Bergamo, Italy

**Objective:** *Loxosceles rufescens* (LR) is a spider indigenous to the Mediterranean Europe. The therapeutic response involves a multidisciplinary approach that involves general practitioners, toxicologists, emergency doctors, infectivologists, hyperbaric specialists and plastic surgeons. In Italy *Loxosceles rufescens* is present and often takes refuge in homes. Skin loxoscelism is characterized by cutaneous necrosis, sometimes complicated by soft tissue infection or necrotizing fasciitis. We describe a case of severe necrotizing infection probably caused by a bite by this spider which was treated with pharmacological therapy, hyperbaric oxygen therapy (HBOT) and rehabilitation.
**Case report:** A 44-year-old woman arrived at the emergency department (ED) with hyperpyrexia and vesicles on her swollen aching left ankle and foot. She explained that the lesion had started as a small insect bite that gradually extended to a large purulent spot and then to the whole foot with pain and oedema within 48 hours. She had not felt the bite. *Streptococcus agalactiae* infection was diagnosed and treated with antibiotics, morphine, fasciotomy and vacuum assisted closure therapy that was performed for one month. A debridement and a fasciotomy of the fifth metatarsal were performed. Finally, the Poison Center

was consulted and a diagnosis of LR bite was suspected. The patient was admitted to the infective disease ward and due to worsening and rapid local evolution with increasing pain, it was decided, in agreement with the hyperbaric medicine center, to perform two sessions of HBOT daily at 2.8 ATA. HBOT was performed for three weeks for a total of 22 sessions. Other therapy included: antibiotics, clonazepam, pregabalin, acetaminophen, ebastine, hydroxyzine and a regenerating cream. An autologous skin graft was applied and HBOT was continued. During the HBOT cycles, the lesion decreased with injury delimitation. Full functionality of the limb has been achieved with rehabilitation.
**Conclusion:** Symptoms of loxoscelism tend to appear late and diagnosis is frequently delayed. If the correct diagnosis is delayed, HBOT may still contribute to the recovery and prevent the loss of the affected limb. The poison control center is the reference center for the diagnosis of loxoscelism and for information on the pharmacological management. Hyperbaric oxygen treatment promotes the delimitation of the lesion and is important for recovery. HBOT results in a decrease in pain and in a faster demarcation of the eschar.

## 74. Compartment syndrome after Italian viper bite: two case reports

Lucia Bernasconi[a], Monica Carnovale[a], Davide Lonati[b], Benedetta Brolli[a], Valentina Negrini[a], Cristina Grazioli[a], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS. Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Compartment syndrome is a rare complication occurring after European viper bites. It may be secondary to extensive oedema or thrombosis at the bite site, leading to increase in the intra-compartment pressure causing perfusion compromise and tissue ischemia. Children seem to have higher risk of this complication due to the potential severity of envenomation. We present two cases of compartment syndrome after a viper bite treated with decompressive fasciotomy.
**Case series:** Case 1: A 6-year-old female, was admitted to the emergency department (ED) 2 hours after a snake bite on the left foot. On admission, grading severity score (GSS) was 1 and laboratory tests were normal except for slightly elevated D-dimer (789 ng/ml). Three hours later the oedema spread to the thigh, and she manifested bilateral ptosis. The patient was transferred to a tertiary care hospital to receive specific antidote; at hospital arrival GSS was 3 and, she was intubated due to worsening neurological condition. One vial of Viekvin® antivenom was administered 7 hrs after the initial bite. Despite antidotal therapy, local symptoms worsened with appearance of ischemic areas; measured compartment pressure confirmed the diagnosis of compartment syndrome and urgent surgical decompression with fasciotomy was performed. The patient recovered without any major limb sequela. Case 2: A 38-year-old female, presented to hospital with GSS 1 three hours after a snake bite to the right foot. The patient was initially discharge after 36 h of observation due to amelioration of local manifestations and unremarkable lab tests. She returned 48 h after discharge with extensive oedema, from ankle to proximal thigh, of the bitten limb that developed over the previous day, associated with severe pain and a large hematoma. Laboratory tests showed anemia (Hb 9 g/dL), with normal platelets count, white blood cells and D-dimer (467 ng/mL). One vial of Viper Venom Antitoxin, was urgently administered, but despite antivenom therapy compartment syndrome developed, and surgical fasciotomy was performed. The clinical course was further complicated by local infection of the surgical wound, but she recovered with major sequelae.
**Conclusions:** In these cases, antivenom was administered at GSS 3, in the first case because it was not available in the ED and in the second due to late hospital presentation. This may have been responsible for insufficient therapeutic response. These cases highlight the importance of prompt administration of antivenom at GSS 2, to avoid severe local evolution, and the need of antivenom availability across Italian hospitals. When compartment syndrome develops, fasciotomy remains the best therapeutic approach to avoid local sequelae.

## 75. Failure of viper antivenom therapy and the need for an effective antidote: an Italian pediatric case series

Lucia Bernasconi[a], Davide Lonati[b], Azzurra Schicchi[b], Benedetta Brolli[a], Cristina Grazioli[a], Valentina Negrini[a], Monica Carnovale[b], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS. Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Antivenom availability in Italian emergency departments (ED) varies greatly and no comparative data on effectiveness are available. Moreover, viper envenomation may be due to 4 different species (*Vipera aspis is the* most common) and may be severe, especially in children. We evaluate envenomed pediatric cases in which the clinical toxicologist decided to administer different antivenoms to increase the probability to counteract the vipera venom toxic effects.
**Methods:** Pediatric patients (1–14 years) referred to the Poison Control Center (January 2014–September 2022) requiring administration of more than one type of antivenom were retrospectively evaluated. Ineffectiveness was defined as worsening of local/systemic symptoms after 8 h. Age; sex; time between bite and ED-admission; antivenom/number of vials, grading severity score (GSS) at first/second antidote administration; outcome; adverse effects were collected.
**Results:** Six cases were included [mean age 5.8 (2–10) years, males 83.3%]. Viper-Venom-Antitoxin® was administered as first antivenom in all cases. Five cases received a second antidote because of worsening edema to avoid compartment syndrome; in 1 case because of severe neurotoxicity (cranial nerves palsy and dysphagia) (Table 1). All patients improved after administration of the second antidote and no compartment syndrome complicated our cases. No acute or delayed adverse reactions were recorded.
**Conclusion:** All pediatric patients requiring a second antivenom were previously treated with Viper-Venom-Antitoxin®. This antivenom is monovalent against *Vipera berus* and its potency is not comparable to $ED_{50}$ considered as gold standard by the World Health Organization. European-viper-venom-antiserum® is no

Table 1. Details of pediatric patients requiring more than one type of viper antivenom

| Case no. | Gender, age | Time elapsed from bite to ED presentation (hours) | GSS at time of first antidote administration | First antivenom, number of vials | GSS at time of second antidote administration | Time elapsed from bite to second antivenom administration (hours) | Second antivenom, number of vials |
|---|---|---|---|---|---|---|---|
| 1 | M, 6 | 20 | 2 | Viper Venom Antitoxin[↓], 1 | 3 | 30 | European viper venom antiserum®, 1 |
| 2 | M, 2 | 4 | 2 | Viper Venom Antitoxin[↓], 1 | 3 | 48 | European viper venom antiserum®, 1 |
| 3 | M, 4 | 5 | 2 | Viper Venom Antitoxin[↓], 1 | 3 | 30 | European viper venom antiserum®, 1 |
| 4 | M, 10 | 3 | 3 | Viper Venom Antitoxin[↓], 2 | 3 | 27 | Viekvin®, 2 |
| 5 | M, 5 | 7 | 2 | Viper Venom Antitoxin[↓], 1 | 3 | 18 | ViperFAV®, 1 |
| 6 | F, 8 | 5 | 2 | Viper Venom Antitoxin[↓], 1 | 3 | 24 | ViperaTAb®, 1 |

GSS: grading severity score.

longer available in Europe. ViperaTAb®/Viekvin®/ViperFAV® showed better clinical efficacy in our experience [1]. These cases highlight the need of further clinical data on variation of antivenom efficacy by country and the urgent need for an effective antidote against all types of Italian vipers, to ensure appropriate treatment of envenomed patients.

## Reference

[1] Bolsi G, Lonati D, Schicchi A, et al. Antidote treatment in viper envenomation in Italy: a comparison of 4 antivenoms during a 6 year study. Clin Toxicol. 2020;58:594.

# 76. Portuguese man o' war: heart attack! First case of *Physalia physalis* cardiotoxicity reported in Italy

Valentina Negrini[a], Cristina Naturale[b], Monica Carnovale[a], Cristina Grazioli[a], Elena Mattiuzzo[b], Giulia Scaravaggi[b], Valeria M Petrolini[b], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute. Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** *Physalia physalis* belongs to the class of Hydrozoa. It is a colonial organism native to the tropical and subtropical areas of Atlantic Ocean, characterized by a pneumatophore, from which hang long tentacles with nematocysts containing one of the most powerful toxins of marine fauna. The venom is composed of a protein, neurotoxic and cardiotoxic complex, which is inactivated by heat at temperatures great than 55 °C/131 °F. Contact with nematocysts causes instant and durable pain. Erythematous skin lesions in a linear pattern replicating the tentacle shape, often associated with oedema and giant urticaria, usually accompany it. The most important systemic symptoms include asthenia, nausea and vomiting, loss of consciousness, seizures, arrhythmias and bronchial asthma. No antidote is available.

**Case report:** On July 17, in Sicily, a 68-year-old woman, after a contact with a Portuguese man o' war developed skin lesions, nausea and vomiting, followed the day after by severe asthenia, mental confusion and hypotension. She referred to Pavia Poison Control Center (PCC) that, considered the risk of neurologic and cardiologic sequelae, sent her to the local Emergency Department to monitor vital signs and laboratory tests. During the night, the patient developed a high frequency atrial fibrillation, treated with electrical cardioversion. On July 19, she reported fever and signs of local infection of the skin lesions, accompanied by leucocytosis and increased C-reactive protein (CRP), so, local and systemic antibiotic therapy was started. During the night, two episodes of paroxysmal supraventricular tachycardia occurred, treated with sinus massage. After that, symptoms progressively improved until resolution on July 21, when the patient was discharged.

**Conclusion:** Warming of the Mediterranean's water allows new oceanic and tropical species to find a favourable environment and this exposes the population to new risks of envenomation. Our patient developed several symptoms of *P. physalis* toxicity. The cutaneous lesions are characteristic. From a systemic perspective, the arrhythmic events were predominant. Atrial fibrillation and ventricular tachycardia were identified as a cardiotoxic effect of *Physalia*'s venom; non-pharmacological treatments were chosen, because of the risk of unknown interactions between medications and the toxin. All the systemic manifestations resolved after 72 hours. In consideration of the clinical evolution, the initial indication from Pavia PCC was confirmed: ED access to monitor vital signs and electrocardiography until complete resolution of systemic symptoms, laboratory tests, support therapy and, if needed, antibiotics.

# 77. Fatal stings

Wui Ling Chan

Emergency Department, Khoo Teck Puat Hospital, Singapore, Singapore

**Objective:** Insects responsible for the majority of the serious sting-related reactions belong to the order Hymenoptera. Typically, the patient will not be able to identify the culprit insect, which makes targeted therapy (e.g., immunotherapy) difficult. Reactions to hymenoptera stings range from uncomplicated local reactions to large local reactions and anaphylaxis [1]. Literature review shows that patients with large numbers of wasp stings can result in multi-organ failure (MOF) and its severity appears to be dependent on the number of stings [2]. In one local study, insect venom hypersensitivity was responsible for 32.8% of anaphylaxis cases presenting to the immunology/allergy centre, of which honeybee and wasp stings comprised 45% of the insect venom anaphylaxis [3]. We report a fatality associated with multi-organ failure after multiple insect stings.
**Case report:** A 62-year-old gentleman, with history of hypertension and ischemic heart disease, presented to the Emergency Department (ED) complaining of pain and breathlessness after he was stung multiple times by insects. His vital signs were stable. On examination, there were multiple discrete sting marks with a central area of haemorrhage seen over his face, trunk and limbs. There were no stings lodged within these lesions. He was treated with intravenous (IV) antihistamines, steroids and opioid analgesia. A nasoendoscopy was performed and showed no upper airway concerns. However, he deteriorated rapidly within the next 20 hours and developed MOF. He succumbed to his illness 3 days after initial presentation despite maximal supportive care in the intensive care unit (ICU). Treatment in the ICU included: intubation, triple inotropic support, hemodialysis, IV N-acetylcysteine, IV vitamin K and IV antibiotics.
**Conclusion:** Insect venom hypersensitivity and its associated systemic complications may be underdiagnosed. This case highlights the importance of awareness of this condition. These patients need an extended period of observation and can deteriorate rapidly. Regular, close monitoring, in addition to maximal supportive management will be the strategy in managing such patients.

## References


[1] Freeman T. UpToDate: bee, yellow jacket, wasp and other hymenoptera stings: reaction types and acute management [cited 2022 Oct 10]. Available from: https://www.uptodate.com/contents/bee-yellow-jacket-wasp-and-other-hymenoptera-stings-reaction-types-and-acute-management.

[2] Yanagawa Y, Morita K, Sugiura T, et al. Cutaneous hemorrhage or necrosis findings after *Vespa mandarinia* (wasp) stings may predict the occurrence of multiple organ injury: a case report and review of literature. Clin Toxicol. 2007;45:803–837.

[3] Thong BY, Cheng YK, Leong KP, et al. Anaphylaxis in adults referred to a clinical immunology/allergy centre in Singapore. Singapore Med J. 2005;46:529–534.


# 78. Ivermectin toxicosis in dogs: circumstances, clinical signs and severity of poisoning


Nicola Bates, Zoe Tizzard and Nick Edwards

Veterinary Poisons Information Service, London, United Kingdom


**Objective:** Ivermectin is used in veterinary medicine as a broad-spectrum ecto- and endoparasiticide. Toxicosis is characterised by neurological signs; some breeds such as collies are more susceptible due to a deletion in a gene which changes expression of P-glycoprotein allowing increased uptake of ivermectin into the brain. Ivermectin is lipophilic and mainly excreted in faeces. We reviewed canine cases of ivermectin exposure.
**Methods:** A retrospective study of cases with follow up information involving ivermectin exposure in dogs reported to the Veterinary Poisons Information Service (1985-2022). Cases involving praziquantel were included as praziquantel is of low toxicity and unlikely to have contributed to signs or outcome. Severity was scored using the Poison Severity Score (PSS) modified for dogs.
**Results:** Overall 148 cases (137 oral, 8 parenteral, 1 ear, 2 skin) were included (ivermectin/praziquantel =18). The most common circumstances of exposure were ingestion of a large animal product (57.4%, in feed $n=2$) or faeces of treated animals (horse, cattle, sheep, pig, alpaca) (9.5%) and therapeutic error (12.8%). Overall, 117 dogs (79.1%) developed signs. The dose was estimated in 35 oral cases; in symptomatic ($n=22$) and asymptomatic ($n=13$) dogs the estimated median dose was similar (2.3 and 2.7 mg/kg, respectively). Common signs were ataxia (44.6%, 66/148), blindness (43.2%), muscle tremor (35.1%), mydriasis (23.8%) and vomiting (21.1%). Median duration of effects was 48 hours (range 3–240 hours, $n=52$). Where specified ($n=18$), blindness lasted <24 hours to 10 days (median 64 hours). Overall PSS was asymptomatic 20.9%, mild 19.6%, moderate 22.3%, severe 25.7% and fatal 11.5% (9 died, 8 euthanased). For collie/collie crosses ($n=30$) severity was asymptomatic 13.3%, mild 30.0%, moderate 20.0%, severe 13.3% (one dog tested negative for double recessive gene for ivermectin sensitivity) and fatal 23.3% (5 died, 2 euthanased). The severity in the 22 symptomatic dogs that received intravenous lipid emulsion was mild 22.7%, moderate 45.5%, severe 22.7% and fatal 9.1% (1 died, 1 euthanased).
**Conclusion:** Ivermectin products intended for large animals are a particular risk for dogs. Exposures occur after direct ingestion (often dropped or spilled while treating a large animal), mixed with feed or via ingestion of faeces of treated animals. Over half of symptomatic dogs developed ataxia and/or blindness. Overall, the severity of poisoning was high (59.5% had PSS ≥2). The fatality rate was higher in dogs described as collie/collie crosses (23.3%) and lower in dogs that received lipid emulsion (9.1%), compared to the case series overall (11.5%).

# 79. Nitroscanate toxicosis in cats and dogs


Nicola Bates, Zoe Tizzard and Nick Edwards

Veterinary Poisons Information Service, London, United Kingdom


**Objective:** Nitroscanate is a broad spectrum veterinary anthelmintic available over the counter as 100 mg and 500 mg tablets. The therapeutic dose in dogs is 50 mg/kg orally and it is not for use in puppies under 2 kg or 6 months. Products for cats are not available in the UK but 25 mg/kg has been used. We reviewed cases of nitroscanate exposure in cats and dogs.
**Methods:** A retrospective study of cases with follow up information involving nitroscanate exposure in cats and dogs reported to the Veterinary Poisons Information Service (1992–2022). Severity for dogs was scored using the Poison Severity Score (PSS) modified for dogs.
**Results:** There were 65 canine cases of which 27 dogs (41.5%) were under 2 kg and/or 6 months (all were symptomatic). In 15 of these cases (55.6%) the owner had given the nitroscanate. Only four dogs (6.2%) remained well; the dose was 100–243.9 mg/kg. The median dose in symptomatic dogs was 112.4 mg/kg (range 16.7–500 mg, $n=48$). The most common signs were ataxia (36/65, 55.4%), emesis (40.0%), lethargy (24.6%), disorientation (24.6%) and elevated liver enzymes (16.9%). Overall, 96.7% of symptomatic dogs recovered. Time to

recovery was 6 hours to 19 days (median 42 hours, $n = 20$). PSS was asymptomatic 6.2%, mild 66.2%, moderate 15.4%, severe 9.2% and fatal 3.1%. PSS in puppies <2 kg and/or <6 months was asymptomatic 0, mild 63.0%, moderate 14.8%, severe 18.5% and fatal 3.7%. A 1.1 kg, 2.5 month old Cavalier King Charles Spaniel died after 454.6 mg/kg and a 2 kg Pomeranian was euthanased after 100 mg. There were 26 feline cases. Four cats (15.4%) were asymptomatic; the dose was 26.3–125 mg/kg ($n = 3$). The median dose ingested in symptomatic cats was 122 mg/kg (range 44.4–333.3 mg/kg, $n = 12$). Common signs were ataxia (76.9%) and emesis (19.2%). The median recovery time was 48 hours (range 12–72 hours, $n = 9$). Overall, 19 cats recovered and 3 were euthanased (11.5%). The dose in two fatal cases was 25.6 and 166.7 mg/kg. The third cat was euthanased after gradual deterioration over a week.

**Conclusion:** Ataxia was the most common sign in cats and dogs, with a higher incidence in cats. Nitroscanate toxicosis occurred in all puppies where it was contraindicated due to age or body weight. Most dogs had only mild toxicosis, with higher incidence of severe poisoning in puppies. The fatality rate in cats (11.5%) was higher than in dogs (3.1%), but feline case numbers were small.

## 80. Use of rivastigmine to treat scopolamine toxicity: a case report

Samantha S. Klein and Robert S. Hoffman

Ronald O. Perelman Department of Emergency Medicine, Division of Medical Toxicology, New York University School of Medicine, New York, NY, USA

**Objective:** The use of physostigmine is limited in the US by ongoing market shortages. In patients with significant antimuscarinic toxicity, the use of rivastigmine is uncommonly reported [1–3]. We present a patient successfully treated with rivastigmine to further support this alternative treatment.

**Case report:** A 31-year-old woman was hospitalized for intractable abdominal pain and provided with a scopolamine patch on arrival for symptom control. The patient began to display signs of altered mental status and agitation about 6 hours later with no response to antipsychotics or benzodiazepines. Her vitals were: blood pressure 135/74 mmHg; heart rate 126 beats/minute; 22 breaths/minute; temperature 36.2 °C. On examination, she was agitated and pulling at her IV and monitor lines. She had dilated, nonreactive pupils (6 mm), dry, flushed skin, and was actively hallucinating that there were small children running around her room. The scopolamine patch was removed two days after the patient's symptoms began, once it was suspected to be the source of her agitation. Given the physostigmine shortage, the patient was given pyridostigmine without response. The poison center was contacted for help managing the patient's altered mental status and we recommended oral rivastigmine for antimuscarinic toxicity reversal. The patient received three doses of 3 mg oral rivastigmine, 1 hour apart. On reassessment, 6 hours after her last dose, her mental status had returned to baseline, her tachycardia resolved, and she did not display any further signs of antimuscarinic toxicity during her hospital stay.

**Conclusion:** Central nervous system toxicity from antimuscarinic agents can be severe. During a shortage of physostigmine, other reversal agents are needed. In a rat model, rivastigmine reversed scopolamine-induced memory impairment [4]. We present a patient with significant antimuscarinic toxicity successfully treated with oral rivastigmine to further support this practice.

### References

[1] Van Kernebeek MW, Ghesquiere M, Vanderbruggen N, et al. Rivastigmine for the treatment of anticholinergic delirium following severe procyclidine intoxication. Clin Toxicol. 2021;59:447–448.

[2] Hughes AR, Moore KK, Mah ND, et al. Letter in response to Rivastigmine for the treatment of anticholinergic delirium following severe procyclidine intoxication. Clin Toxicol. 2021;59(9):855–856.

[3] Sandia S I, Ramírez V J, Piñero A J, et al. Treating 'devil's breath' intoxication: use of rivastigmine in six patients with toxic psychoses due to non pharmaceutical scopolamine. Eur Neuropsychopharmacol. 2017;27:833–834.

[4] Bejar C, Wang RH, Weinstock M. Effect of rivastigmine on scopolamine-induced memory impairment in rats. Eur J Pharmacol. 1999;383:231–240.

## 81. Status epilepticus in the setting of an intentional ingestion of propranolol: a case report

Samantha S. Klein[a] and Mark K. Su[b]

[a]Ronald O. Perelman Department of Emergency Medicine, Division of Medical Toxicology, New York University School of Medicine, New York, NY, USA; [b]Department of Health and Mental Hygiene, New York City Poison Control Center, New York, NY, USA

**Objective:** Seizures are a known potential complication of propranolol overdose. Status epilepticus induced by intentional overdose is less frequently reported [1]. We describe a case in which a patient presented with status epilepticus after an overdose of propranolol.

**Case report:** A 26-year-old woman with a history of post-traumatic stress disorder (PTSD) presented to the emergency department (ED) after an intentional ingestion of her propranolol during a suicide attempt. She had called her psychiatrist to tell him what she had done and he immediately called Emergency Medical Services (EMS). When they arrived, she was noted to have a generalized tonic-clonic seizure and was endotracheally intubated in the field for airway protection. Upon arrival to the ED, she had a second seizure. Her initial vital signs were: blood pressure 85/58 mm/Hg; heart rate 64 beats/minute; respiratory rate 12; temperature 36.2 °C; and oxygen saturation 100% ($FiO_2$, 100%). Her electrocardiogram showed first-degree AV block with a QRS interval of 114 ms and PR interval of 220 ms at a rate of 52 beats per minute. The patient was given intravenous glucagon 5 mg and a glucagon infusion (5 mg/h). Despite glucagon administration, norepinephrine and high dose insulin infusion of 1 unit/kg/h were required due to hemodynamic instability. She was admitted to the intensive care unit and had four more seizures overnight. The following day, she was transferred to a facility with continuous electroencephalogram (EEG) monitoring. She did not experience further seizures at the receiving facility and her infusions were down titrated and ultimately discontinued 3 days after her overdose. She remained stable and did not display further signs of toxicity during her admission.

**Conclusion:** Propranolol is the most lipophilic of all beta-adrenergic antagonists which allows rapid entry into the central nervous system (CNS). The exact mechanism of how it exerts these CNS effects, including seizures, is unclear. There is evidence that propranolol is concentrated in synaptic vesicles and impairs synaptic function by inhibition of membrane ion pumps including sodium-potassium ATPase, calcium ATPase and magnesium ATPase pumps. These actions may explain some of the effects noted in propranolol overdose [2]. While uncommon, it appears

that propranolol in overdose may lead to the development of status epilepticus.

## References


[1] Lauterbach M. Clinical toxicology of beta-blocker overdose in adults. Basic Clin Pharmacol Toxicol. 2019;125:178–186.

[2] Gopalaswamy UV, Satav JG, Katyare SS, et al. Effect of propranolol on rat brain synaptosomal Na(+)-K(+)-ATPase, Mg(2+)-ATPase and Ca(2+)-ATPase. Chem Biol Interact. 1997;103:51–58.


# 82. Performance of the ICU requirement score (IRS) in predicting the need for ICU admission of intoxicated adult patients: the INTOXICATE study


Samanta M. Zwaag[a], Claudine C. Hunault[a], Dylan W. de Lange[a,b], Ana Ferrer-Dufol[c], Arzu Topeli[d], Elin Lindqvist[e,f], Patrick Druwé[g], Gabija Laubner-Sakalauskiene[h], Muhammed Elhadi[i], Richard Rezar[j] and Stuart Baker[k,l]

[a]Dutch National Poisons Information Centre (NPIC), University Medical Center Utrecht, Utrecht, Netherlands; [b]Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, Netherlands; [c]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza University, Zaragoza, Spain; [d]Hacettepe University Ankara, Ankara, Turkey; [e]Department of Anaesthesiology and Intensive Care, South Hospital Stockholm, Stockholm, Sweden; [f]Department of Clinical Science and Education, South Hospital Stockholm, Karolinska Institutet, Stockholm, Sweden; [g]Department of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium; [h]Faculty of Medicine, Toxicology Centre, Republican Vilnius University Hospital, Vilnius University, Vilnius, Lithuania; [i]Faculty of Medicine, University of Tripoli, Tripoli, Libya; [j]Department of Cardiology and Intensive Care Medicine, Paracelsus Medical University of Salzburg, Salzburg, Austria; [k]Intensive Care Unit, Redcliffe Hospital, Redcliffe, Queensland, Australia; [l]Faculty of Medicine, University of Queensland, Brisbane, Queensland, Australia



**Objective:** To assess the performance of the intensive care unit (ICU) requirement score (IRS) for acutely intoxicated adults in an international ICU cohort with calibration analysis to demonstrate model accuracy.

**Methods:** Data from the INTOXICATE study, an international multi-center cohort, collected from September 2020 to July 2022 were used. Variables are age, blood pressure, heart rate, exposure, Glasgow Coma Score (GCS), presence of dysrhythmia, respiratory failure, liver cirrhosis and/or second ICU diagnosis and ICU requirement (defined as receiving mechanical ventilation and/or vasopressors for at least an hour) and/or death during hospital stay [1]. Exclusion criteria are age below 18 years, ICU stay of less than 4 hours and/or ICU requirement before ICU admission. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were obtained with complete case analysis (CCA). C-statistic, intercept and slope of the calibration plot were obtained with pooled analyses of multiple imputed datasets ($m = 5$) with 10 iterations. All analysis were performed in RStudio version 1.3.1093.

**Results:** Of the 998 patients enrolled, 205 were excluded. Sensitivity and specificity were 0.92 (CI: 0.87–0.96) and 0.31 (0.27–0.36), respectively. PPV and NPV were 0.34 (0.29–0.38) and 0.91 (0.86–0.95), respectively ($n = 655$). C-statistic was 0.72 (0.67–0.76) and the intercept and slope of the calibration plot were −0.70 and 0.65, respectively ($n = 793$).

**Conclusion:** The IRS has a high sensitivity and a good NPV similar to other studies [2,3] indicating that the model can be used to reduce unnecessary admissions in an international ICU population. The calibration needs to be optimized and the model recalibrated by adjusting the intercept and potentially the slope in order to increase its precision. More patients are needed for more precise performance estimates.


## References


[1] Brandenburg R, Brinkman S, de Keizer NF, et al. The need for ICU admission in intoxicated patients: a prediction model. Clin Toxicol. 2017;55:4–11.

[2] Böll R, Romanek K, Schmoll S, et al. Independent validation of the ICU requirement score in a cohort of acutely poisoned adults. Clin Toxicol. 2018;56:664–666.

[3] El Gharbi F, El Bèze N, Jaffal K, et al. Does the ICU Requirement Score allow the poisoned patient to be safely managed without admission to the intensive care unit? – a validation cohort study. Clin Toxicol. 2022;60:298–303.


# 83. The emerging cloud: a survey of vapers, their health, and the associated burden on the UK health system


Lachlan J. Sund, Paul I. Dargan and David M. Wood

Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom



**Objective:** Recent work in the UK has demonstrated that the prevalence of current cannabinoid vaping exceeds that of the US, a factor previously associated with the E-cigarette or Vaping Associated Lung Injury (EVALI) outbreak in the US [1]. Given there have only been sporadic reports of EVALI in the UK, we aimed to identify symptoms amongst UK vapers that were reported in US EVALI cases and to determine the healthcare burden associated with these symptoms.

**Methods:** A voluntary online survey of individuals aged 16 and over within the UK was conducted, via a market research company. Anonymised data were collected on respondent demographics, vaping and smoking status, vaping products used, symptomatology (shortness of breath (SOB), cough, chest pain, fever/high temperature, chills, lethargy/fatigue, nausea, vomiting, palpitations, bloody sputum), healthcare attendances (accident and emergency, general practitioner or other health clinic) and diagnoses given.

**Results:** In total 2477 complete responses were analysed (Table 1); 397 respondents defined themselves as "current" vapers, median age was 37 years (IQR 29–51) and 215 (54.2%) were male. "Current" vapers who used cannabinoid-based products alone or in combination, accounted for a higher number of presentations per healthcare attendant for all symptoms, with the exception of palpitations and bloody sputum.

**Conclusion:** This survey identified that current UK vapers experience a number of symptoms reported in US EVALI cases. Current UK vapers of cannabinoid-based products and nicotine-free e-liquids in combination were more likely to seek medical attention for cough and SOB, and cannabinoid-based products were associated with a higher healthcare burden. Clinicians most frequently diagnosed lower respiratory tract infections, asthma/

Table 1. Key findings in a survey of individuals aged 16 and over within the UK on the use of e-liquid and symptomatology.

| | |
|---|---|
| Products used, by "current" vapers: N (%)/prevalence of concurrent cigarette smoking *N* (%[A])*n* = 397[A] within each group | Nicotine-based + nicotine-free e-liquids: 150 (37.8%)/92 (61.3%)<br>Cannabinoid-based products, nicotine-based and nicotine-free e-liquids: 98 (24.7%)/ 81 (82.7%)<br>Nicotine-based e-liquids: 92 (23.2%)/42 (45.7%)<br>Nicotine-free e-liquids: 20 (5.04%)/9 (45.0%)<br>Cannabinoid-based products + nicotine-based e-liquids: 16 (4.0%)/15 (93.8%)<br>Cannabinoid-based products: 13 (3.27%)/8 (61.5%)<br>Cannabinoid-based products + nicotine-free e-liquids: 8 (2.02%) /6 (75.0%) |
| Symptom prevalence amongst "current" vapers within previous 12 months | Cough (34.7%), lethargy/fatigue (25.9%), shortness of breath (23.4%), chest pain (12.3%), nausea (12.1%), chills (12.1%), fever/high temperature (8.6%), palpitations (7.6%), vomiting (5.8%), bloody sputum (3.8%) |
| Number of "current" vapers who sought medical attention for each symptom within previous 12 months: *N*/Total healthcare attendances[B] *N* (%)[B] *n* = 383 | Shortness of breath: 49/130 attendances (33.9%)<br>Cough: 31/61 attendances (15.9%)<br>Chest pain: 31/42 attendances (11.7%)<br>Lethargy/fatigue: 25/45 attendances (11.7%)<br>Fever/high temperature: 15/31 attendances (8.1%)<br>Palpitations: 13/26 attendances (6.8%)<br>Nausea: 10/18 attendances (4.7%)<br>Chills: 10/16 attendances (4.2%)<br>Vomiting: 8/12 attendances (3.1%)<br>Bloody sputum: 2/2 attendances (0.5%) |
| "Current" users of products that were more or less likely to seek medical attention for specific symptoms[C] (Relative Risk)[C] In comparison to other "current" user groups | Cannabinoid-based products + nicotine-free e-liquids<br>– Shortness of breath (RR 3.3 95% CI 1.3, 8.1)<br>– Cough (RR 5.2 95% CI 2.0, 13.6)<br>Cannabinoid-based products– Shortness of breath (RR 2.63 95% CI =1.1, 6.2)<br>Nicotine-based + nicotine-free e-liquids<br>– Shortness of breath (RR 0.48 95% CI 0.3, 0.9)<br>– Cough (RR 0.40 95% CI 0.2, 0.9) |
| Most frequent diagnoses | Respiratory tract infection *n* = 39<br>Asthma/chronic obstructive pulmonary disease *n* = 23<br>Anxiety/panic attack *n* = 8 |

chronic obstructive pulmonary disease (COPD), or anxiety/panic attacks rather than vaping associated pathology.

## Reference

[1] Sund LJ, Wood DM, Archer JRH, et al. The unseen cloud – a survey of vaping practices and the acquisition of vaping products within the United Kingdom. QJM. 2023;116:99–106.

# 84. Clinical characterization and prognosis outcomes of carbon monoxide poisoning in Spain. The AMICO study

Antonio F. Caballero-Bermejo[a], Belén Ruiz-Antorán[a], Cristina Ramió Lluch[b], Maria Eulàlia Guerrero González[b], Antonio Dueñas-Ruiz[c], Catalina Homar Amengual[d], Maria Àngels Gispert-Ametller[b], Aránzazu Sancho-López[a], Rosa Capilla Pueyo[e], Emilio Salgado García[f], Antonio Dueñas-Laita[c] and Jordi Puiguriguer Ferrando[d]

[a]Clinical Pharmacology Department, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain; [b]Emergency Department, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [c]Clinical Toxicology Unit, Hospital Universitario Río Hortega, Valladolid, Spain; [d]Emergency Department, Clinical Toxicology Unit, Hospital Universitario Son Espases, Palma, Spain; [e]Emergency Department, Hospital Universitario Puerta De Hierro Majadahonda, Madrid, Spain; [f]Emergency Department, Clinical Toxicology Unit, Hospital Clínic Barcelona, Barcelona, Spain

**Objective:** Carbon monoxide (CO) poisoning debuts with heterogenous symptoms and is clearly underdiagnosed in Europe. The most serious complication is delayed neurologic sequelae (DNS), which occurs in up to 30% of patients. We describe clinical characteristics of CO poisoning and identify prognostic factors of developing delayed neurologic sequelae (DNS) after an initial episode of CO poisoning.

**Methods:** A retrospective review of all cases of pure CO poisoning (those poisoned by fire smoke were excluded) presenting to the Emergency Department of 3 tertiary hospitals in Spain during the last 10 years. We analyzed demographics and clinical characteristics at the time of the episode. In patients with follow-up data available, we evaluated the appearance of DNS and its relationship with different variables in the initial exposure to CO.

**Results:** In total 194 cases were identified. Median age was 35.9 years (IQR, 17.8–49.9); 54.7% were female and 182 cases (93.8%) were accidental. The leading causes of poisoning were malfunctioning braziers (27.8%) and poor combustion of a faulty boiler (27.8%). Eight (4.1%) patients required hospitalization, 5 patients (2.6%) were admitted to the ICU and none died. Main symptoms were headache (58.2%), dizziness (54.1%) and loss of consciousness (28.4%). Initial mean (SD) Glasgow Coma Score (GCS) was 14.3 (2.4). Median first carboxyhemoglobin (COHb) levels were 12.5% (IQR, 5.97–17.8). Of the 31 patients (16.0%) with available follow up, 9 patients (29.0%) developed DNS, 8 of these (88.9%) presented magnetic resonance imaging (MRI) alteration. The following have been identified as predictive factors for the development of DNS: GCS (mean (SD) 13.2 (4.2) in patients with DNS versus 14.7 (1.1); $p < 0.001$), the presence of nausea and vomiting (50% of patients with these symptoms developed DNS versus 15.8% in patients without digestive symptoms, $p = 0.041$) and confusion (55.6% with initial confusion developed DNS versus 18.2% in patients without initial confusion, $p = 0.037$). No statistically significant differences were found in the other variables analyzed.

**Conclusion:** GCS, the initial presence of nausea and vomiting, and confusion appear to be clinical predictors of the

development of DNS. Due to the high incidence of DNS (29% in our cohort), we consider it essential to establish multidisciplinary clinical protocols for the follow-up of these patients. The identification of factors related to a higher risk of developing DNS could facilitate early recognition of the patients who are candidates for this follow-up.

## 85. Improving prognosis in *Amanita phalloides* intoxication – are two antidotes needed?

Daniela Pelclova[a], Katerina Kotikova[a], Jaroslav Klan[b], Eva Kieslichova[b], Peter Ondra[c], Jan Zofka[d] and Vladimira Gebauerova[e]

[a]Department of Occupational Medicine, Toxicological Information Centre, First Medical Faculty of the Charles University and General University Hospital in Prague, Prague, Czech Republic; [b]Institute of Forensic Medicine and Toxicology, First Medical Faculty of the Charles University and General University Hospital in Prague, Prague, Czech Republic; [c]Department of Forensic Medicine and Medical Law, Palacky University and Faculty Hospital Olomouc, Olomouc, Czech Republic; [d]Institute of Health Information and Statistics of the Czech Republic, Prague, Czech Republic; [e]Institute of Forensic Medicine, University Hospital Ostrava, Ostrava, Czech Republic

**Objective:** Mushrooms intoxications in the Czech Republic represent a persistent problem, as collecting wild mushrooms is a popular hobby. The treatment and outcome in cases from the past three years was studied.
**Methods:** The inquiries to the Toxicological Information Centre (TIC) in the years 2019–2021, discharge reports and data from toxicological laboratories, performing mushroom identification, including spore identification in the meal, gastric or gut content and/or amatoxins in serum and urine using liquid chromatography-mass spectrometry (LC-MS) were analysed.
**Results:** The number of calls due to mushrooms increased from an average 80 calls (1.6% of total calls) in 1990–1991 to 550 calls yearly (2.4%) in 2019–2021, when an average 125 patients/year were hospitalized for mushroom intoxication. Average yearly counts of mycological analyses in 2019–2021 reached 245 and concerned an average 185 patients/year. Among 207 analyses of biological samples, only 13 samples in 12 patients detected amatoxins (serum 1, urine 12). No post-mortem analysis was performed. TIC provided silibinin for 10 patients, 8 were also treated with N-acetylcysteine (NAC) (Table 1). Supportive extracorporeal treatment was used in 4 patients; patients 1 and 3 were on the waiting list but finally all subjects recovered without liver transplant.
**Conclusion:** In the past 3 years, no lethal mushroom intoxication was recorded by the Institute of Health Information and Statistics of the Czech Republic, unlike in 1990–1991 when mortality was 25.9%. One reason is the higher awareness of the public and shortened time-interval to hospital admission with gastrointestinal elimination of toxins and treatment. Secondly, new antidotes are used. NAC is commonly available as first line antidote, however silibinin acts by several mechanisms. A prospective study is needed to estimate the best order and necessity of combined treatment with both antidotes.

### Acknowledgement

Cooperatio 207041-3 Pharmacology.

## 86. Rivastigmine for the management of anticholinergic delirium: a case series

Angela L. Chiew[a], Betty S. H. Chan[a] and Katherine K. Isoardi[b]

[a]Department of Clinical Toxicology, Prince of Wales Hospital, Sydney, Australia; [b]Clinical Toxicology Unit, Princess Alexandra Hospital, Brisbane, Australia

**Objective:** Anticholinergic agents are commonly taken in overdose and anticholinergic delirium (ACD) is a common complication. ACD is a spectrum of mild agitation to severe behavioural disturbance. The management of ACD often involves chemical sedation with some patients requiring large doses to settle delirium. Physostigmine, an acetylcholinesterase inhibitor that crosses the blood-brain barrier has been shown to be effective in the management of ACD. However, it has a short duration of action and its availability is limited in many countries. Rivastigmine has been proposed in a few case reports as an alternative agent to manage ACD [1,2] and is available as a dermal patch and oral tablet. We report a case series of patients with ACD who were managed with rivastigmine (oral and/or dermal patch) from two toxicology units from January 2019 to June 2022.
**Case series:** Thirty patients were administered rivastigmine for the management of ACD. The median age was 35 years (IQR:

Table 1. Characteristics and treatment in patients treated for amatoxin intoxication.

| No | Sex/Age (years) | Body weight (kg) | Mushroom (pieces) | Onset of symptoms/ admission (hours) | Peak AST (μkat/L) | Peak ALT (μkat/L) | Peak bilirubin (mmol/L) | Peak INR | Peak creatinine (μmol/l) | Hospital stay (days) | Antidote | Extracorporeal treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M/6 | 23 | 1/2 | 10/17 | 177.9 | 158.2 | 68 | 3.25 | 153 | 12 | Silibinin, NAC | Yes |
| 2 | M/36 | 78 | 1/2 | 12/17 | 4.2 | 4.0 | 25.5 | 1.01 | 93 | 2 | Silibinin | No |
| 3 | M/52 | na | 3 | 8/40 | ≥40 | ≥95 | na | na | ≥560 | 13 | Silibinin | Yes |
| 4 | F/18 | na | 1 | 10/17 | 2.0 | 3.5 | 12 | 1.29 | 70 | 9 | NAC, Silibinin | No |
| 5 | M/45 | 105 | 2 | 12/40 | 123.6 | 148.7 | 43.4 | 3.24 | 194 | 9 | Silibinin, NAC | Yes |
| 6 | M/42 | 75 | 4–5 | No/4 | ≥24.0 | ≥10.2 | ≥38.6 | 1.15 | ≥128 | 12 | Silibinin, NAC | No |
| 7 | M/37 | 75 | 1 | No/3 | 0.48 | 0.64 | 6.6 | 0.86 | 67 | 3 | NAC, silibinin | No |
| 8 | F/68 | 68 | 2 | No/3 | 0.6 | 1.2 | 15.9 | 1.15 | 62.7 | 6 | NAC, silibinin, V-PNC | No |
| 9 | F/72 | 110 | 3 | No/3 | 81.7 | 106.6 | 132.5 | 4.48 | 66 | 8 | NAC, silibinin | No |
| 10 | M/83 | 60 | 4 Small | 11/48 | 56.8 | 63.8 | 46 | 2.08 | 115 | 9 | Silibinin, NAC | No |
| 11 | M/44 | 107 | 5–6 Small | 10/24 | 40.7 | 56.2 | 46.9 | 3.25 | 153 | 8 | NAC, silibinin | Yes |

ALT: alanine aminotransferase; AST: aspartate aminotransferase; na: not available; NAC: N-acetylcysteine

26–48y) and half were females. Other features consistent with anticholinergic toxicity present included tachycardia ($n = 21$), urinary retention requiring catheterisation ($n = 25$) and temperature >37.5 °C ($n = 4$). Most patients were administered physostigmine ($n = 26$) prior to rivastigmine administration. Twenty-two patients were managed with dermal rivastigmine (most commonly 9.5 mg/24 h), and 8 with 6 mg oral rivastigmine. Additional parenteral sedation or physostigmine was required in 15/22 given dermal rivastigmine and 1/8 given oral. No patients had bradycardia or gastrointestinal symptoms following rivastigmine administration. Two patients had seizures; both had also received physostigmine.

**Conclusion:** ACD can be difficult to manage and a longer acting, readily available agent such as rivastigmine may be useful given physostigmine's limited availability. In our series the dermal formulation of rivastigmine appeared less effective, which is likely due to its slow onset with peak rivastigmine concentration achieved with the dermal versus oral formulation, at 8.1 hours versus 1.4 hours, respectively [3]. Oral rivastigmine appears to be a useful antidote in the management of ACD.

## References

[1] Van Kernebeek MW, Ghesquiere M, Vanderbruggen N, et al. Rivastigmine for the treatment of anticholinergic delirium following severe procyclidine intoxication. Clin Toxicol. 2021;59:447–448.

[2] Hughes AR, Moore KK, Mah ND, et al. Letter in response to rivastigmine for the treatment of anticholinergic delirium following severe procyclidine intoxication. Clin Toxicol. 2021;59:855–856.

[3] Kurz A, Farlow M, Lefèvre G. Pharmacokinetics of a novel transdermal rivastigmine patch for the treatment of Alzheimer's disease: a review. Int J Clin Pract. 2009;63:799–805.

# 87. Emergency provision of botulism-antitoxin-heptavalent serum throughout the National Health System: the Italian experience of the National Antidotes Stockpile

Giulia Scaravaggi[a], Valeria M. Petrolini[a], Davide Lonati[a], Azzurra Schicchi[a], Monica Carnovale[a], Francesca Zaffino[b], Olha Maystrova[a] and Carlo A Locatelli[a]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [b]Directorate General for Health Prevention, Ministry of Health, Roma, Italy

**Objective:** In Italy heptavalent-botulism-antitoxin (HBAT) is imported (extra-EU) and supplied by the Ministry of Health (MoH) for the intangible extraordinary endowment of antidotes for CBRN events (e.g., botulinum toxins as biological weapons). Nevertheless, food-borne botulism is frequent in Italy (approximately 50% of all European cases) due to the consumption of improperly home-canned foods [1]. Thus, HBAT (50 mL vial, heptavalent against toxins A-G available in Italy from September 2018) is located in strategic stockpiles throughout Italy to be rapidly mobilized to hospitals. The extraordinary (not for biological attack) mobilization procedure requires the clinical evaluation by Pavia Poison Control Centre (PPCC) and an on-time MoH authorization. We evaluate HBAT extraordinary mobilizations (HBAT-EM) over 4-years.

**Methods:** Clinical characteristics of the botulism case (e.g., form, number of vials, adverse reaction, outcome) and location of hospitals and national stockpile were evaluated for all HBAT-EM between September 2018 and September 2022.

**Results:** HBAT was mobilized for 130 patients (1 vial/patient in all cases; median HBAT-EM/year 26, range 3-58) with suspected botulism. The source was food-borne in 120/130 cases (92.3%; 78/120 male; median age 50.5 years), wound botulism 2/130 cases (1.5%; 2/2 male; median age 47 years), infant botulism in 8/130 cases (6.2%; 5/8 female; median age 101 days). Laboratory confirmed cases were 90/130 (69.2%), while botulism was excluded in 8/130 (6.2%; Guillain-Barré 4/8 cases; Miller-Fisher Syndrome 3/8 cases; myasthenia gravis 1/8 cases). Adverse effects (6/130 cases; 4.6%) were acute in 2.3% (mild hypotension 1/3, mild myalgia 1/3, fever 1/3) and delayed (15–40 days after IV-administration) in 2.3% (thrombocytopenia 1/3, fever 1/3, urticaria 1/3); thrombocytopenia is reported for the first time. Most patients recovered, but death occurred in 5 cases (3.8%). HBAT-EM involved 6 national stockpiles (Rome 39/130, Pavia 25/130, Taranto 21/130, Bologna 19/130, Naples 19/130, Catania 4/130, Genova 3/130, located in 7 different Italian regions) for 81 different NHS hospitals located in 16 Italian regions.

**Conclusion:** The geo-localization of national stockpiles ensures a rapid and efficient supply of appropriate botulism treatment. National stockpiles, established for unconventional events, are an essential facility in order to have the necessary antidote HBAT in cases of "natural" botulism. Follow-up performed up to 40 days after HBAT administration allows identification of adverse effects. The organization of Italian national stockpiles combines clinical toxicological expertise and antidote supply in order to facilitate diagnostic and therapeutic appropriateness.

## Reference

[1] Anniballi F, Auricchio B, Fiore A, et al. Botulism in Italy, 1986–2015. Euro Surveill. 2017;22:30550.

# 88. The EU early warning system on new psychoactive substances: 25 years of early warning and response in Europe

Joanna de Morais, Michael Evans-Brown, Ana Gallegos, Rachel Christie, Rita Jorge, Gregorio Planchuelo and Roumen Sedefov

European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal

**Objective:** The European Union Early Warning System (EU EWS) on New Psychoactive Substances (NPS) operated by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in close cooperation with Europol, has operated since 1997. It was the first regional early warning system to be established to monitor new psychoactive substances (NPS) and has been recognised as a model for national, regional and international early warning systems.

**Methods:** The EU EWS rapidly detects, assesses and responds to health and social threats caused by NPS. Data collected and analysed include event-based data on seizures by law enforcement, collected samples and serious adverse events linked to NPS. These data are complemented by annual reports, which include aggregated data from law enforcement seizures and poisonings.

**Results:** By September 2022, the EMCDDA was monitoring more than 910 NPS. The number of substances in circulation remains high, with approximately 400 previously reported NPS detected in 2021. Following a period of diminishing law enforcement seizures in Europe, the availability of NPS in Europe has reached historical levels, with more than 8.5 tonnes seized in Member States in 2021. At least in part, this increase has been driven by a large increase in law enforcement seizures of synthetic cathinones, in particular 3-chloromethcathinone (3-CMC) and 3-methylmethcathinone (3-MMC). Information from suspected poisonings in certain parts of Europe suggests that the incidence of poisoning related to 3-MMC reported to poison centers has increased significantly between 2020 and 2021 compared to previous years and that this coincides with an increased availability and use of this substance. In addition, in 2020 and 2021 concerns continued to be raised over the adulteration of illicit drugs with NPS, such as reports of low-THC cannabis adulterated with synthetic cannabinoids and detections of NPS in fake medicines, in particular benzimidazole opioids in fake oxycodone tablets.
**Conclusion:** The EU EWS plays a central role in supporting national- and EU-level preparedness and responses to NPS. Given the growing complexity of the NPS market and its strong links with the broader illicit drug market, there is a need to ensure that Europe continues to strengthen its ability to detect, assess, and respond to emerging threats in a timely and effective way in order to prevent or reduce the public health and social harms caused by NPS. Poison centres play a central role in detecting, characterising, responding, and evaluating the effectiveness of response measures to emerging toxicological issues related to NPS.

## 89. ChemSex context and substance abuse: a case series

Benedetta Brolli[a], Cristina Grazioli[a], Azzurra Schicchi[b], Giulia Scaravaggi[c], Pietro Papa[d], Antonella Valli[d], Ilaria Giardini[d], Francesca Crema[e] and Carlo A Locatelli[c]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute. Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Experimental Medicine PhD Program, Toxicology Unit, Pavia Poison Control Centre - National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, University of Pavia, Pavia, Italy; [c]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [d]Laboratory of Analytical Toxicology, Clinical Chemistry Service, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [e]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Chemsex is a practice in which drugs are abused in order to improve and prolong sexual performance. It is more common in men who have sex with men (MSM)/transgender communities. Substances commonly used are cathinones, GHB/GBL, poppers, 3,4-methylenedioxymethamphetamine (MDMA), ketamine, and sildenafil, usually ingested, smoked, sniffed, or injected. Rectal administration is also used. We aimed to evaluate the frequency of chemsex inquiries to our Poison Control Centre (PCC) in the last 12 years in order to evaluate the diffusion of the phenomenon, to better characterize clinical features and the more frequently abused substances.

Table 1. Patient characteristics, analytical data, treatment and outcome in 61 patients who abused substances in a chemsex context.

| Patient's characteristics | Median [25°,75°]/% |
|---|---|
| Gender | 100% M |
| Age (years) | 35 [19–63] |
| Clinical manifestations at emergency department admission | |
| Cardiorespiratory symptoms | 72% |
| Neuroexcitatory symptoms | 54% |
| Neuroinhibition | 37.7% |
| Rhabdomyolysis | 19.7% |
| Seizures | 16.4% |
| Miosis | 11.5% |
| Hyperthermia | 9.9% |
| Liver enzyme alteration | 8% |
| Mydriasis | 4.9% |
| Renal failure | 1.6% |
| Declared substances | |
| Cathinones (16 different types) | 65.6% |
| Gamma-hydroxybutyrate/gamma-butyrolactone (GBH/GBL) | 27.9% |
| Substance not specified | 18.3% |
| Cocaine | 16.4% |
| Alcohol | 9.8% |
| Benzodiazepines/neurodepressants | 9.8% |
| MDMA/derivatives | 9.8% |
| Ketamine/ other dissociatives | 6.5% |
| Synthetic cannabinoids | 5% |
| Amphetamine/methamphetamine/derivatives | 5% |
| Cannabis/tetrahydrocannabinol (THC) | 5% |
| Other drugs | 5% |
| Nitrates | 3.3% |
| Lysergic acid diethylamide (LSD)/lysergic acid 2,4-dimethylazetidide (LSZ) | 3.3% |
| Laboratory analysis (plasma and/or urine determination) | |
| Cathinones | 98% |
| GHB/GBL | 24.6% |
| Cocaine | 19.7% |
| Amphetamine/methamphetamine/derivatives | 16.3% |
| Cannabis/THC | 11.5% |
| MDMA/derivatives | 8.2% |
| Opiates | 6.6% |
| Benzodiazepines/neurodepressor | 6.6% |
| Ketamine/other dissociatives | 3.3% |
| Other drugs | 3.3% |
| Levamisole | 3.3% |
| Synthetic cannabinoids | 3.3% |
| LSD/LSZ | 1.6% |
| Treatment | |
| Benzodiazepines | 55% |
| Major sedation (propofol/remifentanil/fentanyl/curare) | 19.7% |
| Naloxone | 9.8% |
| Flumazenil | 8.2% |
| Orotracheal intubation | 1.6% |
| Physical restraint | 1.6% |
| Length of hospitalisation (days) | 3 days [1, 32] |
| Outcome | |
| Recovery | 100% |

**Methods:** We designed a retrospective observational study including all patients referred in 2010–2022 to our PCC who abused substances in a "chemsex" context. For all included patients we collected data about (I) drugs declared by the patient, (II) substances determined by laboratory analysis, clinical and biological parameters on admission and during hospitalization, treatment and outcome.
**Results:** In total 61 patients were included (Table 1). During the study years the distribution of the cases was: 2010 (1/61), 2011 (3/61), 2012 (3/61), 2013 (2/61), 2014 (3/61), 2015 (6/61), 2016 (1/61), 2017 (5/61), 2018 (7/61), 2019 (10/61), 2020 (4/61), 2021 (11/61), 2022 (5/61).
**Conclusion:** An increasing trend of chemsex phenomenon has been observed in recent years. Substances most frequently used

are cathinones and GHB. There is high variability in clinical picture that can be characterized by neuroexcitatory symptoms if new psychoactive substance (NPS) abuse is prevalent or neuroinhibitory in case of GHB abuse. High variability is also detected in the different substances abused, in many cases without accordance between declared substance and that determination by second level toxicological analysis. The laboratory support able to perform second level analysis enables physicians to make the correct diagnosis and to identify new molecules.

## 90. Acute tolfenpyrad poisoning reported to Taiwan National Poison Center: a case series

Nai-Yu Chen[a], Jou-Fang Deng[a] and Chen-Chang Yang[a,b]

[a]Department of Medicine, National Poison Center & Division of Clinical Toxicology & Occupational Medicine, Taipei Veterans General Hospital, Taipei City, Taiwan; [b]College of Medicine, Institute of Environmental & Occupational Health Sciences, National Yang Ming Chiao Tung University, Taipei City, Taiwan

**Objective:** Tolfenpyrad, a mitochondrial complex I electron transport inhibitor, is used as an insecticide. Knowledge about the clinical characteristics and treatment of tolfenpyrad poisoning is limited to a few case reports, and measurement of serum/urine tolfenpyrad concentration is only available in postmortem analysis [1]. In this case series, we describe the clinical profile of four fatal cases with intentional oral tolfenpyrad ingestion reported to Taiwan National Poison Center (PCC-Taiwan) between 2015 and 2022.
**Case series:** Case 1. A 71-year-old woman who ingested an unknown amount of tolfenpyrad was found unconscious by her family. She was in cardiac arrest and could not be revived after cardiopulmonary resuscitation. Case 2. A 76-year-old woman who drank 100 mL of tolfenpyrad was found with loss of consciousness, vomiting, and seizures by her family. When she arrived at the emergency department (ED), she had hypothermia, mydriasis, and profound shock with severe lactic acidosis. She was discharged in a moribund state and later died at her home. Case 3. A 65-year-old woman who drank 170 mL of tolfenpyrad presented with nausea, vomiting, dyspnea, and cold sweat. She was sent to the ED in thirty minutes. Initial vital signs were stable, but she soon developed respiratory failure. Laboratory data showed severe metabolic acidosis and acute renal failure. Hypothermia (32.5 °C) was observed within four hours and she died 23 hours post-exposure. Plasma tolfenpyrad level was 463 ng/mL thirty minutes post-exposure, whereas serial serum tolfenpyrad concentrations measured by liquid chromatography/mass spectrometry ranged from 62.2 to 66.7 ng/mL between 30 minutes and 18 hours post-exposure. Case 4. An 80-year-old man who drank 100 mL of tolfenpyrad was found to be in a comatose state with some vomitus next to him. Twenty minutes later, he was sent to the ED with respiratory failure, bradycardia, and mydriasis. He passed away four hours later.
**Conclusion:** The clinical manifestations of tolfenpyrad poisoning include disturbance of consciousness, gastrointestinal symptoms, respiratory failure, mydriasis, unstable hemodynamics, metabolic acidosis, and hypothermia. The case fatality rate from tolfenpyrad poisoning was 100% among the four cases reported to PCC-Taiwan. Given the extremely high toxicity of tolfenpyrad, identification of possible predictors of severity and effective treatment of tolfenpyrad poisoning are warranted.

### Reference

[1] Hikiji W, Yamaguchi K, Saka K, et al. Acute fatal poisoning with tolfenpyrad. J Forensic Leg Med. 2013;20:962–964.

## 91. From heroin to prescription opioids: opioid poisoning in Australia over the last three decades

Katherine Z. Isoardi[a] and Geoffrey K. Isbister[b,c]

[a]Clinical Toxicology Research Group, University of Newcastle, Newcastle, Australia; [b]Clinical Toxicology Research Group, University of Newcastle; [c]Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle, Newcastle, Australia

**Objective:** Opioid-related harm has risen in Australia in recent decades. Despite this, there is little research describing the clinical burden of opioid poisoning to Australian hospitals. We aimed to investigate hospital presentations with opioid poisoning over three decades.
**Methods:** This prospective cohort study investigates opioid poisoning presentations to a clinical toxicology unit over 32 years. The Toxicology Service database was searched for all adult patients (>15 years) with an opioid exposure between 1990 and 2021. Data regarding opioid exposure, naloxone administration, intubation, intensive care unit (ICU) admission, length of stay and death were extracted.
**Results:** There were 4492 presentations in 3574 patients (median age 36, 57.7% female) over the period, increasing from an average of 93 presentations each year in the first decade to 199 in the third decade. Deliberate self-poisonings accounted for 3694 presentations (82.2%). Heroin was dominant in the 1990s, peaking in 1999 before decreasing. Prescription opioids then rose, with codeine (almost always in paracetamol combination) predominating until 2018, after which oxycodone presentations exceeded them. Methadone consistently increased from an average of six presentations each year in the first decade to 16 in

Table 1. The commonest opioids resulting in 4492 opioid-related presentations to a clinical toxicology unit from 1990–2021.

| Opioid | Codeine | Oxycodone | Heroin | Methadone | Morphine | Tramadol |
|---|---|---|---|---|---|---|
| Presentations | 2618 | 724 | 496 | 347 | 206 | 195 |
| Deliberate self poisoning | 2488 (95%) | 639 (88%) | 169 (34%) | 172 (50%) | 165 (80%) | 178 (91%) |
| Co-ingestions | 2608 (99%) | 644 (89%) | 322 (65%) | 255 (73%) | 177 (86%) | 168 (86%) |
| Naloxone | 171 (7%) | 205 (28%) | 293 (59%) | 207 (60%) | 106 (51%) | 22 (11%) |
| Intubation | 106 (4%) | 44 (6%) | 43 (9%) | 31 (9%) | 28 (14%) | 12 (6%) |
| Seizure | 19 (<1%) | 4 (<1%) | 16 (3%) | 7 (2%) | 2 (1%) | 18 (9%) |
| Death | 6 (<1%) | 0 | 9 (2%) | 2 (1%) | 8 (4%) | 0 |
| ICU admission | 52 (2%) | 60 (8%) | 34 (7%) | 47 (14%) | 26 (13%) | 9 (5%) |
| Median LOS | 16 h | 17 h | 12 h | 19 h | 24 h | 16 h |

ICU: intensive care unit; LOS: length of stay.

the last decade. Naloxone was administered in 990 (22.0%) presentations and 266 (5.9%) were intubated, both highest with heroin and methadone, then oxycodone (Table 1). ICU admissions increased from 5% or less between 1990 and 2014 to 16% in 2021. Codeine resulted in less severe effects, most morbidity and mortality was due to co-ingested paracetamol; methadone resulted in the most severe effects overall. The median length of stay was 17 hours (IQR:9–27 hours). There were 28 deaths (0.6%).
**Conclusion:** Opioid presentations increased in number and severity over three decades, and the type of opioid changed. Oxycodone is currently the main opioid of concern, causing more severe toxicity than codeine. Methadone poisoning increased and was the most severe.

## 92. Naloxone requirements of confirmed para-fluorofentanyl exposures in emergency department patients with illicit opioid overdose

Kim Aldy[a], Alex Krotulski[b], Jeffrey Brent[c], Sharan Campleman[a], Alison Meyn[a], Stephanie Abston[a], Rachel E. Culbreth[a], Barry Logan[b], Paul Wax[a], Alexandra Amaducci[d], Bryan Judge[e], Michael Levine[f], Diane Calello[g], Joshua Shulman[h], Adrienne Hughes[i], Evan Schwarz[j] and Alex F. Manini[k]; on Behalf of the Fentalog Study Group

[a]American College of Medical Toxicology, Phoenix, AZ, USA; [b]Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation, Willow Grove, PA, USA; [c]University of Colorado School of Medicine, Aurora, CO, USA; [d]Lehigh Valley Health Network/USF Morsani College of Medicine, Allentown, PA, USA; [e]Spectrum Health/Michigan State University, Grand Rapids, MI, USA; [f]University of California– Los Angeles, Los Angeles, CA, USA; [g]Rutgers New Jersey Medical School, Newark, NJ, USA; [h]University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [i]Oregon Health and Science University, Portland, OR, USA; [j]Washington University School of Medicine, St. Louis, MO, USA; [k]Icahn School of Medicine at Mount Sinai, New York, NY, USA

**Objective:** Para-fluorofentanyl (PFF), a fentanyl analog, is a schedule 1 drug with no accepted medical use in the US. PFF is commonly found in combination with illicit fentanyl, but occasionally alone, and may reflect a change in the use of precursors in illicit fentanyl manufacture. We aimed to examine the naloxone requirements of confirmed PFF exposures in emergency department (ED) patients with illicit opioid overdose (OD).
**Methods:** This is a secondary data analysis from the ToxIC Fentalog Study, an ongoing prospective multicenter cohort at 8 participating medical centers across the United States. Adult patients with suspected acute opioid OD are enrolled, clinical data is gathered, and residual blood samples collected as part of routine clinical care were analyzed qualitatively by liquid chromatography quadrupole time-of-flight mass spectrometry for the presence of over 900 psychoactive substances. For this analysis, we included only confirmed illicit opioid OD (positive PFF and/or fentanyl). Bivariate analyses were conducted to determine sociodemographic and clinical differences between cases with PFF present and cases without PFF. Multivariable log-linear regression analyses were conducted among cases who received naloxone to determine the association between PFF and naloxone dose requirements while adjusting for other covariates (i.e., age, sex, race/ethnicity, and other non-fentanyl opioid present). Sex-stratified analyses were also conducted. All analyses were conducted in R 4.1.2 and approved by a central IRB (WIRB).
**Results:** Between 21 September 2020 and 30 September 2022, 537 patients met the inclusion criteria, and 422 samples contained fentanyl and/or PFF. The PFF analyte was detected in 87 of these cases (20.6%). A higher percentage of patients positive for PFF received the first dose of naloxone in a healthcare facility (26.5%) compared to patients negative for PFF (11.2%) ($p < 0.01$). In the multivariable model, PFF was associated with approximately 33% less naloxone required compared to those without PFF (Est: -0.40; 95% CI: −0.68, −0.13) after adjusting for covariates. In the sex-stratified analyses, PFF was associated with less naloxone required for males (Est: −0.57; 95% CI: −0.94, −0.21) but this association was not statistically significant for females.
**Conclusion:** PFF was present in over one-fifth of ED patients with confirmed illicit opioid OD. PFF was associated with approximately one-third lower naloxone requirements compared to fentanyl alone. Based on these data, PFF may be less potent than fentanyl. More research is needed on the clinical consequences of PFF exposure.

## 93. Illicit substance use requiring chemical sedation: a prospective cohort study of 1125 patients presenting to Emergency Departments with analytically confirmed psychoactive substance exposure

Sarah Hodgson[a], Rachelle Abouchedid[a], Rebekka Syrjanen[b], Jennifer Schumann[b] and Shaun L. Greene[a]

[a]Victorian Poisons Information Centre, Melbourne, Australia; [b]Victorian Institute of Forensic Medicine, Melbourne, Australia

**Objective:** Chemical sedation is commonly employed in pre-hospital and hospital settings to control behavioural disturbance secondary to illicit substance use, however the practice is variable and chemical sedation is associated with adverse outcomes. We examined use of chemical sedation in 1125 Emergency Department patients with suspected or reported illicit drug use.
**Methods:** Data was extracted from a human research ethics committee approved registry comprising de-identified clinical and biochemical data on a convenience sample of illicit drug presentations to Emergency Departments in Victoria, Australia [1]. Blood samples were analysed using combined liquid chromatography, with tandem mass spectrometry for 575 pharmaceutical and psychoactive substances (including 324 novel psychoactive substances).
**Results:** Overall, 376/1125 (33%) patients received sedation and/or antipsychotics in the pre-hospital and/or hospital environment. Benzodiazepines were the most commonly administered agent in both contexts. Sedatives were more commonly detected in the group requiring no chemical sedation (81% versus 61%, $p < 0.0001$), as were opioids (35 versus 26%, $p = 0.004$). Methamphetamine was the most commonly detected stimulant (66% of cases, $n = 748$). There was no significant difference in frequency of methamphetamine detection between those requiring chemical sedation (264/376, 70%) and the non-sedated group (408/624, 65%) ($p = 0.126$). Patients self-reporting methamphetamine use were more likely to be administered chemical sedation (35 versus 16%, $p < 0.0001$), despite no significant difference in median methamphetamine concentration between groups: 0.12 mg/L (sedated) versus 0.14 mg/L (non-sedated), $p = 0.118$.

**Conclusion:** Despite published evidence of adverse effects [2], practice diverged from current Australian evidence-based recommendations, with benzodiazepines most commonly administered for chemical sedation in patients with suspected or confirmed illicit substance use. Patients *self-reporting* methamphetamine use experienced an increased incidence of chemical sedation, despite a lower median blood methamphetamine concentration in this group. This may relate to specific stigma and discrimination methamphetamine-users face in Australia [3]. Prescribing may be unduly influenced by healthcare practitioners' stigma towards certain illicit substances.

## References


[1] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

[2] Isbister GK, Calver LA, Page CB, et al. Randomized controlled trial of intramuscular droperidol versus midazolam for violence and acute behavioral disturbance: the DORM study. Ann Emerg Med. 2010;56:392–401.

[3] Cohn A, O'Connor R, Lancaster K, et al. Media and political framing of crystal methamphetamine use in Australia. Drugs Educ Prev Policy. 2020;27:261–270.


# 94. Sodium nitrite: an emerging public health concern in the United Kingdom


Gillian A. Cooper[a], Sally M Bradberry[b], Euan A. Sandilands[c], Ruben H. K. Thanacoody[d] and Laurence A. Gray[a]

[a]National Poisons Information Service, Cardiff, United Kingdom; [b]National Poisons Information Service, Birmingham, United Kingdom; [c]National Poisons Information Service, Edinburgh, United Kingdom; [d]National Poisons Information Service, Newcastle, United Kingdom



**Objective:** To report on sodium nitrite-related enquiries received by the UK National Poisons Information Service (NPIS) with the intention of promoting a public health message to healthcare providers.

**Methods:** A retrospective observational study of telephone enquiries received between 1 January 2008 and 31 August 2022 was performed. Enquiries involving sodium nitrite/nitrate were extracted and examined.

**Results:** The NPIS received 114 enquiries relating to potential exposure to sodium nitrite during the study period. Sixty-four related to suspected deliberate self-harm; 28 reported completed suicide or potential exposure secondary to self-harm, 19 related to accidental exposures, and 3 involved patients that were threatening to self-harm. No cases of deliberate self-harm were reported before 2018. The Internet was recorded as the source of sodium nitrite in 10 cases, but was unspecified in 40 cases. The dose, where reported ($n = 20$) ranged from approximately 5–50 g. Twenty-two patients (44%) were in cardiac arrest at the time of enquiry, 35 (70%) received methylene blue. Death was reported in 16 (32%), complete recovery in 8 (16%), and "scarred lung" in 1 case. Outcome was unknown in 25 (50%) cases (7 of which reported prolonged cardiac arrest at time of enquiry). Co-ingested agents were reported in 13 cases, none of which were anti-emetics (sometimes advised in online "suicide kits"). Twenty-eight enquiries reported suicide or secondary exposure following deliberate self-harm. Of these, 18 identified a fatality that was not apparently related to one of the cases above (2019 = 3; 2020 = 6; 2021 = 5; 2022 = 4). If these data are tallied with case reports resulting in death, the peak incidence occurred in 2020 ($n = 10$).

**Conclusion:** Sodium nitrite enquiries account for a small proportion of total enquiries discussed with the UK NPIS, but the data suggest that these cases frequently involve cardiac arrest and/or death. There were no cases noted before 2018. Despite the limitations of poisons centre data when estimating poisoning incidence this report suggests a potential worrying emerging trend in the UK.


# 95. Collaborative public health responses to suicide prevention: sodium nitrite


Jared A. Brown[a], Ingrid Berling[b], Thanjira Jiranantakan[b], Nicholas A. Buckley[b] and Andrew Dawson[b]

[a]Toxicity Response, Epidemiology and Surveillance, Sydney, Australia; [b]NSW Poisons Information Centre, Sydney, Australia



**Objective:** Internet publications and social media promoting the use of sodium nitrite for suicide and euthanasia began in 2017. Increases in self-poisoning followed and have been published in Australia and worldwide. We investigated updated time trends and characteristics of deliberate self-poisonings with sodium nitrite/nitrate in Australia to examine early impacts of public health interventions for suicide prevention.

**Methods:** Retrospective observational study of the National Coronial Information System (July 2000–December 2021) and New South Wales (NSW) Poisons Information Centre and NSW Health public health notifications. We examined survival, date, gender, age, setting, geographical location, history of a terminal or psychiatric illness, product, and toxicology results; and public health activities led by NSW Health.

**Results:** A sudden step-increase in poisonings was seen from September 2017 (and the first death), peaking in 2020 with 36 and reducing to 17 in 2021. We identified 102 suicides in total, who were mostly male (63%) with a bi-modal age distribution (peak age-adjusted rates of 20–29 and >80 years). There were a further 21 non-fatal deliberate self-poisonings, peaking in 2020


Table 1. Demographic data related to deliberate self-harm cases involving sodium nitrate.

| | | | Gender | | | | |
|---|---|---|---|---|---|---|---|
| Year | Number of enquiries | Cases | Male | Female | Unknown | Average age (range) | Fatal |
| 2018 | 4 | 4 | 3 | 1 | 0 | 28.5 (22–42) | 1 |
| 2019 | 20 | 15 | 8 | 7 | 0 | 25.2 (17–41) | 5 |
| 2020 | 19 | 15 | 9 | 5 | 1 | 29.3 (19–49) | 4 |
| 2021 | 7 | 6 | 2 | 4 | 0 | 26.2 (21–36) | 2 |
| 2022(to August 31) | 14 | 10 | 5 | 5 | 0 | 30.4 (20–43) | 4 |
| Total | 64 | 50 | 27 | 22 | 1 | 27.8 (17–49) | 16 |

with 8 and reducing to 5 in 2021. Most cases (83%) had a psychiatric illness and no terminal illness (91%). All cases with product information available reported use of pure compounds and purchased online. Many cases had incorrect documentation of sodium nitrate. Public health interventions included alerting clinicians and coroners. Changing product scheduling and enforcement, surveillance of online retailers and reporting to regulators and online marketplaces. A directive was issued to increase antidote stocking of methylene blue across NSW hospitals and to store in the Emergency Department (ED) and issuing of clinical guidelines, with proposals to NSW Ambulance to stock methylene blue and to update protocols for toxic cardiac arrest. As well as advocacy to the eSafety commissioner and police intervention on websites and social media promoting use.
**Conclusion:** The promotion of suicide methodology was associated with a dramatic change in harms from sodium nitrite. State public health actions to date have focused on enhanced surveillance, means restriction, improved antidote stocking, and clinical education. These appear to have reduced the number of poisonings but further surveillance is needed to observe if this is sustained. National and international collaboration is needed for monitoring and rapid responses to promoted lethal substances.

## 96. Accidental clozapine ingestions are of concern

Colette Degrandi and Cornelia Reichert

National Poisons Centre, Tox Info Suisse, Associated Institute of the University of Zurich, Zurich, Switzerland

**Objective:** Clozapine is an antipsychotic drug, mainly used as second-line treatment in schizophrenia. Moderate and severe symptoms can occur even after a therapeutic dose (300–900 mg/day in 2–4 doses), especially in patients older than 50 years [1]. We investigated the effects of accidental ingestion of clozapine. These ingestions often occur due to exploratory behavior in toddlers, and medication errors in older children and adults.
**Methods:** Retrospective review of accidental clozapine ingestion reported by physicians to our National Poisons Centre from 1997 to 2021 with high causality. Severity was graded according to the Poisoning Severity Score.
**Results:** There were 234 accidental clozapine ingestions. Clozapine was the primary agent in 221 cases including 134 single substance ingestions. Moderate and severe cases were characterized by agitation or coma, with complications of aspiration pneumonia and rhabdomyolysis. Convulsions were rare. In children $\leq$6 years clozapine was the primary agent in 47 cases; 41 were single substance ingestions. Thirty children developed no or minor symptoms, 9 had moderate (dose known 6/9: 50–300 mg; average 117 mg; median 100 mg) and 2 severe symptoms (maximum 100 mg and maximum 200 mg). The six children with multiple substance ingestions developed minor symptoms. In adults and children >12 years clozapine was the primary agent in 174 cases; 118 patients were >50 years old (68%). No or minor symptoms occurred in 95 patients (54% >50 years, $n = 51$); 44 developed moderate (82% >50 years, $n = 36$) and 34 severe symptoms (88% >50 years, $n = 30$). There was one fatality. A 82-year-old male received 100 mg clozapine, 1.25 mg lorazepam and therapeutic doses of paracetamol and ibuprofen. He developed coma and died the following day. Of the 174 cases in adults and children >12 years, 93 were single substance ingestions. The dose was known in 20/27 asymptomatic patients (50–400 mg; average 194 mg; median 150 mg), 25/32 patients with minor symptoms (50–1000 mg; average 252 mg; median 200 mg), 15/21 patients with moderate symptoms (75–900 mg; average 362 mg; median 350 mg) and 9/13 patients with severe symptoms (200–800 mg; average 467 mg, median 400 mg).
**Conclusion:** Moderate and severe courses occur at any age after accidental clozapine ingestion of therapeutic doses, but patients >50 years are at higher risk. This is of particular concern in healthcare institutions, where medication therapeutic errors occasionally occur.

### Reference

[1] Krämer I, Rauber-Lüthy C, Kupferschmidt H, et al. Minimal dose for severe poisoning and influencing factors in acute human clozapine intoxication: a 13-year retrospective study. Clin Neuropharmacol. 2010;33:230–234.

## 97. Paracetamol medication errors are associated with a high risk of hepatotoxicity in children aged 0–6 years: a retrospective cohort study

Alaa Daoud, Christina Gade, Søren Bøgevig, Mikkel B. Christensen, Kim P. Dalhoff and Tonny S. Petersen

Department of Clinical Pharmacology, Copenhagen University Hospital - Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** Paracetamol is the most prescribed analgesic and antipyretic drug in children. When prescribed and used in single or repeated supratherapeutic doses it may cause liver injury. However, medication errors leading to overdoses in children are poorly explored. In this study, we examined the prevalence of prescribing and administration errors with paracetamol in young children.
**Methods:** In this retrospective cohort study, we included children aged 0–6 years hospitalized for suspected paracetamol poisoning in the Capital Region of Denmark from 2010 to 2017 as previously published [1]. We manually reviewed the medical charts using standardized abstraction forms and analyzed the data using R version 4.0.2.
**Results:** Out of the 297 children hospitalized with suspected paracetamol overdose 25 (8.4%) had an admission due to medication errors with 13 occurring in-hospital and 12 at home. The median age was 2 (IQR: 1–4) years, and boys were overrepresented (64%). Paracetamol was used to treat pain in 11 children including four for postoperative pain and to treat fever in 8 children. In 36% of the cases paracetamol was prescribed by a physician in a supratherapeutic dose and the rest were due to administration errors by parents at home or by medical staff during hospitalization. Repeated supratherapeutic overdoses accounted for 64% of the cases. The administration route most used was oral (40%) and intravenous (28%) followed by suppositories (12%). The estimated administered dose of paracetamol per day was 82.5 (IQR: 38.5–100.7) mg/kg. The peak paracetamol concentration measured during hospitalization was 0.10 (IQR: 0.07–0.12) mmol/L. In total 48% were treated with N-acetylcysteine and none developed anaphylactoid reactions. The peak International Normalized Ratio (INR) and alanine aminotransferase (ALT) were 1.3 (IQR: 1.2–1.5) and 24.0 (IQR: 19.0–47.0), respectively. Two children developed severe hepatotoxicity after physician prescription errors. All fully recovered and no deaths occurred.
**Conclusion:** Paracetamol medication errors accounted for less than 10% of the suspected paracetamol overdose cases. Prescription errors were particularly associated with a high risk of hepatotoxicity, which indicates a need for preventive measures.

## Reference

[1] Gade C, Bøgevig S, Daoud A, et al. Has the time come to stop routine N-acetylcysteine treatment in young children in Denmark? A review of 300 suspected paracetamol overdoses in children aged 0–6 years. Acta Paediatr. 2022;111:667–674.


# 98. Randomized crossover study comparing the pharmacokinetics of two different nicotine salt concentrations and free-base nicotine using an open vape pod system


Samuel E. Christen[a,b], Laura Hermann[c], Elias Bekka[c], Celina Vonwyl[a,b], Felix Hammann[c], Vera van der Velpen[c,d], Manuel Haschke[c,d] and Evangelia Liakoni[c]

[a]Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern; [b]Graduate School for Health Sciences, University of Bern, Bern, Switzerland; [c]Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [d]Institute of Pharmacology, University of Bern, Bern, Switzerland



**Objective:** Popular "pod system" electronic cigarettes commonly use nicotine salt-based e-liquids that cause less irritation when inhaled and can deliver higher nicotine concentrations than the free-base nicotine used in older electronic cigarettes [1]. Since smokers titrate their intake to maintain desired nicotine levels, e-liquids delivering high concentrations might benefit smokers seeking to quit. It is debated, however, whether and how different formulations (salt versus free-base) influence systemic absorption of nicotine [2].
**Methods:** In this randomized, double-blind, within-subject crossover study, 20 non nicotine-naïve participants were switched among three e-liquids (free-base nicotine 20 mg/mL, nicotine salt 20 mg/mL, nicotine salt 40 mg/mL) using a refillable pod system and a standardized vaping protocol (one puff every 30 seconds, 10 puffs total). Blood samples were drawn over 180 minutes; craving, satisfaction, withdrawal and respiratory symptoms were assessed using questionnaires. Serum nicotine concentrations were measured using liquid chromatography-tandem mass spectrometry (LC-MS/MS) and pharmacokinetic data were evaluated by noncompartmental analysis using Monolix.
**Results:** The pharmacokinetic results of the first 8 participants (5 males, 3 females; age 24 ± 3.2 years (mean ± SD)) are shown in Table 1. No serious adverse events were observed.
**Conclusion:** Free-base 20 mg/mL formulations achieved lower exposure than nicotine salt 20 mg/mL formulations, while 40 mg/mL nicotine salt formulations produced blood concentrations similar to cigarette smoking. The findings can contribute to the debate regarding e-liquids' regulation and their potential use in smoking cessation.



## References

[1] Leventhal AM, Madden DR, Peraza N, et al. Effect of exposure to e-cigarettes with salt vs free-base nicotine on the appeal and sensory experience of vaping: a randomized clinical trial. JAMA Netw Open. 2021;4:e2032757.
[2] Gholap VV, Kosmider L, Golshahi L, et al. Nicotine forms: why and how do they matter in nicotine delivery from electronic cigarettes? Expert Opin Drug Deliv. 2020;17:1727–1736.


# 99. Variation in sensitivity to diethylene glycol poisoning can be explained by variation in tissue diglycolic acid (DGA) uptake due to expressional differences in dicarboxylate transporters


Kenneth McMartin, Julie Tobin, Courtney Jamison and Corie Robinson

Louisiana State University Health Sciences Center – Shreveport, Shreveport, MO, USA



**Objective:** In animal studies on the toxicities of diethylene glycol (DEG) and its toxic metabolite diglycolic acid (DGA), remarkable differences in susceptibility to renal toxicity were observed in identically-dosed rats. In both studies, only about 60% of the rats showed acute kidney injury (AKI), yet all of these rats showed marked accumulation of DGA in tissues, while no DGA accumulated in rats without injury. DGA is taken into tissues via the sodium-dependent dicarboxylate transporters (NaDCs). When NaDC-1, which is apically expressed, is inhibited or knocked down in human kidney cells, uptake and toxicity of DGA is reduced. We hypothesize that the variation in sensitivity to tissue DGA retention and to DEG/DGA toxicity might be explained by differential expression of NaDC-1 in rat kidneys.
**Methods:** Two experiments were conducted where Wistar-Han rats were either gavage dosed with DEG (6 g/kg every 12 h for 7 days) or with single doses of DGA (300 mg/kg). Kidney tissue was harvested after euthanasia and preserved in formalin. Tissue slices were homogenized and RNA was isolated using an RNAstorm FFPE RNA Isolation Kit. The resulting RNA was analyzed for NaDC-1 mRNA by reverse transcription polymerase chain reaction (rt-PCR). Results were compared between groups that were identically dosed, but showed DGA accumulation and renal toxicity, with those that showed no DGA accumulation and no toxicity.
**Results:** Of the 10 rats treated with DEG, 6 developed AKI while of the 10 rats dosed with DGA, 7 developed AKI. All 13 rats showed markedly increased DGA concentrations in kidneys, whereas there was no DGA in the kidneys of the other rats. Analysis of NaDC-1 mRNA showed a significantly higher level in the kidneys of rats with DGA accumulation compared to those observed in the rats that has no DGA in the kidney tissue and did not show kidney toxicity.
**Conclusion:** These studies indicate that the likelihood of renal toxicity following dosing with either DEG or DGA is closely linked


Table 1. Nicotine pharmacokinetics by e-liquid formulation (median (range); bold numbers indicate significant differences ($p < 0.05$) between groups).

| | Free-base nicotine 20 mg/mL | Nicotine salt 20 mg/mL | Nicotine salt 40 mg/mL | *p*-Value |
|---|---|---|---|---|
| $C_{max}$ (ng/mL) | 4.8 (1.5–7.8) | 9.3 (2.8–18.7) | 15.7 (2.5–29.0) | **0.012** |
| $T_{max}$ (min) | 2 (2–30) | 2 (2–2) | 2 (2–5) | 0.109 |
| AUClast (ng*min/mL) | 346.3 (129.7–673.6) | 585.1 (264.9–783.2) | 752.9 (158.3–1289.1) | **0.048** |
| Terminal half-life (min) | 199.5 (133.5–292.4) | 170.5 (100.9–346.5) | 137.5 (80.2–221.7) | 0.164 |

AUClast: area under the curve up to last measured concentration; $C_{max}$: maximum observed concentration; $T_{max}$: time of $C_{max}$

with an enhanced ability to take up DGA into tissues via the NaDC-1 transporter. Variability in DEG toxicity also occurs in humans, as has been reported in multiple epidemiological studies. It is possible that the human variability may also be linked with differences in the ability of tissues to take up DGA.

## 100. Quetiapine overdose, good or bad, or just more of the same?

Geoffrey K. Isbister and Shane Jenkins

Clinical Toxicology Research Group, University of Newcastle, Newcastle, Australia

**Objective:** Quetiapine is increasingly prescribed for a broad range of indications and this availability has made it one of the commonest drugs ingested in overdose. There is ongoing concern about it causing QT prolongation in overdose. We report the epidemiology, complications and outcomes for quetiapine overdose in a tertiary toxicology service.
**Methods:** We extracted all cases of quetiapine poisoning presenting to the Hunter Area Toxicology Service for January 1987 to October 2021, and the numbers of other antipsychotic overdoses. Data recorded prospectively in a clinical database was extracted, including demographics, dose, co-ingestants, clinical effects, complications, treatments and outcomes.
**Results:** Over a 21 year period, quetiapine only being available from 2001, there were 2235 admissions for quetiapine overdose. This far exceeded any other antipsychotic, the next most common four being olanzapine (1000), pericyazine (570), thioridazine (399) and chlorpromazine (396). The median age was 35 years (interquartile range [IQR]: 24–44 years); 1492 (67%) were females. Quetiapine alone was ingested in 456 overdoses, and the commonest co-ingestants were alcohol, paracetamol, diazepam, mirtazapine and valproate. The median dose ingested was 1000 mg (interquartile range [IQR]: 350–2600; range: 25–30000 mg), which was higher for quetiapine alone overdoses, median 1400 mg ([IQR]:600–3600 mg). A decreased level of consciousness was the commonest effect with 233 (10.4%) having a Glasgow Coma Score (GCS) $< 9$ and 219 (9.8%) being intubated. Hypotension occurred in 173 (7.7%) admissions, with 20 (0.9%) given inotropes. Delirium occurred in 139 (6.2%) admissions and seizures in 38 (1.7%). Arrhythmias occurred in 13 admissions (0.6%), with no cases of Torsades de Pointes or ventricular fibrillation, and only one ingesting quetiapine alone who developed new onset atrial fibrillation. The median length of stay was 18 hours ([IQR]:11.5–32h), 267 (11.9%) were admitted to intensive care unit (ICU) and three (0.3%) died in hospital.
**Conclusion:** Quetiapine is the commonest psychotropic taken in overdose and causes coma, delirium and hypotension. Quetiapine overdoses result in more healthcare resources utilised than other overdoses for coma, hypotension and delirium, with over 10% requiring ICU and a high intubation rate. However, arrhythmias are very rare and undue focus on QT prolongation unnecessary.

## 101. Wound botulism following intravenous methamphetamine use

Balveena K. Dhaliwal[a], Andrew Henderson[b], Jessica Qiu[b] and Naren Gunja[c]

[a]Western Sydney Toxicology Services, Kellyville, Australia; [b]Department of Neurology, Westmead Hospital, Sydney, Australia; [c]Western Sydney Toxicology Services, Sydney, Australia

**Objective:** Wound botulism is rarely encountered in developed countries. We report a case of wound botulism in an intravenous drug user. Early clinical recognition and treatment with antitoxin is essential to reduce morbidity and mortality in wound botulism [1,2].
**Case report:** A 35-year-old male presented to a tertiary Emergency Department with a two-day history of nonspecific neurological symptoms. He complained of lethargy, difficulty swallowing, increased salivation, and numbness to his mouth. He last injected methamphetamine intravenously 2 days previously, after which his symptoms began. On initial assessment, he was afebrile, blood pressure 130/70 mmHg, with oxygen saturations 100% on room air. A neurological examination demonstrated cranial nerve deficits with ptosis, abnormal gag reflex, with difficulty swallowing. He was alert with a Glasgow Coma Score (GCS) of 15. There was superficial thrombophlebitis of the left antecubital fossa, the injection site. A blood culture was obtained. Neuroimaging was normal. The following day, the patient developed progressive neurological features with bilateral tongue weakness, absent gag reflex, bilateral ophthalmoplegia with gaze paresis, increasing drowsiness and respiratory failure requiring intubation and ventilation. The blood culture demonstrated growth of *Clostridium botulinum* on day 4. The patient was treated with penicillin and botulinum antitoxin. There was gradual improvement in his neurological status and he was extubated after 14 days, and discharged clinically well 26 days later. *Clostridium botulinum* Type B was detected by public health on his drug paraphernalia.
**Conclusion:** Wound botulism is most commonly implicated with black tar heroin [3,4]. Botulinum toxin type A is the most common toxin type in wound botulism [3]. Neurological signs of botulism such as ptosis and altered phonation might be interpreted as mental status changes associated with drug use but botulism needs to be considered in intravenous drug users with focal neurological signs.

### References

[1] Hatami F, Shokouhi S, Mardani M, et al. Early recovery of botulism: one decade of experience. Clin Toxicol. 2021;59:628–632.
[2] Sobel J. Diagnosis and treatment of botulism: a century later, clinical suspicion remains the cornerstone. Clin Infect Dis. 2009; 48:1674–1675.
[3] Waltenburg M, Larson V, Naor E. Notes from the field: botulism type B after intravenous methamphetamine use—New Jersey, 2020. MMWR. 2020;69:1425–1426.
[4] Peak CM, Rosen H, Kamali A, et al. Wound botulism outbreak among persons who use black tar heroin—San Diego County, California, 2017–2018. MMWR. 2019;67:1415–1418.

## 102. A case of foodborne botulism type E

Karolien De Leener[a], Bram Depelseneer[b], Jonas Moens[a], Dominique Vandijck[a] and Anne-Marie Descamps[b]

[a]Belgian Poison Centre, Brussels, Belgium; [b]ZNA Middelheim, Antwerp, Belgium

**Objective:** To present a laboratory-confirmed case of foodborne botulism type E. In Belgium botulism type B is predominant in humans.
**Case report:** A 67-year-old woman, with known arterial hypertension, Hashimoto thyroiditis and cholecystectomy, presented to

the emergency department (ED) with sudden progressive weakness. The evening before, a reheated catfish meal (not canned) was consumed. Physical examination showed the presence of multiple symmetrical cranial nerve palsies with diplopia, dysarthria, bilateral ptosis, hyperreflexia and weakness of the upper and lower limbs. Laboratory tests showed a slightly decreased renal function. Cerebral computerised tomography (CT) scan showed no peculiarities. Upon Intensive Care Unit (ICU) admission, faeces, gastric fluid and blood were sent to the national reference laboratory for botulinum testing. The Poison Centre was called and the botulism antitoxin was ordered. In the differential diagnosis myasthenic problems were also considered. Respiratory distress developed with increased oxygen dependence and she required intubation and mechanical ventilation. Botulism Antitoxin Heptavalent BAT® was administered within 24-hours of onset of symptoms. Electromyography (EMG) suggested axonal motor neuropathy. Additional lumbar puncture was suggestive for Guillain-Barré, despite contradictory clinical presentation. Therefore, intravenous immunoglobulins were administered (day 3 and 4) but were stopped after confirmation for botulinum neurotoxins type E in the gastric fluid and blood. No neurotoxins were detected in the faeces, or the residue of the consumed meal. The patient recovered from day 6 onwards. On day 8 neurotoxins were no longer detectable in the blood, but were detectable in the faeces. The patient was extubated on day 9 but due to weakness, non-invasive ventilation was continued for 1 day. A persistent hoarseness was noticed due to intubation, but this resolved completely. Rehabilitation was started on day 13 as she was unable to get up or walk independently. A new EMG (day 27) showed normalisation of neuropathy. The patient left the hospital fully recovered after 31 days.

**Conclusion:** Early treatment with BAT® neutralises circulating neurotoxins, positively influencing the course of disease. As tests to confirm the presence of neurotoxins in blood or faeces take several days, the decision to start prophylactic treatment should therefore be made based on the anamnesis and clinical presentation upon admission. Due to the presence of a symmetrical, descending, flaccid paralysis the Poison Centre was called to deliver BAT® and treatment was started and the patient recovered completely.

## 103. Severe neurological sequelae of carbon monoxide poisoning

Balveena K. Dhaliwal[a], Chong Wong[b] and Naren Gunja[a]

[a]Western Sydney Toxicology Services, Sydney, Australia; [b]Department of Neurology, Westmead Hospital, Sydney, Australia

**Objective:** Carbon monoxide poisoning can cause delayed neurological sequelae (DNS), a potentially permanent encephalopathy with cognitive impairment and movement disorders [1]. Death secondary to DNS is rarely reported.

**Case report:** A previously healthy 59-year-old man presented to a regional emergency department after he was found obtunded at home, where he was exposed to carbon monoxide from a wood burning heater. He was last seen well 8 hours prior. On initial assessment, vital signs were Glasgow Coma Score (GCS) 3, blood pressure 110/60 mmHg, heart rate 120 bpm, and oxygen saturations 80% (room air). Venous blood gas showed pH 7.39, $pCO_2$ 30mmHg, lactate 7 mmol/L, bicarbonate 15 mmol/L, and carboxyhaemoglobin 19.8%. He had been treated with 4 hours of high flow oxygen, 15 L/min, via a non-rebreather prior to this. Electrocardiogram (ECG) demonstrated sinus tachycardia. Troponin was elevated at 670 ng/L. He was intubated and ventilated with $FiO_2$ 100%. Serial carboxyhaemoglobin concentrations declined to 12.4%, 1.5 hours after positive pressure ventilation, and 7.7% 3 hours later. Hyperbaric oxygen therapy was discussed but not commenced. Neuroimaging with a brain computerised tomography (CT) scan was normal. He recovered well and was successfully extubated 24 hours later. He was discharged home 3 days later with a documented normal neurological examination. Following a lucid interval of 1 week, he represented to a tertiary hospital 3 weeks later with a 2-week history of decline in motor and cognitive function, with slow movements, slurred speech and progressive confusion. Brain magnetic resonance imaging (MRI) demonstrated areas of gliosis in bilateral globus pallidi with non-specific diffuse white matter changes within supratentorial compartment, consistent with neurological sequelae of carbon monoxide poisoning. There was gradual functional decline and he was transferred to a nursing home facility, requiring high level of care, 8 weeks later.

**Conclusion:** DNS sequelae may develop 2-40 days in up to 40% of survivors of acute carbon monoxide poisoning [2]. The most common feature on MRI is symmetrical bilateral basal ganglia abnormality [2]. There is currently no optimal evidence-based treatment for carbon monoxide associated DNS [1,2]. Prompt treatment of carbon monoxide toxicity may reduce its occurrence.

### References

[1] Spina V, Tomaiuolo F, Celli L, et al. A case of carbon monoxide-induced delayed neurological sequelae successfully treated with hyperbaric oxygen therapy, N-acetylcysteine, and glucocorticoids: clinical and neuroimaging follow-up. Case Rep Neurol Med. 2019; 2019:9360542.

[2] Oh S, Choi SC. Acute carbon monoxide poisoning and delayed neurological sequelae: a potential neuroprotection bundle therapy. Neural Regen Res. 2015;10:36–38.

## 104. Factors associated with hospitalization for acute recreational drug toxicity

Viktoria T. Aasgaard, Maria Abrahamsen, Mette Brekke and Odd Martin Vallersnes

Department of General Practice, University of Oslo, Oslo, Norway

**Objective:** Though acute recreational drug toxicity can frequently be managed in primary care or by simple means in emergency departments [1], the condition may rapidly deteriorate and give rise to complications requiring hospital admission. This may be difficult to predict. In this study, we aim to identify factors related to the need of hospitalization among patients presenting with acute recreational drug toxicity to a primary care emergency clinic.

**Methods:** In a retrospective observational study at the Oslo Accident and Emergency Outpatient Clinic (OAEOC), the main primary care emergency clinic in Oslo, Norway, we included all patients presenting with acute recreational drug toxicity in the period 2014–2020, except lone ethanol poisoning, poisoning inflicted by others, and suicide attempts. The patients were identified by reviewing the patient registration lists in the clinic's electronic patient records system. We registered clinical features, treatment, and toxic agents taken. Diagnosis of toxic agents was based on the assessment of the doctor treating the patient as noted in the patient records, mainly based on information from the patient and/or the patient's companions.

**Results:** Among 12,149 included patients, 9374 (77.2%) of whom were men, 1823 (15.0%) were transferred to hospital for medical review and 551 (4.5%) transferred to a psychiatric hospital.

Transfer to hospital for medical review was most common among patients with hyperthermia (temperature ≥39.0 °C) (73.6%), arrhythmia (63.0%), coma (Glasgow Coma Scale (GCS) score <8) (57.7%), seizures (31.1%), chest pain (30.1%), hypotension (systolic blood pressure ≤90 mmHg) (23.6%), tachypnoea (respiratory rate ≥20/min) (23.0%), vomiting (21.3%), or bradycardia (heart rate <50/min) (20.7%), among patients given sedation (38.6%) or naloxone (20.4%), and when the toxic agent involved was gamma-hydroxybutyrate (GHB) (35.2%) or methadone (20.5%). Transfer to a psychiatric hospital was most common among patients with psychosis (64.2%) and hallucinations (35.6%).
**Conclusion:** Transfer to hospital was often needed for patients with hyperthermia, arrhythmia, GCS <8, seizures, chest pain, psychosis, or hallucinations, when sedation was required, and when GHB was reportedly taken. Rapid hospital admission should be considered if any of these conditions occur.

## Reference

[1] Vallersnes OM, Jacobsen D, Ekeberg Ø, et al. Outpatient treatment of acute poisoning by substances of abuse: a prospective observational cohort study. Scand J Trauma Resusc Emerg Med. 2016;24:76.

# 105. The association between alcohol co-ingestion and clinical outcome of deliberate self-poisoning patients visiting the emergency department

Seon Hee Woo, Gyu Won Kim, Woon Jeong Lee, Dae Hee Kim and Jun Young Lee

Incheon St. Mary's Hospital, The Catholic University of Korea, Incheon, South Korea

**Objective:** Alcohol is one of the most commonly co-ingested agents in deliberate self-poisoning (DSP) patients visiting the emergency department (ED). The increased impulsivity, aggressiveness, and disinhibition caused by alcohol ingestion may have different clinical features and outcomes in cases of DSP. This study investigated whether alcohol co-ingestion affects clinical features and outcomes of DSP patient in the ED.
**Methods:** We retrospectively investigated DSP patients who visited our ED from January 2010 to December 2016 in a single-center. Patients were classified into two groups: with (ALC+) or without alcohol co-ingestion (ALC-). We compared clinical features of DSP according to co-ingestion of alcohol and analyzed factors related to discharge against medical advice (AMA) of DSP.
**Results:** A total of 689 patients were included in the study, with 272 (39.5%) in the ALC + group. More ALC + group patients were male, middle-aged (45–54 years old), and arrived at the ED at night. The rate of discharge AMA from ED was higher in the ALC + group (130; 47.8%) than the ALC − group ($p = 0.001$). There were no significant differences in poisoning severity score between the two groups ($p = 0.223$). Multivariate analysis showed that the alcohol co-ingestion (odds ratio [OR] = 1.42; 95% confidence interval [CI], 1.01–1.98), alert mental status (OR =1.65; 95% CI, 1.17–2.32), past psychiatric history (OR =0.04; 95% CI, 0.01–0.28), time from event to ED arrival >6 hours (OR =0.57; 95% CI, 0.37–0.88) and age >65 years (OR =0.42; 95% CI, 0.23–0.78) were independent predictive factors of discharge AMA ($p = 0.043$, $p = 0.004$, $p = 0.001$, $p = 0.010$ and $p = 0.006$, respectively).
**Conclusion:** Alcohol co-ingestion was associated with the outcome of discharge AMA in DSP patients. Emergency physicians should be aware that DSP patients who have co-ingested alcohol may be uncooperative and at high risk of discharge AMA.

# 106. Baron von Münchausen in a bullet proof vest

Marc Stevens[a], Erik Lindeman[a] and Andreas Blomgren[b]

[a]Swedish Poisons Information Centre, Solna, Sweden; [b]Swedish Medical Products Agency, Uppsala, Sweden

**Objective:** To describe a case of claimed cyanide ingestion with multiple presentations.
**Case report:** A 23-year self-described "gangster" presented at the emergency room (ER) wearing a bulletproof vest, claiming to have swallowed a ziplock bag with powdered heroin ("10 g") and a home-made capsule of potassium cyanide ("300 mg") inside. On his phone was the webpage of an online vendor of laboratory chemicals where he claimed to have bought the potassium cyanide ("100 g"). He claimed he swallowed the package to conceal it on the mistaken assumption that a police raid of his apartment was about to occur. He would not disclose the intended purpose of the cyanide. The patient showed no symptoms of poisoning, but the potential danger coupled with his very threatening behaviour was highly distressing to the staff. After consultation with the poison centre (PC) a gastroscopy was performed under general anaesthesia where a ziplock bag was indeed discovered in the ventricle. To ensure extraction without leakage a mini-gastrotomy was performed. The extracted bag was given to the police who, however, decided not to have its contents analysed or to further pursue the case. During the following 10 months the patient presented a further four times claiming to have swallowed a cyanide capsule, with increasingly incoherent explanations as to why. A ziplock bag was extracted by gastrotomy on a further three occasions and after the police had again decided against investigation of bag 2; bags 3 and 4 were sent to the PC on request. A pharmacist and analytical chemist working at the PC performed the analysis of the extracted substances in collaboration with the laboratory at the Swedish Medical Products Agency. Infrared (IR) spectroscopy was performed on commercial samples of sodium and potassium cyanide and compared to spectra from the ingested samples to identify tell-tale absorption peaks from cyanide (CN) groups. When no such peaks could be identified, both samples were analysed by gas chromatography-mass spectrometry (GC-MS) and obtained spectra were compared to a commercial library. Subsequent analysis by nuclear magnetic resonance spectroscopy (NMR) confirmed the presence of sustained-release valproate in bag 3 and of a paracetamol suppository in bag 2. On the fifth presentation the patient was treated with whole-bowel irrigation instead of surgery.
**Conclusion:** The case illustrates that, although analytical findings cannot be used to predict future outcomes, they provide an opportunity to adjust prior assumptions and keep making sound judgments in the ever-changing and sometimes baffling landscape that is clinical toxicology.

## 107. Recreational use of nitrous oxide – a growing concern in Europe

Joanna de Morais[a], Leon van Aerts[b], Michael Evans-Brown[a], Ana Gallegos[a], Rachel Christie[a], Rita Jorge[a], Thomas Néfau[a], Gregorio Planchuelo[a], Roumen Sedefov[a], Caroline Victorri-Vigneau[c], Rasa Povilanskienė[d], Kari Grasaasen[e], Dorte Fris Palmqvist[f], Deirdre Mongan[g], Nicki Killeen[h] and António Óscar Duarte[i]

[a]European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal; [b]Section Pharmacology, Toxicology and Biotechnology, College ter Beoordeling van Geneesmiddelen, Medicines Evaluation Board, Utrecht, Netherlands; [c]Clinical Pharmacology Department, Center for Evaluation and Information on Pharmacodependence – Addictovigilance, Nantes University Hospital, Nantes, France; [d]Drug Precursors Control and Risk Assessment Division, Drug, Tobacco and Alcohol Control Department of Lithuania, Vilnius, Lithuania; [e]Danish Health Authority, Copenhagen, Denmark; [f]Department of Anaesthesia and Intensive Care, Danish Poison Information Centre, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark; [g]Health Research Board, Dublin, Republic of Ireland; [h]Health Service Executive, Dublin, Republic of Ireland; [i]Divisão de Relações Internacionais, Serviço de Intervenção nos Comportamentos Aditivos e nas Dependências, Lisbon, Portugal

**Objective:** Nitrous oxide, commonly known as laughing gas, is used medically as an analgesic and anaesthetic. It has been used recreationally for its brief euphoric effects for over 200 years, however, in the last decade there has been a large increase in its recreational use and, more recently, an increase in reported serious health and social harms in some countries. The situation in seven European countries has been analysed, including epidemiology, health and social harms, policy responses, and lessons learned. This can be used to inform relevant stakeholders on how to respond to nitrous.
**Methods:** Case studies on the situation with nitrous oxide in Denmark, France, Ireland, Lithuania, the Netherlands, and Portugal were developed based on the information collected by the national Early Warning Systems within their networks and literature. For the case study of the United Kingdom, open-source data were used. In addition, relevant information was retrieved from PubMed and Web of Science.
**Results:** Easy availability, low price, short-lived effects, and perception as a safe and socially acceptable drug might explain growing popularity of nitrous oxide. The market has expanded in recent years with a range of specialised Internet shops, partly offering it under the disguise of "party accessories", but also openly when the legal situation permits. Social media is also used to promote and sell it. In some cases, the supply has moved from shops to social media following measures to restrict its supply. Of special concern is that most use of nitrous is by young people, including teenagers inexperienced with drug use. The current situation has led to an increase in frequent and heavy use and an increase in poisonings reported to poison centres. According to the French Addictovigilance network the number of notifications linked to nitrous increased from 10 in 2018 to 358 in 2021. Harms include frostbites, barotrauma, serious neurological toxicity (such as myeloneuropathy), cardiovascular consequences (such as thrombo-embolic events), psychiatric disorders, and driving under the influence. More recently, harms are fuelled by a switch from small to large cylinders.
**Conclusion:** Poison centres and the French Addictovigilance system played a key role in detecting, monitoring, and responding to the issue of nitrous oxide. Its growing recreational use is a public health concern requiring an integrated multi-sectoral approach to reduce demand, availability, and risks. The responses might include prevention, monitoring, treatment, and legislative actions. Data sharing at EU level to monitor this issue is needed.

## 108. Predicting the need for intensive care unit (ICU) admission in acutely intoxicated adult patients at the Emergency Department (ED)

Claudine C. Hunault[a], Samanta M. Zwaag[a], Irma S. van den Hengel-Koot[a], Saskia J. Rietjens[a], Laura Hondebrink[a], Douwe Dekker[a,b] and Dylan W. de Lange[a,c]

[a]Dutch National Poisons Information Centre (DPIC), University Medical Center Utrecht, Utrecht, Netherlands; [b]Department of Emergency Medicine, University Medical Center Utrecht, Utrecht, Netherlands; [c]Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, Netherlands

**Objective:** Admissions for acute intoxications are frequent at the Emergency Department (ED) while the associated mortality for those patients admitted at an Intensive Care Unit (ICU) is relatively low. An ICU requirement score (IRS) has been previously developed to predict the need for ICU admission [1]. The IRS was based on data from intoxicated patients already at the ICU. Our objective was to assess the prognostic value of the IRS predictors in acutely intoxicated patients arriving at the ED.
**Methods:** Data of adult acutely intoxicated patients presenting at the ED between 1 January 2015 and 31 December 2020 were collected retrospectively in a single university hospital. The primary outcome was "ICU admission". The logistic model included predictors that were included in the IRS: age, heart rate, systolic blood pressure, Glasgow Coma Score (GCS), co-morbidities, second diagnosis at admission, exposures (alcohols; analgesics; antidepressants; street drugs; sedatives; poisons like carbon monoxide (CO) or arsenic or cyanide; other toxins not otherwise specified; combination of 2 or more exposure types; unknown exposure). We choose "alcohol only" as reference category. Results are expressed in Odds Ratios (OR) with 95% Confidence Intervals (CI). We computed the Area Under the Curve (AUC) statistics for all patients (group 1), and for patients without cardiopulmonary resuscitation (CPR) or mechanical ventilation at the ED (group 2).
**Results:** Overall 1140 ED visits were included. The patients' mean age was 38 years (SD =15.3); 150 patients were admitted to the ICU (13.2%). "Combination" was the most common exposure category ($n = 501$), followed by "street drugs (only)" ($n = 142$), "alcohol (only)"($n = 123$), "sedatives (only)" ($n = 85$), "other toxins (only)" ($n = 55$), "analgesics (only)" ($n = 52$), "unknown exposure" ($n = 32$), "poisons (only) like CO, arsenic, cyanide)" ($n = 30$), and "antidepressants (only)" ($n = 19$). Significant predictors for ICU admission were heart rate (OR =1.02, 95% CI 1.01;1.03), GCS score (OR =0.79, 95% CI 0.76;0.83), second diagnosis (OR =3.5, 95% CI 1.71;7.4) and exposure categories. Exposure categories that were most predictive for ICU admission were "other toxins" (OR =19.6, 95% CI 4.6;83.2), "combination" (OR =12.2, 95% CI 3.6;41.6), "sedatives" (OR =8.2, 95% CI 1.9;34.7) and "poisons like CO, arsenic, cyanide" (OR =7.6, 95% CI 1.4;41.1). The AUC to predict ICU admission was 0.82 (0.78;0.86) in group 1 and 0.81 (0.76;0.85) in group 2.
**Conclusion:** Some of the predictors included in the IRS do have a prognostic value to predict ICU admission in acutely intoxicated patients at the ED.

## Reference

[1] Brandenburg R, Brinkman S, de Keizer NF, et al. The need for ICU admission in intoxicated patients: a prediction model. Clin Toxicol. 2017;55:4–11.

# 109. Gamma-hydroxybutyrate (GHB) intoxication: clinical diagnosis versus laboratory findings

Didrik Skjelland[a], Benedicte M. Jørgenrud[b], Karsten Gundersen[c], Mari Asphjell Bjørnaas[d], Mette Brekke[a], Vivian M. Dalaker[a], Håvard Furuhaugen[b] and Odd Martin Vallersnes[a]

[a]Department of General Practice, University of Oslo, Oslo, Norway; [b]Department of Forensic Sciences, Section of Drug Abuse Research, Oslo University Hospital, Oslo, Norway; [c]Department of Medicine, Lovisenberg Diaconal Hospital, Oslo, Norway; [d]Department of Acute Medicine, Oslo University Hospital Ullevaal, Oslo, Norway

**Objective:** Intoxication with gamma-hydroxybutyrate (GHB) may need urgent medical treatment. The clinical manifestations are heterogenous and the level of consciousness often unstable with rapid fluctuations between agitation and coma. We investigate the accuracy of the clinical diagnosis of GHB compared to laboratory findings in blood samples.
**Methods:** In this ongoing, prospective study we include patients ≥16 years of age admitted to hospital with a clinical diagnosis of GHB intoxication. The diagnosis was made by the doctor treating the patient based on the clinical picture and/or information from the patient and/or the patient's companions. Blood samples were taken at admission and analyzed using ultrahigh performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS).
**Results:** Fifty patients were included. Median age was 37 years (IQR 24–42); 30 (60%) were male. GHB was detected in 35 patients (70%). Furthermore, benzodiazepines were found in 39 (78%), amphetamines in 36 (72%), ethanol in 20 (40%), cocaine in 19 (38%), tetrahydrocannabinol (THC) in 15 (30%), morphine in 5 (10%), 3,4-methylenedioxymethamphetamine (MDMA) in 5 (10%), codeine in 2 (4%), and methadone in 2 (4%). No patients had taken GHB only. Naloxone and/or flumazenil were administered to 11 patients (22%), while 4 patients (8%) required sedation. Eighteen patients (36%) were treated in the intensive care unit (ICU), 1 patient (2%) was ventilated, whereas none were intubated. At admission, median Glasgow Coma Scale (GCS) score was 6, and 19 patients (38%) presented with GCS ≤4. In 21 patients (42%) rapid changes in GCS was observed, and 16 patients (24%) were agitated. Two patients (4%) reported hallucinations. Eight patients (16%) had bradypnoea and 6 (12%) were tachypnoeic.
**Conclusion:** GHB was found in blood samples in 70% of patients with a clinical diagnosis of GHB intoxication. All patients were co-intoxicated with other substances, mainly amphetamines and benzodiazepines. Nearly 40% presented with GCS ≤4 and as many showed rapid changes in the level of consciousness, both findings are considered characteristic for GHB intoxication, although the impact of other CNS depressants and stimulants should not be underestimated. Two out of three patients were in need of observation only, and among the patients admitted to the ICU, none were intubated, and only one needed mechanical ventilation.

# 110. A febrile syndrome with a broad differential diagnosis

Juan Ortega Pérez[a], Meritxell Vidal Borràs[b], Carlos Rafael Álvarez Ferrer[a], Catalina Homar Amengual[a], María del Carmen Rodríguez Ocejo[a], Maria Codinach Martín[b], Bernardino Comas Díaz[a] and Jordi Puiguriguer Ferrando[a]

[a]Hospital Universitario Son Espases, Palma de Mallorca, Spain; [b]Institut Català d'Oncologia Girona, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain

**Objective:** To report a case of fever in a patient receiving multiple drugs and signs suggestive of neuroleptic malignant syndrome.
**Case report:** A 61-year-old woman with a history of diabetes mellitus type 2, a borderline personality disorder and depressive syndrome arrived at the emergency room by ambulance due to an altered level of consciousness and fever. Her son told us that she was shivering, and disorientated. Her usual therapy was aripiprazole 20 mg, topiramate 100 mg every 8 hours, metformin 425 mg at breakfast, venlafaxine 300 mg at breakfast and trazodone 100 mg at night. When she arrived she presented tachycardia (130 bpm), axillary temperature 39.6 °C, respiratory rate 40/minute, oxygen saturation 80% and blood pressure 135/75 mmHg. She had generalized rigidity, reactive mydriatic pupils, Glasgow Coma Score (GCS) 7 and unresponsive to physical stimuli. Oxygen with a 100% reservoir mask was prescribed. Two blood cultures, urine culture, blood count, coagulation, kidney and liver function, chest X-ray, concentrations of aripiprazole, trazodone, venlafaxine and topiramate were performed. She was given intravenous paracetamol (1 g) and cooling measures initiated to reduce temperature. She progressively worsened, so sedation, orotracheal intubation and mechanical ventilation were performed, followed by cerebral computerised tomography (CT) scan and a lumbar puncture. She was given intravenous piperazillin-tazobactam (4 g). In this situation, we diagnosed fever without etiology and possible neuroleptic malignant syndrome and she was transferred to the intensive care unit. Laboratory tests showed leukocytes with neutrophilia, creatinine 2.45 mg/dL, creatine kinase 526 U/L, arterial blood gas pH 7.33, $pCO_2$ 21 mmHg, $pO_2$ 74 mmHg, and lactic acid 6.6 mmol/L. We prescribed a dose of dantrolene. All cultures were negative. She has low blood concentrations of aripiprazole, desvenlafaxine and trazodone; the topiramate concentration was slightly elevated. After 48 hours she improved and was transferred to the Internal Medicine department. She was discharged after 7 days.
**Conclusion:** This patient may have had neuroleptic malignant syndrome, a rare but serious complication of the use of drugs that act on dopamine receptors in the central nervous system. She was taking aripiprazole and venlafaxine although her blood concentrations were low. Neuroleptic malignant syndrome is an idiosyncratic entity, however, and occurs regardless of drug concentrations. It has a high mortality rate. In addition to hyperthermia, patients have decreased level of consciousness, autonomic instability and motor symptoms such as rigidity, bradykinesia, and seizures. As treatment, support measures are importance with the aim of reducing temperature, correcting hydration and electrolyte imbalance and ventilatory support. Depending on the case, dantrolene and bromocriptine could be considered.

## 111. Iatrogenic medication errors – still a problem

Mandy Gollmann, Michael Deters and Anne Stürzebecher

Poison Information Centre Erfurt, Erfurt, Germany

**Objective:** Poison information centres are contacted not only by medical care facilities when they have an intoxicated patient, but also frequently when medication errors occur in those facilities themselves. The aim of the study was to show how often medication errors still happen in medical care facilities. Furthermore, the cause of these medication errors and potential risk was investigated.
**Methods:** A retrospective study, we identified and analysed medication errors occurring in medical care facilities between 2013 and 2020. Data were categorized into cause of medication error, drugs involved, and estimated potential risk of toxicity to assess the potential harm to the patient.
**Results:** In total, 1,242 cases of medication error were identified in medical care facilities during the study period (0.8% of all exposures). We registered an increase of 57.7% from 2013 to 2020. The main reason for medication errors was unintentional misuse (e.g., incorrect dosing 33.9%). Further reasons were confusion of drugs for different patients (26.7%), action-based slip (21.9%), wrong medical indication (10.6%), and wrong administration route (6.9%). The most frequent drug classes involved were antipsychotics (19.6%), antiepileptics (10.8%), and antidepressants (6.1%). Quetiapine, clozapine, acetaminophen and valproic acid were the most common drugs involved. The medication errors led to a minor estimated risk of toxicity in 34.9%; a moderate or severe risk occurred in 10.0 and 8.0%, respectively. In 38.4% the risk was unpredictable, whereas in just 8.7% of the cases no adverse effects were expected. Methotrexate and baclofen were most often associated with a severe estimated potential risk.
**Conclusion:** The study shows that medication errors in medical care facilities are a persistent problem and should be monitored continuously for patient safety. Incorrect dosing is common and poses a potential risk, especially for drugs with a narrow therapeutic range. In particular, methotrexate incorrect dosing (daily instead of weekly dose) occurs again and again, despite numerous risk assessments and warnings [1]. To avoid medication errors, the personnel in medical care facilities should receive regular training on medications in general. In addition, the medication process should always be questioned and optimized.

### Reference

[1] European Medicines Agency. New measures to avoid potentially fatal dosing errors with methotrexate for inflammatory diseases. EMA/587673/2019. 21 October 2019 [cited 2022 Oct 9]. Available from: https://www.ema.europa.eu/en/medicines/human/referrals/methotrexate-containing-medicinal-products.

## 112. Severity of voluntary and accidental methanol intoxication associated with methylated spirit ingestion: a retrospective study in a French poison control center

Geraldine Meyer[a], Dominique Savary[b], Marie Deguigne[a] and Alexis D'Escatha[a]

[a]Poison Control Center, Angers, France; [b]Emergency Department, Angers University Hospital, Angers, France

**Objective:** Ingestion of methylated spirit, a mix of ethanol and methanol, can cause methanol intoxication and blindness because of formic acid which is the main metabolite of methanol. The aim of the study is to characterize the severity of methanol intoxication in cases of methylated spirit ingestion using retrospective data from a poison control center.
**Methods:** Data from all calls between 1 January 2010 and 30 April 2019 in the poison control center of Angers (France) concerning methylated spirit ingestion were included with the exception of co-ingestion with alcohol. Variables collected were circumstances of ingestion, symptoms and severity scores, blood methanol analysis, presence of metabolic acidosis and the use or not of fomepizole. Descriptive analysis and logistic models assessing the association between intoxication severity with relevant variables were carried out.
**Results:** We identified 128 cases. Accidental ingestions represented 58 cases (45.3%) which were of zero or low severity. The volume of methylated spirit ingestion was low, a sip or less. Voluntary ingestions represented 70 cases (54.7%) including 16 cases of medium and high severity with coma, convulsions, aspiration pneumonia, acute renal failure and/or serious metabolic acidosis. In the serious intoxication subgroup, mean volume ingested was 842 mL. No significant link between biological markers of methanol intoxication and the severity of symptoms was found. Evolution of intoxications was always positive and without sequelae, even without fomepizole treatment, except for one patient with chronic intoxication who had blindness at admission.
**Conclusion:** In a large poison control center database, accidental ingestion of methylated spirit was always benign. In France, commercial methylated spirit is restricted to 5% or less of methanol, which could explain this result. Voluntary ingestions can result in serious symptoms but our study suggests that they are mostly related to alcohol intoxication. For chronic ingestion, methanol intoxication might occur due to accumulation of methanol which has a longer half-life than alcohol. Restricting the concentration of methanol in methylated spirit could help prevent serious acute intoxication by ingestion.

## 113. Palytoxin poisoning during the pandemic

Ágnes Bakos and Ildikó Urbán

Péterfy Sándor Hospital, Budapest, Hungary

**Objective:** Palytoxin is a potent marine toxin. Human poisoning is caused by consumption of palytoxin-contaminated seafood, inhalation of vapours from palytoxin-contaminated water, skin and eye contact. Symptoms of poisoning are non-specific respiratory, musculoskeletal, cardiovascular and neurological symptoms [1] and may mimic viral infection. We present a palytoxin poisoned patient in the COVID-19 era.
**Case report:** A 45-year-old man was admitted to our department at night because he had high fever (39 °C), chills and nausea. His past medical history included bronchial asthma. The day before, he took a sauna in the morning and cleaned his son's aquarium in the afternoon. On examination, we did not detect any abnormalities and the patient had no other complaints. He had no contact with an infected or febrile person. His COVID-19 antigen rapid and polymerase chain reaction (PCR) tests were negative. Laboratory results showed leucocytosis with high levels of

neutrophils, slightly elevated urea, creatinine, lactate dehydrogenase, and creatine kinase, but C-reactive protein and procalcitonin were normal. The electrocardiogram (ECG) detected biphasic T wave in the inferior leads without increase in the cardiac enzymes. The chest X-ray was negative. Arriving at our department, his son, who was an amateur aquarist, told us that there was Zoanthid coral in the aquarium, which contain palytoxin. The patient cleaned the stones of aquarium without protective equipment inhaling the contaminated steam of water and had dermal contact. The next day he had a mild cough and uncertain chest complaints, but his fever resolved. He received supportive therapy and his laboratory results and condition improved. The patient was discharged from our department in a good condition on the third day. Finally, his microbiological tests were also negative.
**Conclusion:** Palytoxin poisoning is rare in our country and due to nonspecific symptoms can cause problems with differential diagnosis, particularly during a pandemic. Although no tests were performed to detect the presence of palytoxin, based on the patient's medical history, symptoms and laboratory tests, we assumed that our patient suffered from palytoxin poisoning.

## Reference

[1] Pelin M, Brovedani V, Sosa S, at al. Palytoxin-containing aquarium soft corals as an emerging sanitary problem. Mar Drugs. 2016;14:1–22.

# 114. Necrotizing fasciitis in a parenteral drug user

Victoria Lobo Antuña[a], David Rodrigo Domiguez[a], Marta Lobo Antuña[b], Sofia Russo Botero[a], Miriam Ripoll Martínez[a] and Benjamin Climent[a]
[a]Consorcio Hospital General Universitario de Valencia, Valencia, Spain; [b]Hospital Fundación Jiménez Díaz, Madrid, Spain

**Objective:** Slamming, a form of chemsex, is an increasingly widespread practice that is associated with great risks. We present an intravenous drug user with complications of an accidental needlestick injury.
**Case report:** A 53-year-old intravenous drug user with a history of human immunodeficiency virus (HIV) presented to the Emergency Department with progressive pain in the posterior region of the left thigh that had become disabling within 72 hours. The patient reported regular use of α-pyrrolidinopentiophenone (α-PVP, colloquially called flakka in Spain) in the past year in the context of slamming, using only the upper extremities as sites of injection. He denied injecting his lower limbs for these purposes. Upon arrival he was hemodynamically stable. He presented an increased perimeter of the proximal right lower limb with slight erythema and edema on the posterior aspect of the thigh; neurovascular examination was normal. The upper limbs showed multiple necrotic lesions compatible with punctures. Laboratory tests revealed significant elevation of acute phase reactants (procalcitonin 0.42 ng/mL, C-reactive protein 29.3 mg/dL [0–0.5 mg/dL]) and a computerised tomography (CT) scan of the limb showed findings consistent with cellulitis and necrotizing myofasciitis with a myofascial abscess in the posterior region of the adductor muscle. Broad-spectrum antibiotic therapy (meropenem 1 g/8 h + linezolid 600 mg/12 h) was started and urgent surgical debridement and drainage were performed. Methicillin-resistant *Staphylococcus aureus* (MRSA) was isolated in the sample obtained, with negative blood cultures, antibiotics were adjusted to clindamycin with favorable evolution and progressive improvement of the patient's clinical condition.
**Conclusion:** Intravenous drug use is increasingly widespread in the sexual context. Methamphetamine, mephedrone or ketamine are the most commonly used drugs for these purposes. α-PVP is a synthetic stimulant drug of the cathinone class that, due to its stimulating profile, is also frequently used in this context [1]. Our patient stated that he complied with the recommendations for safe practice, however, quick acting effects of this drug led him to accidentally puncture himself with a used needle. This case depicts that this type of practice is still not risk-free despite the increasing education of drug users. Apart from the expected pharmacological effects of the drug, other concerns relate to the psychosocial impact and transmission of infectious agents by the parenteral route.

## Reference

[1] Schreck B, Guerlais M, Laforgue E, et al. Cathinone use disorder in the context of slam practice: new pharmacological and clinical challenges. Front Psychiat. 2020;11:705.

# 115. Cocaine body packer: a case report

Gabija Valauskaite[a], Haris Jakavicius[b], Gabija Laubner-Sakalauskiene[b] and Robertas Badaras[b]
[a]Department of Intensive Care Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [b]Toxicology Center, Republic Vilnius University Hospital, Vilnius, Lithuania

**Objective:** A body packer is a person who ingests pouches or packages of psychoactive substances (usually cocaine) to transport it. International smuggling of cocaine via body packers is an increasing problem worldwide. It is a very dangerous method to transport cocaine, since there is a high risk of package rupture inside the body, leading to overdose and sudden death. We report a case of a man who ingested and tried to transport 90 cocaine packages from South America to Europe.
**Case report:** A 27-year-old man was brought to the emergency department by customs police officers from Vilnius airport with a suspicion of psychoactive substances transportation via packages inside his body. He was travelling from French Guiana to Latvia with stopovers in Paris and Lithuania. When airport customs officers suspected him of being a body packer, he denied an illegal transportation of drugs and agreed to be examined by clinical toxicologists in Republic Vilnius University Hospital. Upon admission he was conscious, oxygen saturation was 99%, blood pressure 135/84 mmHg, and heart rate 99 beats per minute. There was no evidence suggesting an acute intoxication. Laboratory tests were without clinical changes. Psychoactive drug tests were also negative. Plain abdominal radiography suggested intensive multiple shadows with clear boundaries present inside the colon. To confirm the suspicion of body packing, an abdomen and pelvic computerised tomography (CT) scan was done. It revealed multiple ingested foreign bodies (up to 90) distributed from the caecum to the rectum. When the case was confirmed, the patient admitted that he was carrying 90 packages of diameter 3.5 × 1.5 cm. After half an hour he started eliminating the packages. The patient was hospitalized in the acute poisoning department. The decision was made not to use any medication to stimulate faster elimination of packages and let them leave the body naturally, however precautions were made, including heart rate monitoring and personnel supervision. The packages were

successfully eliminated in two days and the patient was discharged back to law enforcement.
**Conclusion:** Even though there are recommendations to induce faster gut clearance of foreign bodies using medication it can be done naturally. It is also important to take precautions such as heart rate monitoring to register tachycardia in a case of package rupture as well as personnel supervision to ensure a rapid response if packages leak and clinical signs occur.

## 116. The teratogenic risk of caffeine in pregnancy

Mariapina Gallo, Georgios Eleftheriou, Andrea Giampreti, Lorella Faraoni, Marco Cirronis, Maria Gioia Contessa and Giuseppe Bacis

Bergamo Poison Control Center, ASST Papa Giovanni XXIII, Bergamo, Italy

**Objective:** Caffeine, a methylxanthine alkaloid, is the most widely used stimulant substance in the world. Caffeine induces stimulation of the central nervous system and cardiac muscle, and relaxation of smooth muscle. Caffeine acts on physical and cognitive performance, as well as mood, memory, and alertness. In adults, caffeine is principally metabolized in the liver through the $CYP1A_2$ enzyme. During pregnancy, the $CYP1A_2$ is downregulated so the rate of caffeine metabolism decreases from the first to the third trimester of pregnancy. At the end of pregnancy, the half-life of caffeine is three to four times longer than in the non-pregnant state. Caffeine rapidly crosses the placental barrier and is not metabolized by the fetus, therefore its clearance depends on the maternal rate of metabolism. We reviewed the literature on teratogenic risks in pregnancy.
**Methods:** In order to identify literature on the topic EMBASE and MEDLINE were searched. Searches were executed using Ovid search engine and limited to the English language.
**Results:** Animal studies have shown that caffeine exposure can cause birth defects, premature labor, preterm delivery, reduced fertility, and increase the risk of low-birth-weight offspring. In the last few decades, studies have been conducted addressing the risk of caffeine exposure during human pregnancy. Considering the risk of spontaneous abortion from exposure to caffeine, two recent systematic reviews reported an increased risk respectively by 14%, in a linear fashion with every 100 mg/day increase in caffeine consumption, and by 19%, for every increase in caffeine intake of 150 mg/day. Observational and cohort studies reported conflicting data on the impact of caffeine on birth weight. Two meta-analyses, however, found that maternal caffeine intake during pregnancy was associated with an increased risk of low birth weight as compared with the reference group (no or very low caffeine intake), with a dose-response of 7% increase for each 100 mg/day. In a recent narrative caffeine consumption was significantly associated with negative outcomes, including miscarriage, stillbirth, low birth weight, and small for gestational age. Negative outcomes were identified at lower levels of consumption and increased in a dose-dependent manner. Even moderate caffeine consumption (200 mg per day) was alleged to be unsafe.
**Conclusion:** Assessing consequences of caffeine exposure during pregnancy is extremely difficult in light of biologic and epidemiologic considerations. Overall, low levels of caffeine consumption are not consistently associated with any fetal risks. Furthermore, more rigorous research with prospective designs are needed to mitigate some of the methodologic weaknesses in the current body of evidence.

## 117. Massive caffeine ingestion without severe poisoning: a case report

Georgios Eleftheriou[a], Raffaella Butera[b], Mariapina Gallo[b], Andrea Giampreti[b], Lorella Faraoni[b], Marco Cirronis[a], Maria Gioia Contessa[a], Eliana Margutti[c] and Giuseppe Bacis[a]

[a]Bergamo Poison Control Center, ASST Papa Giovanni XXIII, Bergamo, Italy; [b]Poison Control Center, ASST Papa Giovanni XXIII, Bergamo, Italy; [c]Emergency Department, ASST Papa Giovanni XXIII, Bergamo, Italy

**Objective:** Caffeine overdose have been reported with fatal doses from 10 g and higher. We present a man with delayed presentation to the emergency-department (ED) after ingestion of 120 caffeine tablets (0.2 g caffeine/tablet) who suffered mild cardiotoxicity and renal failure.
**Case report:** A 42-year-old man with no history of psychiatric illness presented to the ED after ingesting a lethal dose of 24 g of caffeine as a suicide attempt, 22 hours earlier. He reported mild tremors and vomiting. In the ED he had no clinical signs and symptoms and physical examination was normal. Mild hypokalemia 3.2 mmol/L was observed. Laboratory data were consistent with mild renal failure (creatinine 1.38, 2.32 and 1.3 mg/dL, 22 hours, 54 hours and 6 days after ingestion, respectively) and cardiotoxicity (troponin concentration 25.7, 71.2 and 18.6 ng/L, 22, 30 and 54 hours after ingestion; normal levels $<$53 ng/L), with normal electrocardiogram. Creatine kinase activity was 431 U/L and 222 U/L (normal 46–171 U/L), 22 and 54 hours after ingestion. Serum toxicology screen was negative for illegal substances and caffeine concentrations were 40 ng/mL, 15 ng/mL, and then under the limit of quantification (1 ng/mL), at 22 hours, 30 and 54 hours, respectively. He received 2000 mL/day of isotonic sodium chloride solution and remained hemodynamically stable. The clinical course was complicated by nosocomial pneumonia. He was transferred to the Psychiatric Unit 11 days after the overdose.
**Conclusion:** In our case in spite of 340 mg/kg of caffeine, only a mild clinical picture was observed. In the literature, ingestion of 200 mg/kg and plasma concentrations of 100 ng/mL are reported to be lethal [1]. Considering the delay between ingestion and ED presentation, the observed 40 ng/mL of caffeine after 22 hours, could correspond to a lethal plasma concentration after the overdose, because of its half-life 15–16 hours [2]. The mild clinical effects observed may be explained by vasoconstriction induced by caffeine. In our case renal vasoconstriction and antagonism of adenosine are considered to be the principal pathophysiological renal mechanisms involved in the kidney damage observed. In conclusion, our case suggests that further studies are needed to reassess the dose-response relationship in caffeine poisoning.

### References

[1] Cappelletti S, Piacentino D, Fineschi V, et al. Caffeine-related deaths: manner of deaths and categories at risk. Nutrients. 2018; 10:611.
[2] Leson CL, McGuigan MA, Bryson SM. Caffeine overdose in an adolescent male. J Toxicol Clin Toxicol. 1988;26:407–415.

## 118. Autoimmune diseases related to cocaine use: a case series

Macarena L. Míguez Del Águila[a], Gemma Alvarez Martinez[a], Antoni Castro Guardiola[a], Nuria Vilanova Anducas[a], Maria Àngels Gispert-Ametller[b], Ana Merino Ribas[c], Carolina Lorencio Cardenas[d] and Mercè Alsius Suñer[e]

[a]Department of Internal Medicine, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [b]Emergency Department, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [c]Department of Nephrology, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [d]Department of Intensive Care, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [e]Department of Clinical Analysis, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain

**Objective:** Sustained consumption of cocaine or levamisole-adulterated cocaine is related to the development of clinical immune-mediated conditions, mainly localized or systemic vasculitis. Our aim is to report five cases of vasculitis/systemic processes associated with cocaine use.
**Case series:** We performed a retrospective review of clinical, laboratory and histological features of five patients admitted to our center from November 2021 to August 2022, suspected of different immune-mediated clinical conditions associated with cocaine or levamisole-adulterated cocaine exposure. Five cases (1 female and 4 males), 31–44 years of age, were active cocaine users. Cocaine was detected in the urinalysis of all patients, though our reference laboratory was unable to detect positivity for levamisole in urine. On admission, three patients had cocaine-induced midline destructive lesions. Four patients developed vasculitis with skin abnormalities (purpura, helix necrosis, bullous dermatosis, pyoderma gangrenosum). Skin biopsies revealed leukocytoclastic vasculitis in 3 cases, and microvascular thrombosis in two of them. In the remaining cases, no biopsy was performed. Two patients developed polyarthritis. Acute renal disease developed in two cases, and renal biopsy in one revealed IgA nephropathy. Other clinical manifestations were orolingual angioedema, multiple mononeuritis and alveolar hemorrhage. The most critical case included multiorgan failure and subarachnoid hemorrhage. Only one patient developed neutropenia. Antineutrophil cytoplasmic autoantibodies (ANCA) against classic antigens were positive in four cases (3 for proteinase 3 [PR3] and 1 for myeloperoxidase [MPO]), and anti-elastase autoantibodies (HNE) were detected in three of them. The remaining case only tested positive for lupus anticoagulant. Corticosteroids were used in all cases, and in two patients immunosuppressants were also used.
**Conclusion:** Both cocaine and levamisole can induce autoimmune profiles and compromise the function of multiple organs. The most common clinical manifestations described are leukocytoclastic vasculitis, arthralgia, glomerulonephritis and neutropenia. The presence of ANCA at high titers and with mixed immunofluorescence patterns is frequent. The detection of HNE is characteristic of levamisole-induced vasculitis. In addition, other autoantibodies such as antinuclear, anti-DNA or antiphospholipid autoantibodies can be found. Distinguishing primary ANCA vasculitis from those induced by cocaine/levamisole is a clinical challenge [1]. Drug consumption (especially cocaine) should be investigated in all patients with some immune-mediated conditions. The anti-elastase autoantibodies are characteristic of levamisole-induced vasculitis. Clinical improvement depends on ceasing consumption. Severe cases could benefit from immunosuppressive treatment.

### Reference

[1] Lopez J, Lopez A, Alcocer M. Immune-mediated clinical manifestations associated with cocaine levamisole use – a literature review. Int J Clin Rheumatol 2020;15:155–163.

## 119. Severe complications associated with cocaine abuse requiring intensive care unit (ICU) admission

Clara Serrano-Ferrer[a], Angela Ruiz García[a], Diego Beltrán Hernandez[a], Ana Oñoro Morales[a], Alejandra Acha Aranda[a], Ana Ferrer-Dufol[b] and Emilio Nevado Losada[a]

[a]Intensive Care Unit, Principe de Asturias Hospital, Alcalá de Henares, Spain; [b]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza, Spain

**Objective:** Cocaine abuse is associated with a high risk of cardiovascular events. We present 3 cases of cocaine abusers requiring ICU admission for complications.
**Case series:** Case 1. A 40-year-old male with a history of cocaine abuse presented to the emergency department (ED) complaining of chest pain, with irradiation to the jaw and the left arm. The electrocardiogram (EKG) showed sinus rhythm (45 bpm) with ST elevation in inferolateral leads. Cardiac catheterization was performed, showing an ecstatic right coronary artery, with total thrombotic occlusion at the same localization. Thrombi aspiration and dilation were performed. Triple anti-aggregation was initiated, with systemic anticoagulation. No stent was implanted because of the absence of atherosclerotic plaque. He was transferred to the ICU; the only analytical alterations were a medium rise of bilirubin, aspartate aminotransferase (AST) and lactate dehydrogenase (LDH). He was discharged 5 days after admission. Case 2. Emergency services were called by the family of a 42-year-old male with a history of multiple drug abuse after finding him with a low level of consciousness in a kneeling position over his bed. They did not mention how long it had been since they last heard from him. He was transferred to hospital complaining of severe right leg pain. Urine was positive for cocaine, benzodiazepines, and opioids. An echo-Doppler showed permeability of the whole venous system. A computerised tomography (CT) scan showed swelling of all right leg fascia and a decrease of venous contrast. Intramuscular pressure was normal, but pain worsened, so a surgical fasciotomy was undertaken. Blood tests showed renal impairment, hepatic cytolysis, coagulopathy, and thrombocytopenia. Muscle necrosis was evident (creatine kinase 65,900 U/L). On EKG negative T waves were found in V1–V6 leads with normal troponin concentrations. An echocardiogram showed a small left ventricle dilation, the right ventricle quite dilated with mild tricuspid regurgitation, and the aortic root and ascending aortic arch dilated (43, 39 mm). Evolution was uneventful, and he was discharged 7 days after admission. Case 3. The emergency services were called to a 37-year-old male with a history of cocaine and alcohol abuse in cardiorespiratory arrest. The first rhythm was ventricular fibrillation and after cardiopulmonary resuscitation (CPR), he returned to sinus rhythm with ST elevation. Cardiac catheterization showed amputation of the anterior descending coronary arteria. Arterial counter-pulsator (ACtP) and stent were performed. He developed multiorgan failure and died 12 hours after admission. Urine was positive for cocaine.
**Conclusion:** Cocaine use can cause significant cardiac complications requiring multiple investigations and procedures.

## 120. Continuous renal replacement therapy in poisoning

Katja M. K. Lundquist[a], Lotte C. G. Høgberg[b] and Søren Bøgevig[a]

[a]Department of Clinical Pharmacology, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [b]Department of Anaesthesia and Intensive Care, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** The role of continuous renal replacement therapy (CRRT) in poisoning is not clear and hemodialysis (HD) is in general the recommended modality. The efficacy of CRRT machines is still improving and if settings are optimized (e.g., maximum dialysate flow), the gap to HD is minimized markedly. In most intensive care units CRRT is readily available and easier to commence in comparison to HD. The aim of this study was to investigate the reported use of CRRT in poisonings for seven selected pharmaceuticals, salicylic acid, lithium, paracetamol, gabapentin, pregabalin, carbamazepine and valproic acid, before and after the publication of the EXTRIP recommendations [1]. Furthermore, to investigate to the extent important machine parameters are reported in these publications.
**Methods:** Firstly, the literature underlying the EXTRIP recommendations concerning CRRT was identified through the references for each systematic review. Furthermore, a follow-up search (after 1 April 2014) was conducted to compare the EXTRIP reference data with the newest evidence in the area.
**Results:** Fifty articles on CRRT were identified through the EXTRIP work, primarily consisting of case reports. Out of these, the clearance and half-life were found for 18 (36%) and 19 (38%), respectively. Operating parameters were available in varying degrees in the articles; blood flow (Qb) in 40% of articles, dialysate flow (Qd) in 60%, replacement fluid flow (Qr) in 26% and ultrafiltrate flow (Quf) in 23%. In the follow-up search, 24 articles were identified. Clearance was reported in 12.5% and half-life in 29%. Operating parameters were reported as follows; Qb in 54%, Qd in 36%, Qr in 29% and Quf in 40% of relevant articles. In cases where the flow rates were reported sufficiently, the rates rarely reached and generally did not exceed 4000 mL/h.
**Conclusion:** The evidence regarding the use of CRRT as a treatment modality for intoxicated patients is still very sparse. The reports are characterized by heterogenous data in both machine settings, reported values and effect parameters. Both studies before 2014 and newer studies report submaximal operating parameters, which all in all makes the evaluation of the true effect and future role for CRRT in poisoning difficult.

### Reference

[1] EXTRIP. The extracorporeal treatments in poisoning workgroup [cited 2022 Oct 10]. Available from: https://www.extrip-workgroup.org/.

## 121. Management of tetanus: an "off-topic" for a Poison Control Center?

Monica Carnovale[a], Azzurra Schicchi[b], Lucia Bernasconi[a], Valentina Negrini[a], Davide Lonati[b], Valeria M. Petrolini[b], Elena Mattiuzzo[b], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute; Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Tetanus is caused by a neurotoxin produced by *Clostridium tetani*, an ubiquitous bacterium whose spores can contaminate surgical and traumatic wounds, burns, and the umbilical stump. Diagnosis is clinical, possibly supported by laboratory testing. It is a rare disease and there is no consensus on the therapeutic approach. Over the years, our Poison Control Center (PCC) was consulted for the management of this poisoning. Therefore, our aim was to study all cases referred to our PCC to evaluate the clinical presentation leading to toxicologist consultation and the treatment used.
**Methods:** We retrospectively analyzed (January 2012–August 2022) all cases of tetanus referred to our PCC. Data regarding age, sex, exposure route, clinical manifestations, vaccination status and outcome were evaluated. A tetanus case was defined by the presence or history of a wound and at least two of the typical signs (trismus, rigidity, spasms).
**Results:** Sixty patients were included (Table 1). In 49/60 patients (81.7%) the wound was identified: accidental wound in 42/49 (85.7%) patients; animal bite in 4/49 (8.2%); burns in 1/49 (2%); diabetic ulcer in 2/49 (4.1%). Vaccination status was known in 47/60 (78.3%) patients: in 46/47 (97.9%) it was incomplete. Clinical manifestations at first consultation were: trismus/risus sardonicus (85%), rigidity/spasms (66.7%), dysphagia (43%), and rigor nucalis (35%).
**Conclusion:** Although vaccine-preventable, tetanus is still a lethal disease. Our study shows that, even if is not a "typical" poisoning, PCCs can be involved in tetanus management. The main limitation of our study is that, due to the retrospective nature, outcome of many patients remains unknown; a prospective multicenter study can be relevant to identify the best management and therapeutic approach.

Table 1. Patient characteristics, management and outcome in 60 cases of tetanus.

| Patients' characteristics | Median [25–75 percentile]% |
|---|---|
| Age (years) | 75 [61.25–83.5] |
| Gender (M/F) | M 36.7%<br>F 63.3% |
| Time between wound and hospital admission (days) | 8 [7–10.75] |
| Case per years | 5 [4–6.5] |
| Management | |
| Wound debridement | 60/60 (100%) |
| Midazolam infusion | 60/60 (100%) |
| Metronidazole (500 mg/tid) | 60/60 (100%) |
| Tetanus immunoglobulin IM (median dosage 3000 [2500–3000] UI) | 60/60 (100%) |
| IV magnesium for target (magnesium 2–4 mmol/L) | 60/60 (100%) |
| Mechanical ventilationTracheostomy | 19/60 (31.7%)<br>6/19 (31%) |
| Outcome | |
| Partial or total recovery | 26/60 (43.3%) |
| Death | 14/60 (23.3%) |
| Unknown | 20/60 (33.3%) |

## 122. Bromoform ingestion causes gastrointestinal radioopacities, apparent hyperchloraemia and carboxyhaemoglobinaemia

Darren M. Roberts[a], Mina Roberts[b] and Nazila Jamshidi[a]

[a]NSW Poisons Information Centre, Sydney Children's Hospitals Network, Sydney, Australia; [b]Emergency Medicine, The Canberra Hospital, Canberra, Australia

**Objective:** Bromoform ($CHBr_3$) is a colourless liquid used mostly as a reagent and solvent in mineralogy. Bromoform is absorbed via the lungs, skin and gastrointestinal tract but its toxic dose and effects are poorly defined. We report a case of bromoform self-poisoning manifesting gastrointestinal radioopacities, carboxyhaemoglobinaemia and apparent hyperchloraemia.
**Case report:** A 62-year-old male non-smoker with a history of ischaemic heart disease and previous suicide attempts was found in a city park with Glasgow Coma Score (GCS) 7/15. He was transferred to hospital and the initial blood gas noted mild mixed respiratory and metabolic acidosis including pH 7.22, $pCO_2$ 53 mmHg, bicarbonate 17.6 mmol/L, chloride 104 mmol/L, lactate 2.2 mmol/L, base excess −6, anion gap 13, and carboxyhaemoglobin (COHb) 10.9%. Other investigations were notable for leucocytosis $16.6 \times 10^9$/L (neutrophils $15.3 \times 10^9$/L), creatinine 100 μmol/L (baseline 90 μmol/L), ALT 50 U/L, troponin 27 ng/L (reference <26 ng/L), INR 1.3 and negative paracetamol and ethanol concentrations. He received supportive care including low flow oxygen therapy and intravenous fluids and there was a progressive improvement. Approximately, 90 minutes postarrival, he was GCS 14 with normal cardiorespiratory and abdominal examination. He reported ingesting 50 mL of bromoform with suicidal intent. A blood gas at this time showed an improvement with pH 7.27, $pCO_2$ 48 mmHg, bicarbonate 19.1 mmol/L, lactate 1.9 mmol/L and base excess −4.9, although COHb increased to 13.2%. Repeat troponin remained 27 ng/L. Abdominal X-ray demonstrated radioopacities in the small intestine. A blood gas 6 hours post-presentation was similar except for chloride 113 mmol/L. In view of reports of gastric erosions and enterocolitis from poisonings with the related substances chloroform and bromide, he was observed in ICU overnight. COHb peaked at 15.6%. A gastroscopy performed the next day was normal. Approximately 33 hours post-presentation, bloods noted INR 1.6 and ALT 70 U/L and acetylcysteine infusion was commenced. Serum chloride concentrations rose to 150 mmol/L, attributed to assay interference by bromide. Despite ALT increasing to 115 U/L, the patient remained asymptomatic and was transferred to another institution.
**Conclusion:** When ingested, bromoform reacts with gastric hydrochloric acid to liberate bromide, which is radioopaque. Absorbed bromoform is metabolised to bromide, carbon monoxide and carbon dioxide, and eliminated unchanged in the urine. Investigations supporting a significant exposure include blood gases (elevated COHb, hyperchloraemic metabolic acidosis), and abdominal X-rays identifying radioopacities. Blood and urinary bromide concentrations if available confirm the exposure. Management is supportive care; the effect of gastric decontamination or enhanced elimination techniques is not known.

## 123. Sodium nitrite ingestions, mission impossible?

Erik Lindeman, Jasmin Khessib and Johanna Nordmark Grass

Swedish Poisons Information Centre, Stockholm, Sweden

**Objective:** Sodium nitrite (SN) has emerged as a method for suicide in several parts of the world. Detailed practical instructions on administration and dosing are available through dedicated "suicide forums" on the Internet while the chemical itself is available for home delivery through different websites. SN is an oxidizing agent and exposure causes methemoglobinemia (Met-Hb). The clinical course of four SN-suicide attempts is explored in a case series.
**Case series:** The four calls to the Swedish Poison Center (PC) concerning symptomatic sodium nitrite ingestions with suicidal intent are described. All calls occurred from November 2021 through September 2022 and were immediately perceived as exceptional when they occurred. The patients were in their early 20s, two males and two females. The calls to the emergency medical services (EMS) were all placed prior to symptom onset. In cases 1 and 2, the patients themselves called EMS shortly after ingesting SN. In case 3 the EMS call was made from staff at a psychiatric facility. In cases 1–3, the EMS operator received information on the substance and dose consumed and case 1 even asked for "methylene blue" (MB). The PC was "patched in" on these EMS calls and could inform the ambulance staff of the high lethality associated with the ingestion and of treatment needed. In case 4 the call was made by family members who reported that the patient had taken an unknown "suicide powder". In this case the PC was contacted on hospital arrival, when the patient was already deeply unconscious, and helped establish the diagnosis. Case 1 had cardiac arrest on site and cases 2–4 developed cardiac arrest within minutes of arrival to the hospital. Ambulances in Sweden do not carry MB and no patient received MB prior to cardiac arrest. All patients had Met-Hb >90% on presentation and all were pronounced dead within an hour after the initial EMS call. Resuscitative efforts, including the administration of MB, were futile.
**Conclusion:** The management of SN ingestion constitutes a great challenge due to the rapid development of Met-Hb concentrations incompatible with life. Ideally, antidote administration should occur on site. When this is impossible, the speediest possible transport to hospital is warranted, optimally establishing intravenous access *en route*. Hospital staff need to be put on alert and should meet the ambulance, MB at the ready. The PC, when contacted early, could be of use in coordinating this response.

## 124. A fatal case of iatrogenic iodine toxicity

Amanda G. Holford[a,b] and Katherine Z. Isoardi[a,b]

[a]Clinical Toxicology Unit, Princess Alexandra Hospital, Brisbane, Australia; [b]Queensland Poisons Information Centre, Brisbane, Australia

**Objective:** Severe toxicity from povidone-iodine is rare, and results in profound metabolic acidosis likely due to tissue destruction, lactataemia and bicarbonate consumption from the conversion of iodine to sodium iodide. We report a case of fatal iodine toxicity following complications of sclerotherapy.

**Case report:** An elderly man presented to a rural hospital with an altered level of consciousness 6 hours after a seemingly uncomplicated ablation of a large renal cyst with 10% povidone-iodine and 100% ethanol. He was drowsy with a Glasgow Coma Score (GCS) of 14 and complained of feeling intoxicated but denied having ingested any alcohol. He was initially haemodynamically stable although developed resistant hypotension over the next 3 hours and was commenced on noradrenaline (peak 20 μg/min). His admission ethanol concentration was 54 mmol/L. Imaging was performed which confirmed a large amount of residual radio-opaque fluid at the site of the cyst. He was urgently transferred to the tertiary hospital which performed the initial procedure. On arrival to there, he was unwell with cardiovascular collapse. His venous gas demonstrated a profound metabolic acidosis with a spurious hyperchloraemia (pH 7.09, $pCO_2$ 22mmHg, $HCO_3$ 6 mmol/L, anion gap 20, chloride 122 mmol/L), and lactate 15 mmol/L. His creatinine was 172 μmol/L. The residual fluid was percutaneously drained, and he was transferred to intensive care unit (ICU) on multiple maximum dose vasopressor agents (noradrenaline, adrenaline) and commenced on continuous renal replacement therapy 20 hours after the exposure. His iodine concentration peaked at 8940 μmol/L (reference range 0.32–0.63 μmol/L) 14.5 hours post exposure. His chloride remained spuriously elevated (peak 129 mmol/L), following the trend of the iodine concentrations, normalising once the iodine concentration was 1559 μmol/L. Unfortunately, the patient continued to deteriorate despite maximal dose vasopressors and organ support and succumbed on day 3.
**Conclusion:** Povidone-iodine is a commonly used antiseptic agent. When absorbed in large amounts systemically it can result in profound toxicity, an under-recognised complication. Iodide interferes with point of care testing chloride measurements but chloride may be used as a surrogate for very high iodine concentrations (>2000 μmol/L) where timely iodine concentrations are unavailable.

## 125. Gamma-hydroxybutyrate (GHB) intoxication is associated with hypothermia: a case series of 790 patients with analytical confirmation of psychoactive substance exposure

Shaun L. Greene[a], Zeff Koutsogiannis[a], Sarah Hodgson[a], Rebekka Syrjanen[a], Rachelle Abouchedid[a] and Jennifer Schumann[b]

[a]Victorian Poisons Information Centre, Melbourne, Australia; [b]Victorian Institute of Forensic Medicine, Melbourne, Australia

**Objective:** Hypothermia has been reported in self-reported GHB intoxications [1,2]. We examined hypothermia in illicit-drug intoxications with analytically confirmed exposure to GHB compared to intoxications without GHB detection.
**Methods:** Data was extracted from a human research ethics committee approved clinical registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to emergency departments in Victoria, Australia [3]. Blood samples are analysed using combined liquid chromatography/mass spectrometry/time of flight mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances).
**Results:** GHB was detected in 240 (30%) of 790 illicit drug presentations. Median temperature in cases that included GHB detection (Table 1) was significantly lower compared to cases without GHB detection (35.7 versus 36.3 °C, $p < 0.0001$). There was no significant temperature difference between cases that included GHB and methamphetamine versus cases that included GHB without methamphetamine detections (35.7 versus 35.7 °C, $p = 0.2$). Median temperature in cases that included methamphetamine but excluded GHB detection was significantly higher compared to cases that included both methamphetamine and GHB detections (36.2 versus 35.7 °C, $p < 0.0001$). The rate of hypothermia (temperature ≤35.0 °C) was significantly higher in GHB exposures compared to exposures with no GHB detected (31 versus 10%, $p < 0.0001$).
**Conclusion:** GHB intoxication is associated with hypothermia and is independent of co-exposure to methamphetamine.

### References

[1] Chin RL, Sporer KA, Cullison B, et al. Clinical course of gamma-hydroxybutyrate overdose. Ann Emerg Med. 1998;6:716–722.
[2] Miró O, Nogué S, Espinosa G, et al. Trends in illicit drug emergencies: the emerging role of gamma-hydroxybutyrate. J Toxicol Clin Toxicol. 2002;40:129–135.
[3] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

## 126. Gamma-hydroxybutyrate intoxication is associated with bradycardia, but not blood pressure derangement: a case series of 790 patients with comprehensive analytical confirmation of psychoactive substance exposure

Shaun L. Greene[a], Rebekka Syrjanen[a], Rachelle Abouchedid[a], Sarah Hodgson[a], Zeff Koutsogiannis[a] and Jennifer Schumann[b]

[a]Victorian Poisons Information Centre, Melbourne, Australia; [b]Victorian Institute of Forensic Medicine, Melbourne, Australia

**Objective:** Bradycardia [1] and hypertension [2] have been reported in published series of self-reported GHB intoxications. We aimed to examine cardiovascular findings in illicit-drug

Table 1. Descriptive temperature statistics for GHB and non-GHB detection groups.

| Exposure | Number | Median temperature (°C) | Range (°C) |
|---|---|---|---|
| All exposures that INCLUDED GHB detection | 240 | 35.7 | 30.6 – 37.8 |
| All exposures that EXCLUDED GHB detection | 550 | 36.3 | 28.0 – 41.7 |
| All exposures that INCLUDED GHB and methamphetamine detections | 226 | 35.7 | 30.6 – 37.8 |
| All exposures that INCLUDED GHB detections, BUT EXCLUDED methamphetamine detections | 14 | 35.6 | 33.1 – 35.9 |
| All exposures that EXCLUDED GHB detections, BUT INCLUDED methamphetamine detections | 316 | 36.2 | 28.0 – 41.7 |

intoxications with analytically confirmed exposure to GHB compared to intoxications without GHB detection.
**Methods:** Data was extracted from a human research ethics committee approved clinical registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to emergency departments in Victoria, Australia [3]. Blood samples were analysed using combined liquid chromatography/mass spectrometry/time of flight mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances).
**Results:** Gamma-hydroxybutyrate (GHB) was detected in 241 (30%) of 790 illicit drug presentations. Median heart rate in cases that included GHB detection ($n = 241$) was significantly lower compared to cases without GHB ($n = 549$) detection (72 versus 96 bpm, $p < 0.0001$). Median heart rate in cases including both methamphetamine and GHB detection ($n = 225$) was significantly lower compared to cases with methamphetamine ($n = 317$), but not GHB detected (72 versus 92 bpm $p < 0.0001$). The rate of bradycardia (heart rate $\leq$60 bpm) was significantly higher in GHB exposures compared to exposures with no GHB detected (27 versus 5%, $p < 0.0001$). There was no significant difference in median systolic or diastolic blood pressure (BP) between cases with GHB ($n = 241$) and without GHB ($n = 549$) detection (median systolic BP 121 versus 124 mmHg, $p = 0.09$, median diastolic BP 75 versus 76 mmHg, $p = 0.31$). There was no significant difference in the rate of systolic hypotension (BP $\leq$90mmHg) between cases that included GHB ($n = 241$) and cases without GHB ($n = 549$) detection (4.6 versus 4.2%, $p = 0.8$), or hypertension (BP $\geq$160mmHg) (7.5 versus 5.3%, $p = 0.25$). Systolic BP in cases with methamphetamine, but no GHB detected was not significantly different than cases with GHB without methamphetamine detected (median systolic BP 121 versus 125 mmHg, $p = 0.16$).
**Conclusion:** GHB intoxication is associated with bradycardia, but not altered blood pressure. GHB attenuated methamphetamine-induced tachycardia in cases with combined GHB-methamphetamine detected.

## References


[1] Chin RL, Sporer KA, Cullison B, et al. Clinical course of gamma-hydroxybutyrate overdose. Ann Emerg Med.1998;6:716–22.
[2] Munir VL, Hutton JE, Harney JP, et al. Gamma-hydroxybutyrate: a 30 month emergency department review. Emerg Med Australas. 2008;20:521–530.
[3] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.


# 127. Characterisation of illicit drug exposures within an early warning system: medical record documentation performs poorly compared to comprehensive toxicological analysis of biofluid


Rebekka Syrjanen[a], Jennifer Schumann[b], Sarah Hodgson[a], Rachelle Abouchedid[a], Zeff Koutsogiannis[a] and Shaun L. Greene[a]

[a]Victorian Poisons Information Centre, Austin Health, Heidelberg, Victoria, Australia; [b]Victorian Institute of Forensic Medicine, Southbank, Victoria, Australia


Table 1. Sensitivity of medical record documentation of illicit drug exposure compared to comprehensive toxicological biofluid analysis.

| Analytically confirmed exposure (number) | | Percentage of analytically confirmed exposures reported in the medical record at time of ED presentation (sensitivity) (%) |
|---|---|---|
| Novel stimulant including cathinones | 25 | 0 |
| Novel dissociative | 9 | 0 |
| Novel opioid | 8 | 25 |
| Tetrahydrocannabinol (THC) | 202 | 25 |
| Synthetic cannabinoid receptor agonist | 16 | 25 |
| Methamphetamine | 723 | 31 |
| Novel benzodiazepine | 178 | 41 |
| Cocaine | 121 | 45 |
| 3,4-Methylenedioxymethamphetamine (MDMA) | 71 | 48 |
| Ketamine | 39 | 54 |
| Gamma-hydroxybutyrate (GHB) | 242 | 75 |
| Lysergic acid diethylamide (LSD) | 22 | 77 |
| Heroin | 156 | 92 |


**Objective:** Measures of illicit drug use based on Emergency Department (ED) illicit drug presentations are utilised within illicit drug Early Warning Systems (EWS), harm reduction responses and health-care policy. Medical record documentation of illicit drug exposure based on patient self-report and health-care provider interpretation of case history and examination findings, but excluding comprehensive toxicological analysis, may be utilised as an indicator of community illicit drug use within these systems. We examined sensitivity of medical record documentation of illicit drug exposure compared to comprehensive toxicological analysis of biofluid.
**Methods:** Data was extracted from a human research ethics committee approved clinical registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to emergency departments in Victoria, Australia [1]. Blood samples are analysed using combined liquid chromatography/mass spectrometry/time of flight mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances).
**Results:** Overall, 1088 reported or suspected illicit drug presentations with comprehensive toxicological analysis were analysed. At least one illicit drug was detected in 1011 (93%) of cases. There were 1812 separate illicit drug detections; 811 (45%) had been documented as an exposure within the case record. Sensitivity of medical record documentation as compared to comprehensive toxicological analysis varied with drug class (range 0–92%, Table 1). Sensitivity for novel psychoactive substances was poor (range 0–41%). No analytically confirmed novel stimulant exposures and only 25% of novel opioid exposures were documented.
**Conclusion:** Medical record documentation of illicit drug exposure in ED presentations performed poorly compared to comprehensive toxicological biofluid analysis. This has important implications for EWS and health-system responses.


## Reference


[1] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

## 128. Diphenidine, methoxyphenidine and related 1,2-diarylethylamine acute toxicity reported to the Euro-DEN Plus project

David M. Wood[a], Alison M. Dines[b], Matthias E. Liechti[c], Isabelle Giraudon[d], Fridtjof Heyerdahl[e], Knut Erik Hovda[f], Odd Martin Vallersnes[g], Oscar Miro[h], Christopher Yates[i], Euro-Den Plus Research Group and Paul I. Dargan[a]

[a]Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust and Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom; [b]Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [c]Division of Clinical Pharmacology and Toxicology, University Hospital Basel and University of Basel, Basel, Switzerland; [d]European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Lisbon, Portugal; [e]Prehospital Division, Oslo University Hospital and Norwegian Air Ambulance Foundation, Oslo, Norway; [f]Norwegian CBRNE Centre of Medicine, Oslo University Hospital, Oslo, Norway; [g]Department of General Practice, Oslo University and Oslo Accident and Emergency Outpatient Clinic, City of Oslo Health Agency, Oslo, Norway; [h]Emergency Department, Hospital Clínic, IDIBAPS, University of Barcelona, Barcelona, Spain; [i]Emergency Department and Clinical Toxicology Unit, Hospital Universitari Son Espases, Mallorca, Palma, Spain

**Objective:** The new psychoactive substances diphenidine and related 1,2-diarylethylamines ephenidine, methoxyphenidine, isophenidine and fluorolintane, are N-methyl-D-aspartate (NMDA) receptor antagonists. Although there is limited published information on their toxicity, they appear to have similar unwanted effects to ketamine. Based on the availability, reported and potential toxicity of these compounds, the World Health Organization reviewed diphenidine and 2-methoxyphenidine in 2020. Diphenidine was subsequently added to the UN Convention on Psychotropic Substances in 2021, but 2-methyoxyphenidine was not added and remains under UN surveillance. There is limited published information on acute toxicity on these substances; we aim here to summarise the Euro-DEN Plus experience of these compounds.
**Methods:** The Euro-DEN Plus database was retrospectively interrogated to identify presentations from the 62,613 presentations reported between October 2013 and December 2021 involving the self-reported use of diphenidine, ephenidine, methoxyphenidine, isophenidine and/or fluorolintane. The following were extracted for analysis from cases involving use of only one of these NPS with/without alcohol but no other NPS/recreational drugs: demographics, clinical features and outcome (initial disposition from the ED and overall length of hospital stay).
**Results:** We identified six Euro-DEN Plus presentations with use of one of these NPS: methoxyphenidine (5 presentations) and diphenidine (1 presentation). There were no presentations involving ephedrine, isophenidine and/or fluorolintane. The diphenidine case from Munich, Germany in 2015, involved the co-use of cannabis, 4-chloromethcathinone and 5MAPB (1-(benzofuran-5-yl)-N-methylpropan-2-amine). No other drugs were reported to have been used in the methoxyphenidine cases and so further analysis was undertaken on these cases. Three were from London, UK (between 2013 and 2015) and two cases were from Msida, Malta (both in 2019). All five were male and the mean ± SD age was 27.6 ± 6.5 years. The reported clinical features were agitation/aggression (2 patients), hallucinations (2), anxiety (1), and seizures (1). Four were discharged from the ED (3 medically and 1 self-discharged) and one was admitted to hospital. The overall median (IQR) length of stay was 3 h 14 mins (2 h 7 mins to 3 h 34 mins).
**Conclusion:** Presentations with acute toxicity related to the use of diphenidine, methoxyphenidine and related 1,2-diarylethylamines is uncommon in the Euro-DEN Plus project. Identified Euro-DEN Plus presentations had short lengths of stay and most were discharged from hospital. Despite the recent international control of diphenidine and recommendation for enhanced monitoring of 2-methoxyphenidine in 2020/21, there have no reports of acute toxicity related to these NPS since 2019.

## 129. Characteristics of analytically confirmed novel opioid exposures in patients presenting to emergency departments within the state of Victoria, Australia

Shaun L. Greene[a], Rachelle Abouchedid[a], Sarah Hodgson[a], Rebekka Syrjanen[a] and Jennifer Schumann[b]

[a]Victorian Poisons Information Centre, Melbourne, Australia; [b]Victorian Institute of Forensic Medicine, Melbourne, Australia

**Objective:** Illicit use of novel opioids is associated with significant morbidity and mortality, particularly in North America [1]. However, documented illicit exposures to novel opioids within Australia are rare. We describe cases of novel opioid toxicity with analytical confirmation of biofluid analysis in patients presenting to emergency departments (EDs) within Victoria, Australia.
**Methods:** Data was extracted from a human research ethics committee approved clinical registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to EDs in Victoria, Australia [2]. Blood samples are analysed using combined liquid chromatography/mass spectrometry/time of flight mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances).
**Results:** An opioid was detected in 363 (32%) of 1125 reported or suspected illicit drug presentations. Commonly detected opioids included heroin ($n = 159$), methadone ($n = 127$), oxycodone ($n = 29$) and tramadol ($n = 25$). A novel opioid was detected in 0.07% of all cases ($n = 8$). Novel opioids included protonitazene ($n = 5$), butonitazene ($n = 1$), etodesnitazene ($n = 1$), 2-methyl AP-237 ($n = 1$) and beta-U10 ($n = 1$). There were no illicit fentanyl or fentanyl analogue detections. Novel opioid exposure was self-reported in two cases following use of protonitazine and etodesnitazene purchased on-line (in the protonitazene product case, butonitazene was co-detected). Protonitazine was detected in two patients who reported ketamine exposure. 2-Methyl AP-237 was detected in a patient who collapsed following use of multiple unknown substances. Beta-U10 was co-detected with 6-monoacetylmorphine in a patient presenting with respiratory depression following reported heroin use. Within the eight novel opioid cases, co-detections included methamphetamine (n = 5), a novel or pharmaceutical benzodiazepine (n = 5) and a cathinone (n = 1). Four patients (50%) experienced respiratory depression requiring naloxone, including one respiratory arrest. A positive response to naloxone was documented in three cases. There were no deaths, but one patient sustained a hypoxic brain injury.
**Conclusion:** Despite high rates of illicit novel opioid morbidity and mortality in some jurisdictions, novel opioid exposures in patients in presenting to EDs with suspected or reported illicit drug are rare in Victoria. Nitazene opioids comprised the majority of novel opioid detections. No fentanyl analogues were detected.

## References

[1] Centres for Disease Control and Prevention. Drug overdose deaths in the U.S. top 100,000 annually. Centres for Disease Control and Prevention; November 2021 [cited 2022 Oct 10]. Available from: https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/20211117.htm.

[2] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.


# 130. Illicit substance use and physical restraint: a prospective cohort study of 1125 patients presenting to emergency departments with analytically confirmed psychoactive substance exposure


Sarah Hodgson[a], Rachelle Abouchedid[a], Rebekka Syrjanen[b], Jennifer Schumann[b] and Shaun L. Greene[a]

[a]Victorian Poisons Information Centre, Melbourne, Australia; [b]Victorian Institute of Forensic Medicine, Melbourne, Australia



**Objective:** Physical restraint is commonly used in the Australasian healthcare setting to manage behavioural disturbance and risk of harm [1]. However, restraint is associated with significant adverse outcomes and death [2]. We examined use of physical restraint in 1125 patients presenting to Emergency Departments with suspected or reported illicit drug use.
**Methods:** Data was extracted from a human research ethics committee approved registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to Emergency Departments in Victoria, Australia [3]. Blood samples were analysed using combined liquid chromatography with tandem mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances).
**Results:** Physical restraint was used in 109/1125 (9.7%) patients; 13 in the pre-hospital setting only, 64 in hospital only, and 32 in both settings. Methamphetamine was detected in 80/109 (73%) patients requiring restraint; however, this was not statistically different to the non-restrained group (668/1016 patients, 66%, $p = 0.11$). Detection of any stimulant was not statistically different between groups (76% restrained versus 75% non-restrained, $p = 0.9$). However, detection of any opioid (23% restrained versus 33% non-restrained, $p = 0.03$), or any sedative (63% restrained versus 75% non-restrained, $p = 0.01$) was associated with less use of restraint. Patients self-reporting methamphetamine use were more likely to be restrained (38 versus 21%, $p < 0.01$).
**Conclusion:** Despite media and political framing of the methamphetamine user as dangerous [4], this study shows that methamphetamine detection is not associated with an increased need for physical restraint. However patient self-reporting of methamphetamine use was associated with an increased use of restraint, potentially related to the stigma and discrimination this group faces in Australia [5].



## References

[1] Cannon ME, Sprivulis P, McCarthy J. Restraint practices in Australasian emergency departments. Aust N Z J Psychiatry. 2001; 35:464–467.

[2] Mohr WK, Petti TA, Mohr BD. Adverse effects associated with physical restraint. Can J Psychiatry 2003;48:330–337.

[3] Syrjanen R, Schuman J, Fitzgerald J, et al. The emerging drugs network of Australia-Victoria Clinical Registry: A state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

[4] Deen H, Kershaw S, Newton N, Stapin , et al. Stigma, discrimination and crystal methamphetamine ('ice'): current attitudes in Australia. Int J Drug Policy. 2021;87:102982.

[5] Cohn A, O'Connor R, Lancaster K, et al. Media and political framing of crystal methamphetamine use in Australia. Drugs Educ Prev Policy. 2020;27:261–270.


# 131. Counterfeit "Xanax®" tablets in Australia – more than you bargained for?


Rebekka Syrjanen[a], Jennifer Schumann[b], Sarah Hodgson[a], Rachelle Abouchedid[a] and Shaun L. Greene[a]

[a]Victorian Poisons Information Centre, Austin Health, Heidelberg, Victoria, Australia; [b]Victorian Institute of Forensic Medicine, Southbank, Victoria, Australia



**Objective:** In Australia there is increasing evidence of novel benzodiazepines (NBZNs) within counterfeit pharmaceutical products labelled as "Xanax®". Xanax® is not a registered alprazolam preparation available in Australia. We describe cases (with corresponding analysis of biological fluid) of reported "Xanax®" exposure in patients presenting to emergency departments (EDs) in Victoria, Australia.
**Methods:** Data was extracted from a human ethics committee approved clinical registry, focused on the collection of clinical and analytical data from ED presentations involving illicit drug intoxications in Victoria, Australia [1]. Blood samples taken at the time of presentation were analysed using combined liquid chromatography-mass spectrometry/quadrupole time of flight mass spectrometry for 575 common pharmaceutical, illicit and novel substances. The registry was systematically searched for cases of documented "Xanax®" exposure from September 2020 until August 2022.
**Results:** Eighty-eight patients reported exposure to "Xanax®"; 61% were male (median age 23 years, range 16–68 years). In cases where use intent was documented ($n = 67$), 19% reported deliberate self-poisoning. A psychiatric medication was concurrently detected in 24 patients (27%). At least one NBZN was analytically detected in 82% ($n = 72$) of patients reporting "Xanax®" exposure (Table 1). In 54% of these cases a combination of two or more NBZNs were detected. An unreported pharmaceutical benzodiazepine was detected in 44% of patients. Alprazolam was detected in eleven cases. Identities of detected NBZNs varied significantly during the study period.
**Conclusion:** A range of novel and pharmaceutical benzodiazepines were detected following exposure to single counterfeit "Xanax®" tablets, with variation in total number and combination of benzodiazepines over time. Approximately a fifth of patients reported use of these products for self-harm.



## Reference

[1] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

Table 1. Benzodiazepine detections in patients reporting "Xanax®" use ($n = 80$ patients).

| Drug | Number ($n$) | Percentage (%) |
|---|---|---|
| Pharmaceutical benzodiazepines | | |
| Alprazolam | 11 | 13 |
| Clonazepam | 4 | 5 |
| Diazepam | 28 | 32 |
| Nitrazepam | 1 | 1 |
| Novel benzodiazepines | | |
| Bromazolam | 8 | 9 |
| Clobromazolam | 25 | 28 |
| Clonazolam | 35 | 40 |
| Etizolam | 20 | 23 |
| Flualprazolam | 14 | 16 |
| Flubromazepam | 6 | 7 |
| Flubromazolam | 1 | 1 |
| Phenazepam | 20 | 23 |

## 132. Over half of fatalities in 1123 patients presenting to emergency departments with analytically confirmed exposure to a psychoactive substance are associated with heroin use

Rachelle Abouchedid[a], Sarah Hodgson[a], Rebekka Syrjanen[a], Jennifer Schumann[b] and Shaun L. Greene[a]

[a]Victorian Poisons Information Centre, Austin Health, Melbourne, Australia; [b]Drug Intelligence Unit, Victorian Institute of Forensic Medicine, Monash University, Melbourne, Australia

**Objective:** Heroin is consistently identified as the leading illegal drug in overdose deaths, detected in 187 cases in 2020, in Victoria, Australia. In the same year, there were 33 new psychoactive substance (NPS) detections, having quadrupled in the last 3 years [1]. Given rising prevalence, we sought to determine implications of NPS in Intensive Care Unit (ICU) admissions and illicit drug related fatalities.
**Methods:** Data were extracted from a human research ethics committee approved clinical registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to emergency departments in Victoria, Australia [2]. Blood samples are analysed using combined liquid chromatography/mass spectrometry/time of flight mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances).
**Results:** One in seven patients ($n = 160/1123$, 14%) were admitted to ICU, two-thirds were male (108, 68%), with median ages 33.5 years (IQR 25–42 years). Intubation for airway protection and/or respiratory failure was the most common reason for ICU admission. Median hospital length of stay was 58.4 hours (IQR 25.9–103.8 hours). Most patients recovered ($n = 131$, 82%); five (3%) had permanent disability and outcomes were not documented in sixteen (10%). Thirty-two cases (20%) had NPS detections: NPS-benzodiazepine (29, 18%) (bromazolam (5), clobromazolam (3), clonazolam (14), desalkylflurazepam(2), deschloroetizolam (1), estazolam (1), etizolam (7), flualprazolam (6), flubromazepam(5), phenazepam (1)), prototinazene (2), cathinones (3) (N-ethylpentylone (1), ethylone (1), eutylone (1), methylone (1), pentylone (1)) and 5F-Cumyl-PINACA (1). There were eleven deaths; all were associated with out of hospital cardiac arrest; heroin was detected in seven, NPS-benzodiazepine were co-detected in two of these cases. Other deaths ($n = 4$) resulted from suspected asthmatic respiratory arrest with multiple illicit drug detections (cocaine, MDMA, N-ethylpentylone, ethylone, eutylone, clonazolam), massive subarachnoid haemorrhage (MDMA), drug-induced hyperthermia with multi-organ failure (cocaine, MDMA) and completed suicide by hanging (with an associated methamphetamine detection).
**Conclusion:** Out-of-hospital cardiac arrest occurred in all eleven deaths within this cohort. Intubation for airway protection and/or respiratory failure were the most common reasons for ICU admission. NPS-benzodiazepines were detected in one-fifth of admissions. Heroin was the most frequently detected illicit drug in fatalities.

### References

[1] Coroners Court of Victoria. Victorian overdose deaths, 2011–2020 [cited 2022 Octr 10]. Available from: https://www.coronerscourt.vic.gov.au/sites/default/files/2021-07/CCOV%20-%20Overdose%20deaths%20in%20Victoria%202011-2020%20-%2029Jul2021.pdf.
[2] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

## 133. Trends in detections of unregistered benzodiazepines and counterfeit alprazolam in New South Wales, Australia

Jared A. Brown[a], Tracy Ho[a], Thanjira Jiranantakan[a], Una Cullinan[b], Nicole Wright[c], Christopher Ewers[b], Darren M. Roberts[c] and Marissa Parry[a]

[a]NSW Ministry of Health, Sydney, Australia; [b]NSW Health Pathology, Sydney, Australia; [c]NSW Poisons Information Centre, Sydney, Australia

**Objective:** The non-prescribed use of "unregistered benzodiazepines" pose a significant threat to public health, with increasing reports of counterfeit alprazolam products in both Australia and worldwide. Most counterfeit "alprazolam tablets" do not contain alprazolam but instead contain a range of other unregistered/novel benzodiazepines such as etizolam or other drugs. We report on time trends of detections of counterfeit alprazolam and unregistered benzodiazepines in New South Wales, Australia.
**Methods:** We searched the Illicit Drug Analysis Unit, Forensic & Analytical Science Service, NSW Health Pathology dataset (January 2012–February 2022) for police seizures of unregistered benzodiazepines (i.e., benzodiazepines not marketed in Australia); and counterfeit alprazolam (2 mg alprazolam tablet forms of Xanax, Mylan, Kalma, Alprax or Sandoz which: did not contain alprazolam, contained alprazolam with other drugs, or no drugs were present). We summarise data collected following a clinician safety advisory in July 2020 requesting reporting.
**Results:** Unregistered benzodiazepines were first detected in June 2013 in very low numbers, but from late 2018 there was a large increase in detections which has been sustained. Of the 545 samples identified, 394 were tablets, 45 were lollies, 33 were other/unknown, 32 were tablet fragments and 10 were liquids. The most common drugs detected were etizolam ($n = 394$), clonazolam ($n = 80$), flualprazolam ($n = 65$); with a changing pattern

over time. Counterfeit Mylan seizures were most common ($n = 163$), followed by Xanax ($n = 136$), Kalma ($n = 46$), Sandoz ($n = 11$) and Alprax ($n = 1$). Of all counterfeit alprazolam samples, only 10% contained alprazolam. There were rare detections of non-benzodiazepine drugs including amphetamines, tryptamines, cyproheptadine and doxepin. During July–December 2020, there were 91 clinician reports received with 46 confirmed as counterfeit. Brands involved 2 mg forms of Xanax, Mylan and Kalma. Analysis of tablets identified were (in order of frequency): etizolam, flualprazolam, clonazolam, alprazolam, flubromazolam.
**Conclusion:** Data from police seizures showed an increase in unregistered benzodiazepines detected in recent years, primarily from counterfeit alprazolam tablets. These results correspond with findings from other NSW Health surveillance programs which found clinicians can incorporate routine questions about drug appearance during discussions about drug use to aid detection of emerging trends. NSW Health works with stakeholders to provide public and clinician drug information from rapid surveillance data. Multi-agency collaboration is needed to manage this ongoing issue. Given the established presence of unregistered benzodiazepines in circulation and the changing composition, there is an ongoing need to rapidly detect, assess and respond to new substances to reduce public health risks.

## 134. Are novel psychoactive substances (NPS) that share structural motifs with approved compounds more likely to have a psychoactive effect?

Michael Chary
Weill Cornell Medicine, New York, NY, USA

**Objective:** The pace of emergence of novel psychoactive substances (NPS) exceeds the ability of laboratory-intensive approaches to characterize them all as they emerge. This mismatch raises the need to predict the effects of NPS from limited knowledge to judiciously allocate laboratory resources. The Internet provides a plethora of data on NPS. However, it is difficult to distinguish authentic social media posts from nonauthentic ones, raising the need to corroborate statements of NPS effects posted online. The purpose of this study is to determine whether NPS mentioned online as having psychoactive effects are more likely to share structural features with approved therapeutics than NPS explicitly discussed to not have effects.
**Methods:** For each therapeutic approved by the Food and Drug Administration (FDA) as of 1 September 2022 and all designer drugs with reported gas chromatography-mass spectrometry (GC-MS) assays or Wikipedia entries, we acquired the canonical simplified molecular input line entry system (SMILES) structure. To group by structural similarity, we performed k-means clustering on the t-Distributed stochastic neighbor embedding (T-SNE) of each compound's Morgan fingerprint. To analyze descriptions of effects we obtained all publicly available posts from Lycaeum and Bluelight until 2020. This project is part of an ongoing effort to automatically predict NPS toxicity without laboratory data.
**Results:** We acquired the names of 2,988 FDA-approved substances, 777 NPS, 9,288 online posts from Lycaeum, and 5,597,311 posts from Bluelight. We manually curated a 1% random sample of the posts ($n = 56,066$). T-SNE identified 4 groups of structurally similar compounds, one enriched for NPS (60% of NPS, 17% of FDA substances, "Cluster 1"), two with comparable amounts of NPS and FDA-approved substances (22 versus 17% and 11 versus 17%; Clusters 2 and 3), and one mostly FDA-approved substances (7.6 versus 30%, Cluster 4). Clusters 2 and 3 had statistically significantly more NPS stated to have psychoactive effects than those stated to not have effects, a ratio of 3.1:1 ($p = 0.02$, Fisher's exact test with Bonferroni adjustment). The ratio for Cluster 1 was 1:10 and 1:52 for Cluster 4.
**Conclusion:** NPS that share structural motifs with approved compounds are more likely to be described on social media as explicitly having a psychoactive effect. The enrichment we noted for 1% of comments may not hold for the analysis of all Lycaeum and Bluelight posts, even though our sample is larger than that usually used in full studies. We did not consider complex linguistic features like negation. Approximating chemicals as linear static structures may miss informative features.

## 135. Rapid normalization of homocysteine after cessation of nitrous oxide exposure: a case series

Erik Lindeman, Ingi Abdulhameed and Johanna Nordmark Grass
Swedish Poisons Information Centre, Stockholm, Sweden

**Objective:** Oxidation of the cobalt atom in cobalamin is the only known toxic effect of nitrous oxide ($N_2O$). The reaction irreversibly destroys the functionality of the vitamin and makes it toxic to methionine synthase to which cobalamin acts as a cofactor. The toxic depletion of methionine synthase stops the "methionine cycle" that regenerates methionine from homocysteine, leading to accumulation of the latter and deficiency of the former. This is the central pathology in $N_2O$ abuse, leading to a risk of thromboembolic complications (high homocysteine) and defective myelin synthesis (low methionine). Optimal treatment should aim for rapid restoration of methionine cycle function.
**Methods:** In a protocol set up by our Poison Centre, patients with neurologic or thromboembolic complications from $N_2O$ abuse with high homocysteine concentrations on presentation were treated as follows: (1) hospital admission, ensuring abstinence from further $N_2O$ abuse (2) hydroxocobalamin injections 2 mg twice daily (3) antithrombosis prophylaxis or treatment of thromboembolic complications. Parenteral administration of cobalamin was used to rapidly increase concentrations of serum

Table 1. Homocysteine and cobalamin concentrations in patients with nitrous oxide abuse treated with a regimen of hydroxocobalamin and abstinence from further exposure.

| Hospital | Patient 1 | | Patient 2 | | Patient 3 | | Patient 4 | |
|---|---|---|---|---|---|---|---|---|
| Day | Homocysteine | Cobalamin | Homocysteine | Cobalamin | Homocysteine | Cobalamin | Homocysteine | Cobalamin |
| 1 | 129 | 160 | 128 | 180 | 128 | 130 | 257 | 130 |
| 2 | 113 | | | | 95 | | 55 | |
| 3 | 60 | | | | 79 | | 24 | >1100 |
| 4 | 24 | | 15 | 4400 | 30 | >1100 | 16 | |
| 5 | 15 | >1100 | | | 18 | | | |

Homocysteine normal value <15 µmol/L; cobalamin reference range 150–650 pmol/L.

cobalamin to "crowd out" remaining oxidated (and toxic to methionine synthase) forms of the vitamin. The goal of treatment was the normalisation of serum homocysteine indicating a return of methionine cycle function.
**Results:** A convenience sample of patients treated with this protocol is presented in Table 1.
**Conclusion:** In all patients, homocysteine concentrations fell to near the normal range within 4–5 days of treatment. Parenteral hydroxocobalamin was switched to oral dosing on homocysteine normalization or when cobalamin had become highly supratherapeutic. Sustained oral cobalamin is probably of lesser importance for this patient group as they are generally able to absorb cobalamin from a normal diet. Abstinence from all further $N_2O$ use however, is of paramount importance for recovery and should ideally be closely monitored in an outpatient setting by monitoring homocysteine concentrations, which should remain normal.

## 136. Expansion of the Dutch National Calamity Stock with infrequently used (non)-registered antidotes is a great success

Marieke A. Dijkman and Dylan W. de Lange
Dutch Poisons Information Center, Utrecht, Netherlands

**Objective:** In 2018, the Dutch National Calamity Stock of Emergency Medicines was expanded with 11 infrequently used, often sparsely available and/or very expensive (non-)registered antidotes and chelators to overcome unavailability during medical emergencies. These products are available after contact with the Dutch Poisons Information Center (DPIC) which advises on the antidote/chelator indication criteria. Here, we present an analysis of all information requests concerning antidote and chelator deliveries in four years.
**Methods:** A retrospective analysis from 1 August 2018 to 1 September 2022 of the DPIC database.
**Results:** In four years, there were 108 deliveries. In 85 deliveries the antidote/chelator was used to treat the patient. Digoxin-specific antibodies were delivered 31 times; 21 times for suspected (chronic) digoxin poisoning and ten times after ingestion of cardiac glycoside containing plant material. It was administered 15 times and all patients ($n = 15$) had digoxin poisoning. Glucarpidase was delivered 29 times and administered 26 times; 25 times for delayed methotrexate (MTX) elimination during high dose MTX therapy in 23 oncological patients (two patients were treated twice) and once in a patient on low dose MTX with signs of MTX toxicity. Silibinin for the treatment of amatoxin mushroom poisoning was delivered 28 times for 19 incidences often with multiple patients (in total 29 patients). Twenty-six patients were treated with silibinin. In severe cases, multiple deliveries were necessary. Fomepizole was delivered 10 times for 13 patients. It was administered six times for the treatment of toxic alcohol poisoning and once for severe paracetamol poisoning (survived). All seven physostigmine deliveries were administered for the treatment of (suspected) central anticholinergic syndrome; six times following anaesthesia. Hydroxocobalamin was used once to treat sodium azide poisoning (unsuccessfully). Toxogonin® (obidoxime) was delivered to continue the treatment of an organophosphate (diazinon) poisoned patient after the hospital ran out of stock. Unithiol (DMPS) was delivered to continue the treatment of two patients with mercury poisoning. There were no deliveries of succimer (DMSA), sodium calcium edetate and 4-dimethylaminopyridine (4-DMAP).
**Conclusion:** The results of this survey confirms the necessity of the expansion of the National Calamity Stock with infrequently used, often sparsely available and/or very expensive (non-) registered antidotes and chelators

## 137. A survey of antidote availability in Irish hospitals with emergency departments 2022

Conor T. Hurley, Edel Duggan and John X. Herbert
National Poisons Information Centre (NPIC), Dublin, Republic of Ireland

**Objective:** The National Poisons Information Centre (NPIC) currently recommends that Irish hospitals with Emergency Departments follow the Royal College of Emergency Medicine (RCEM)/National Poisons Information Service (NPIS) Antidote Stocking Guidelines [1]. These guidelines classify antidotes into 3 categories, Category A, B and C, which are recommended to be available immediately, within 1 hour and held supra-regionally, respectively. The survey was carried out to obtain an understanding of antidote stocking trends in hospitals with Emergency Departments (EDs) in Ireland, to acquire updated information on the locations of rarely used antidotes and understand the compliance of Irish hospitals with EDs to currently recommended antidote stocking guidelines.
**Methods:** A list of antidotes was created from a review of the 2021 RCEM/NPIS guidelines, TOXBASE® and previous NPIC Antidote Booklets; 41 agents were chosen for the audit and converted to a survey. Where applicable, the survey also contained the RCEM recommended stock level. Respondents were asked to indicate whether they held this level, less than this level or greater than this level. The survey was sent to the 30 hospitals in Ireland with EDs.
**Results:** All (100%) hospitals responded to the survey; 14 hospitals (46.7%) held all the Category A antidotes surveyed. No hospital indicated that they held andexanet alpha (Category B). There was uncertainty regarding the availability of this antidote and it was excluded from further analysis. Five hospitals (16.7%) indicated they held all of the remaining Category B antidotes surveyed. Only 4 hospitals (13.3%) held all Category A & B antidotes surveyed. Ten hospitals held some Category C antidotes with one hospital holding all 6 Category C antidotes surveyed. L-Carnitine was the least-held antidote in Category A or B with only 11 hospitals (36.7%) holding this antidote. All hospitals stocked activated charcoal, N-acetylcysteine, glucagon and protamine sulphate.
**Conclusion:** The survey has shown that there is scope to improve the stocking of antidotes in Irish hospitals. Less than half of the hospitals surveyed hold all of the antidotes required to be immediately available and even fewer hold all those required within one hour. There is also a need to improve the stocking of Category C antidotes.

### Reference

[1] Royal College of Emergency Medicine (RCEM) & National Poisons Information Service (NPIS). 2021. RCEM NPIS antidote guideline update 2021 [online] [cited 2022 October 3]. Available from: https://rcem.ac.uk/rcem-npis-antidote-guideline-update-2021/.

## 138. Carbapenems in valproate toxicity – ready for prime time?

Daniel H. P. Towie[a] and Erik Lindeman[b]

[a]Department of Internal Medicine, Skåne University Hospital, Lund, Sweden; [b]Swedish Poisons Information Centre, Stockholm, Sweden

**Objective:** In the complex process that is valproate (VPA) breakdown, valproic acid glucuronide (VPA-G), formed by glucuronidation of the parent substance, might be termed "the good metabolite". However, VPA-G is itself subjected to substantial metabolism leading to VPA (re)generation. The hydrolase that performs this unique "counter-metabolism" is inhibited by carbapenem antibiotics, the use of which could be of benefit in valproate overdoses to speed up VPA elimination and reduce formation of "bad metabolites" [1]. We present a case of VPA overdose where meropenem was used for this purpose, with determination of VPA half-life during treatment.
**Case report:** A 32-year-old woman with a history of psychiatric disorder was found unconscious at home amidst empty medicine containers (0H). She had access to valproate, promethazine and citalopram and was admitted to hospital at approximately 2H. She was rousable with otherwise stable vital signs and no measures other than observation were instigated initially. Her level of consciousness declined to Glasgow Coma Score (GCS) 3–4 and her oxygen saturation decreased. Serum VPA, measured for the first time at 21H was 464 mg/L, rising to 472 at 27H. Serum ammonium was 27 μmol/L and never rose above 30 μmol/L. The patient underwent cranial computerised tomography (CT) scan examinations of the brain (without oedema), thorax (bilateral aspiration pneumonia) and abdomen (a few undigested pills in the stomach) and the poison centre (PC) was consulted. On PC recommendation the patient was intubated for airway protection, subjected to gastric lavage, and given 50 g activated charcoal. At 28H she was also given levocarnitine (6 g IV followed by 1 g q4h), and meropenem (2 g IV q8h). Serum VPA was followed every 6 h between 35H (388 mg/L) and 59H (37 mg/L). When plotting the serum concentrations versus time, the five points of measurements from 35H onward followed a nearly perfect exponential decline with an $R^2$ of 0.9993, suggesting that the absorption phase was complete and enabling the calculation of half-life. The patient was extubated at 64H and made a complete recovery.
**Conclusion:** During treatment with meropenem the half-life of VPA was 7 h which is significantly shorter than the median population half-life for VPA in therapeutic doses. While our case does not allow us to conclude that meropenem shortened the VPA half-life in our patient or (even if it did) that it affected her outcome; our results suggest this treatment modality deserves our continued attention.

### Reference

[1] Suzuki E, Nakai D, Ikenaga H, et al. *In vivo* inhibition of acylpeptide hydrolase by carbapenem antibiotics causes the decrease of plasma concentration of valproic acid in dogs. Xenobiotica. 2016; 46:126–131.

## 139. Antidotal effect of olanzapine in serotonin toxicity caused by a suicidal 3,4-methylenedioxymethamphetamine (MDMA) overdose

Erik Lindeman[a], Linn Ottosson[b] and Anders Helander[c]

[a]Swedish Poisons Information Centre, Stockholm, Sweden; [b]Department of Anaesthesiology and Intensive Care, Skaraborg Hospital, Skövde, Sweden; [c]Department of Laboratory Medicine, Karolinska Institutet and Karolinska University Laboratory, Stockholm, Sweden

**Objective:** To present a case of MDMA intoxication with serotonin toxicity resistant to standard treatment measures, that responded promptly to administration of the $5HT_2$ receptor antagonist olanzapine [1].
**Case report:** A 22-year-old man with a history of polysubstance abuse was brought to hospital 90 min after a suicidal ingestion of seven "ecstasy" tablets, allegedly containing 300 mg MDMA each (total dose 2.1 g). He was diaphoretic and agitated with body temperature 37.8 °C. Diazepam (25 mg) had no discernible effect on the agitation and acceptable control was achieved with propofol titrated to a total dose of 270 mg at 2 h. Sedation was maintained with propofol infusion of 2 mg/kg/h in the intensive care unit (ICU). Relevant physical signs at 5.5 h were: Glasgow Coma Score (GCS) 4, pulse rate 95/min, blood pressure 170/120 mmHg and saturation 94% (with 3 L $O_2$ by nasal cannula). There was a marked stiffness of the jaw (trismus), neck and back (opisthotonus), which increased on tactile stimulation. His pupils were maximally dilated and unresponsive to light. There was pronounced hyperreflexia in the lower extremities and sustained ankle clonus (>10 beats) inducible by touching the foot. The patient's body temperature was normal at 36.9 °C. A bolus of 10 mg diazepam had no discernible relaxing effect. At 6 h, following poison centre recommendation, he was given 10 mg olanzapine by intramuscular injection. After 10 min, the trismus and opisthotonus had disappeared, ankle clonus was no longer inducible and his pupils, now less mydriatic, reacted briskly to light. During the following 30 min, the propofol infusion was tapered and stopped, his pulse and blood pressure normalized, and oxygen administration discontinued. He was discharged to psychiatric care at 36 h. A urine sample taken at 6 h was analysed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) and contained a high concentration of MDMA (40,100 μg/L; 12,936 μg/mmol creatinine) and the metabolite methylenedioxyamphetamine (MDA) (1,070 μg/L; 345 μg/mmol creatinine).
**Conclusion:** In this case of analytically confirmed MDMA intoxication, symptoms of pronounced serotonin toxicity including truncal rigidity persisted for several hours despite aggressive sedation with GABA agonists. The symptoms promptly disappeared after administration of the $5HT_2$ receptor antagonist olanzapine, suggesting potential usefulness of this substance as a specific antidote in select cases of serotonin toxicity.

### Reference

[1] Lange JHM, Reinders J-H, Tolboom JTBM, et al. Principal component analysis differentiates the receptor binding profiles of three antipsychotic drug candidates from current antipsychotic drugs. J Med Chem. 2007;50:5103–5108.

## 140. Heat stroke associated with 3,4-methylenedioxymethamphetamine (MDMA) overdose treated with olanzapine

Erik Lindeman[a], Maria Daveus[b] and Eva Backman[a]

[a]Swedish Poisons Information Centre, Stockholm, Sweden; [b]Department of Internal Medicine, Kristianstad Central Hospital, Kristianstad, Sweden

**Objective:** Severe serotonin toxicity with heat stroke can be difficult to treat with standard measures such as sedation, paralysation and active cooling. We describe a case where olanzapine, a potent antagonist at the $5HT_2$-receptor (Ki of 1.6 nmol/L) available as an immediate release intramuscular formulation, was associated with rapid resolution of symptoms [1].
**Case report:** A 20-year-old male ingested 14–20 tablets allegedly containing 200 mg MDMA (total dose 2.8–4g) that he had bought as "ecstasy" on the illegal market. He took the tablets on a self-destructive impulse he immediately regretted, calling medical services. His condition deteriorated rapidly during ambulance transport to the hospital when he became confused, diaphoretic, and a peripheral temperature of >40 °C (104 °F) was measured. He was treated with bolus doses of midazolam and cool crystalloids intravenously. On arrival at the hospital, he had Glasgow Coma Score (GCS) 3, pulse 185 beats/min, blood pressure 135/50 mmHg and cold extremities. He had mydriatic pupils, a pronounced stiffness of jaw and legs and generalized muscle tremors. His core temperature was 41.7 °C (107.1 °F). The Poison Centre was contacted via telephone and recommended immediate sedation with propofol, intubation and muscle paralysation (rocuronium), and the administration of olanzapine 10 mg by intramuscular injection as an adjuvant to standard treatment. After intubation, cold gastric lavage was performed, yielding multiple brightly coloured pill fragments. A standard dose of charcoal was administered. Within 10 minutes, his core temperature and pulse rate had dropped to 39.5 °C (103.1 °F) and 120 beats/min respectively. A cooling suit was applied but was never activated because the temperature had normalized (37 °C, 98.6 °F) one hour after arrival at the hospital. His creatine kinase, myoglobin and aminotransferases were minimally elevated, and he was extubated after 12 hours, showing no residual signs of serotonin toxicity (no tremors, hyperreflexia, clonus or rigidity). He remained hospitalized another two days and was treated with antibiotics for a ventilator associated pneumonia.
**Conclusion:** Our case is limited by a lack of confirmatory blood drug concentrations, but case history and symptom development suggest rapidly developing severe serotonin toxicity. There was a remarkably rapid resolution of the symptoms after treatment, and we believe that the administration of the $5HT_2$-antagonist olanzapine played a decisive role in the favourable outcome.

### Reference

[1] Lange JHM, Reinders J-H, Tolboom JTBM, et al. Principal component analysis differentiates the receptor binding profiles of three antipsychotic drug candidates from current antipsychotic drugs. J Med Chem. 2007;50:5103–5108.

## 141. First report of successful treatment of severe serotonin toxicity with levomepromazine

Brenda H. van Koningsveld-Couperus[a], Fellery de Lange[a] and Carina Bethlehem[b]

[a]Department of Intensive Care Medicine, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [b]Department of Intensive Care Medicine and Department of Clinical Pharmacy and Pharmacology, Medical Centre Leeuwarden, Leeuwarden, Netherlands

**Objective:** We present a patient with severe serotonin toxicity who was successful treated with levomepromazine.
**Case report:** A 28-year-old woman was admitted to hospital with serotonin toxicity 4 hours after ingestion of 300 mg tranylcypromine. Initial management with intravenous benzodiazepines, fluid boluses and activated charcoal was not successful and she deteriorated with progressive hyperthermia (41 °C), tachycardia, tachypnea, mydriasis, diaphoresis and nausea. She was subsequently sedated and intubated, and a non-invasive targeted temperature management system was applied. She was paralyzed with a nondepolarizing agent, because of persisting severe neuromuscular hyperreactivity despite high doses of benzodiazepines and propofol. After 36 hours of supportive therapy it was impossible to wean her from neuromuscular blocking agents (NMBA). It was anticipated that her symptoms would persist for at least several days because of the irreversible long-lasting inhibition of monoamine oxidase by tranylcypromine. Prolonged treatment with NMBA cannot only mask seizures but can also lead to intensive care unit (ICU)-acquired weakness. Since the advised antidote cyproheptadine is not available in the Netherlands we searched for an alternative option. Based on case reports chlorpromazine was considered, but this medicine was only available for rectal administration. We then decided to start a similar agent, levomepromazine, because it can be administered intravenously and there is experience with it in our ICU. Like chlorpromazine, levomepromazine is a phenothiazine and it might have a greater affinity for serotonin binding sites in the brain than chlorpromazine [1]. Directly after the first bolus injection of 50 mg there was a clear recovery of her tremors and after initiation of a continuous infusion of 6 mg/hour, therapy with benzodiazepines and propofol could be gradually withdrawn. The next day she was extubated and after cessation of levomepromazine she was discharged home with ambulant care one day later.
**Conclusion:** This is the first report of successful treatment of a patient with severe serotonin toxicity with levomepromazine. Since it can be administered intravenously and ICU physicians are familiar with its use, levomepromazine can be an attractive option to treat patients with severe serotonin toxicity if cyproheptadine is not available.

### Reference

[1] Lal S, Nair NP, Cecyre D, et al. Levomepromazine receptor binding profile in human brain – implications for treatment-resistant schizophrenia. Acta Psychiatr Scand. 1993;87:380–383.

## 142. Primaquine-induced methemoglobinemia treated with N-acetylcysteine: a case report

Lorenzo Losso[a], Francesco Gambassi[b], Brunella Occupati[b], Alessandra Pistelli[b], Andrea Missanelli[b], Cecilia Lanzi[b], Arianna Totti[b], Guido Mannaioni[a] and Alessandra Ieri[b]

[a]Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, University of Florence, Florence, Italy; [b]Medical Toxicology Unit and Poison Control Centre, Careggi University Hospital, Florence, Italy

**Objective:** Primaquine-induced methemoglobinemia is a pathological condition typically characterized by mild-moderate symptoms driven by an increase in methaemoglobin (MetHb) levels (normal value <1%), which can lead to primaquine discontinuation, with major consequences for the management of the underlying disease [1]. Primaquine increases MetHb levels through a pro-oxidant environment promoted by its metabolites [2]. To this aim, we tested the hypothesis that N-acetylcysteine (NAC), by acting as a reducing agent [3,4], would be safe and effective in the treatment of primaquine-induced methemoglobinemia not requiring methylene blue treatment.
**Case report:** We report a 41-year-old woman affected by multiple sclerosis, on treatment with immune-modulatory therapy, who was hospitalized for the management of *Pneumocystis jirovecii* pneumonia (PJP) treated with primaquine 30 mg/day and clindamycin 1800 mg/day. At the time of admission MetHb was <1% and after nine days of treatment, a mild increase in MetHb was observed (9%). After ruling out other causes, including glucose-6-phosphate dehydrogenase (G6PD) deficiency, this increase was ascribed to primaquine. NAC-based antioxidant therapy was introduced at the dose of 3600 mg/day (per os) in order to allow second-line primaquine treatment for PJP. MetHb levels gradually decreased until the physiological range. Given primaquine and its metabolites half-life, NAC therapy lasted one week longer than the duration of primaquine therapy (total 19 days). No adverse drug reactions to NAC therapy were reported.
**Conclusion:** NAC-based antioxidant therapy was safe and effective in this patient for the treatment of primaquine-induced methemoglobinemia.

### References

[1] Kantor GS. Primaquine-induced methemoglobinemia during treatment of *Pneumocystis carinii* pneumonia. N Engl J Med. 1992;327:1461.
[2] Morais M da S, Augusto O. Peroxidation of the antimalarial drug primaquine: characterization of a benzidine-like metabolite with methaemoglobin-forming activity. Xenobiotica. 1993;23:133–139.
[3] Wright RO, Magnani B, Shannon MW, et al. N-acetylcysteine reduces methemoglobin *in vitro*. Ann Emerg Med. 1996;28:499–503.
[4] Ezeriņa D, Takano Y, Hanaoka K, et al. N-Acetyl cysteine functions as a fast-acting antioxidant by triggering intracellular h2s and sulfane sulfur production. Cell Chem Biol. 2018;25:447–459.

## 143. Retrospective evaluation of the effect of oral acetylcysteine on INR in the setting of acetaminophen overdose

Varun Vohra[a], Alisar Aljundi[b], Hala Tokko[b], Ryan Herc[b], Jewel Konja[b], Ali Khanafer[b], Samantha Bauer[c] and Victoria Tutag-Lehr[b]

[a]Michigan Poison & Drug Information Center, Wayne State University School of Medicine, Detroit, MI, USA; [b]Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA; [c]Biostatistics, Epidemiology, and Statistical Design (BERD), Wayne State University, Detroit, MI, USA

**Objective:** Acetaminophen is a widely used analgesic. N-acetylcysteine (NAC) is given in acetaminophen overdose to prevent or mitigate hepatocellular injury. The INR (International Normalized Ratio) is a clinical prognostic indicator used to monitor response to NAC and inform discontinuation of treatment. Reports indicate transient INR increases associated with IV NAC administration, possibly related to the interference of sulfhydryl groups on coagulation factors [1]. The clinical significance remains unclear, however, elevated surrogate markers, like INR, can be misinterpreted as persistent hepatic dysfunction leading to protracted and unwarranted NAC administration. A paucity of evidence exists regarding oral NAC administration and INR changes. We retrospectively evaluated the effect of oral NAC administration on INR in cases of single substance acetaminophen overdose reported to our state poison center.
**Methods:** The Institutional Review Board approved this retrospective case review from our state poison center database of single-entity acetaminophen overdose between 1 January 2016 and 31 December 2016.
**Case inclusion:** Age 1–89 years; documentation of one acetaminophen serum concentration, two or more INR values, and at least one alanine aminotransferase (ALT)/aspartate aminotransferase (AST) within reference range prior to NAC administration.
**Excluded cases:** Pre-existing coagulopathies, hepatic failure/transplant; concomitant use of agents affecting INR, including non-steroidal anti-inflammatory drugs, salicylates, select vitamins, supplements; chronic alcohol use; IV NAC therapy. Data collected included demographics, oral NAC dosage, acetaminophen, INR, AST/ALT, co-morbidities, hospital duration, and medical outcome. Summary statistics described sample characteristics and lab results by blood draw. Generalized linear mixed models with random effects estimated association between oral NAC and INR.
**Results:** There were 96 evaluable cases, median age 19 years (interquartile range [IQR] 16, 32), 72% female, 27% minor, and 46% moderate medical outcomes. Age was the only covariate with a significant association with INR ($\beta = -0.01$; CI $-0.01$, $-0.00$). Adjusted models suggested no association between INR and oral NAC maintenance dose. Associations between INR and NAC do not vary by time. *Post hoc* analyses showed no significant change in INR associated with oral NAC administration.
**Conclusion:** This retrospective evaluation demonstrated no causal inference of oral NAC administration on INR in acetaminophen overdose. The *in vivo* effects of oral NAC administration on INR remain undetermined, warranting a controlled prospective clinical trial including a comparator group, timed INR sampling, and investigation of a potential dose-response effect of oral NAC on INR.

## Reference

[1] Whyte IM, Buckley NA, Reith DM, et al. Acetaminophen causes an increased international normalized ratio by reducing functional factor VII. Ther Drug Monit. 2000;22:742–48.


## 144. High-dose vitamin D supplements – a high risk?


Chantal C. J. Roelen, Antoinette J. H. P. van Riel, Pauline M. Verputten and Dylan W. de Lange

University Medical Center Utrecht, Utrecht, Netherlands



**Objective:** To describe the number and user characteristics of (potential) poisonings with high-dose vitamin D supplements reported to the Dutch Poisons Information Center (DPIC).
**Methods:** A retrospective study of enquiries 2019–2021 on high-dose vitamin D exposures from over-the-counter preparations. Data on patient age, exposure (dosage, acute/chronic), and treatment advice, were extracted from the database and analyzed. Vitamin D supplements were categorized as high dose when they contained ≥25 micrograms (1000 IU)/tablet or ≥10 micrograms (400 IE)/droplet, according to the label.
**Case series:** A total of 245 exposures to high-dose vitamin D supplements were reported. In these 3 years, there was an increase (241%) in exposures with 39, 73 and 133 in 2019, 2020 and 2021, respectively. The mean age was 3 years (IQR 25–75%: 3–4) with only 16 persons ≥18 years. Most cases (80%) involved young children, age 0–4 years, who accidentally ingested an overdose. In the Netherlands, only supplements with a maximum of 75 micrograms (3000 IU) per day are legally allowed [1]. In our study, 10 reported products contained dosages higher than allowed, with one product containing 2500 mcg (100,000 IU) of vitamin D per dose. In 24 cases, the (estimated) vitamin D dose was potentially toxic, causing risk of hypercalcemia. In all these cases, the DPIC advised monitoring of blood calcium concentrations (results unknown to the DPIC). These possible poisonings included 22 children <4 years. Nineteen had ingested one large dose (tablets or liquid), while 3 received chronic high-dose vitamin D supplements due to a medication error by caregivers. The 2 cases involving adults were medication errors in which the supplements were taken daily instead of the recommended weekly or monthly use.
**Conclusion:** The number of exposures to high-dose vitamin D supplements reported to the DPIC has increased in 3 years. In 10% of cases, a possibly toxic amount had been ingested. Due to the higher concentration per tablet, capsule or droplet, children are more at risk of acute intoxication when they get hold of these supplements. Medication errors can lead to chronic intoxication when high-dosed supplements are taken daily instead of weekly/monthly. These chronic poisonings can go unnoticed due to the non-specific symptoms of hypercalcemia.



## Reference

[1] Government Gazette of the Kingdom of the Netherlands. Regulation of the Minister of Health, Welfare and Sport of 12 November 2015, 854424-143049-VGP, amending the commodities act regulation exemption vitamin preparations in connection with vitamin A and D. Government Gazette of the Kingdom of the Netherlands [cited 2022 October 6]. Available from: https://zoek.officielebekendmakingen.nl/stcrt-2015-40994.html.


## 145. Nirmatrelvir and ritonavir exposure and information cases reported to a single statewide United States poison center


Erin E. Ryan, Ladonna A. Gaines and Ann P. Slattery

Alabama Poison Information Center, Children's of Alabama, Birmingham, AL, USA



**Objective:** To evaluate and review the types of cases received by a state poison center regarding the emergency authorization combination use of nirmatrelvir and ritonavir, which is an oral antiretroviral combination used to treat mild or moderate COVID-19 symptoms.
**Methods:** A query was written to pull antiretroviral exposures and information cases handled between 1 January and 30 September 2022 using National Poison Data System (NPDS) antiretroviral generic code 201076 (excluded non-nirmatrelvir/ritonavir cases) and the viral illness generic code 310027 (excluded non-COVID-19 viral illnesses) from our electronic medical records, capturing age and gender of patient, reason for exposure, scenario, clinical effects, and medical outcome. For information cases, only nirmatrelvir/ritonavir and question reason were pulled.
**Results:** The poison center received 21 cases regarding nirmatrelvir/ritonavir during the study period. This included seven information cases, the majority of which ($n = 5$) concerned drug interactions. One caller requested information about therapeutic use and another inquired about potential adverse effects. Exposures to nirmatrelvir/ritonavir were reported in 14 patients (8 female, 6 male) with a mean age of 61.5 years (range 38–89 years). Three exposures were reports of adverse reactions with therapeutic dosing of the drug. One patient reported nausea and headache with the medication; the second patient reported feeling dizzy and weak; the third reported hoarseness. The majority of exposure cases were due to therapeutic errors ($n = 11$), with specific scenarios including inadvertently taking the medication twice ($n = 4$), doses taken too close together ($n = 2$), other incorrect dose ($n = 1$), and other/unknown therapeutic error ($n = 4$). Of the therapeutic errors reported, patients were followed to a known outcome in 8/11 cases. The majority of these patients (5/8) remained asymptomatic. Two patients developed minor effects – headache and nausea after doses were given too close together in a 60-year-old female and dizziness and other unspecified mild symptoms in a 67-year-old female after an unintentional double dose. Moderate effects occurred in a single patient: an 89-year-old female developed rhabdomyolysis and an elevated CK-MB after an unknown dosing error. No major effects were observed.
**Conclusion:** The poison center assisted in patient education and management regarding interactions, adverse effects, and therapeutic misadventures with the introduction of nirmatrelvir/ritonavir as a therapy for COVID-19. Exposure cases related to the drug were due to therapeutic errors or adverse effects and resulted in varied symptoms and largely mild outcomes.


## 146. Wintergreen oil toxicity reported to the UK National Poisons Information Service (NPIS)


Emma Moyns[a], Hayley A. Williams[a], Euan A. Sandilands[b], Laurence A. Gray[c], Ruben H. K. Thanacoody[d] and Sally M. Bradberry[a]

[a]National Poisons Information Service, Birmingham, United Kingdom; [b]National Poisons Information Service, Edinburgh, United Kingdom; [c]National Poisons Information Service, Cardiff, United Kingdom; [d]National Poisons Information Service, Newcastle, United Kingdom

**Objective:** Oil of wintergreen is a volatile oil produced by several plant species and contains 98% methyl salicylate; 1 mL is equivalent to 1.4 g of acetylsalicylic acid. It has been used as a pesticide, flavouring agent and fragrance ingredient. It is also used for topical analgesia and as a rubefacient for muscular and rheumatic pain. We describe cases of wintergreen oil exposure requiring hospitalisation reported to the UK NPIS between 2004 and 2022.
**Case series:** Case 1. A 29-year-old female presented 1 hour after intentionally ingesting 60 mL of wintergreen oil with alcohol. The NPIS was contacted at 8 hours post-ingestion when the patient had been in cardiac arrest for 30 minutes. She had received 300 mL of 8.4% sodium bicarbonate, insulin and dextrose for hyperkalaemia (7.8 mmol/L) and 4 L of intravenous crystalloid. Resuscitation was unsuccessful and discontinued after 45 minutes. Salicylate concentration measured 4-hours post ingestion was 1196 mg/L. Case 2. A 25-year-old male intentionally ingested 15 mL of wintergreen oil over a 2 hour period with alcohol. The salicylate concentration at 2.5 hours post-ingestion was 639 mg/L and the patient was commenced on urinary alkalinisation (1200 mL 1.26% intravenous sodium bicarbonate) upon discussion with the NPIS. The patient was discharged the following day with no sequelae. He re-presented 5 days later after ingestion of a further 100 mL. Salicylate concentration peaked at 1150 mg/dL at 6.5 hours post-ingestion. He was successfully treated with urinary alkalinisation (2 L of 1.26% and 600 mL 8.4% intravenous sodium bicarbonate) and 24 hours of haemodialysis. NPIS experience: Between 2004 and 2022, the NPIS received 17 enquiries involving wintergreen oil, 6 of which originated from hospitals. Four enquiries involved intentional ingestion, two of which are described above. In the two remaining ingestion enquiries, one patient had ingested 35 mL with a salicylate concentration of 629 mg/L at an unknown time post-ingestion. The second patient ingested an unknown volume and had a salicylate concentration of 661 mg/L at 6 hours. Outcomes were unknown in both cases. Of the remaining two enquiries originating from hospital, one involved accidental skin and eye contact in a 1-year-old child and the other involved intentional injection of 5 mL into an unknown body site. No further details were available.
**Conclusion:** Poisoning following wintergreen oil ingestion is rare, but can result in severe, sometimes fatal salicylate poisoning. Early discussion with a poisons centre is recommended.

## 147. Substantial room for improvement in handling medicines in Danish residential institutions

Karen R. Eriksen and Nete B. Hansen

Department of Anaesthesia and Intensive Care Medicine, Danish Poison Information Center, Bispebjerg- and Frederiksberg University Hospital of Copenhagen, Copenhagen, Denmark

**Objective:** The exact number of medication errors in the primary sector is unknown. The Danish Society for Patient Safety reported 22,000 medication errors in 2019 at residential homes. Nursing homes were not included. The current estimated daily cost of hospitalization per patient according to The Danish Health Data Authority is DKK 11,534–26,047 (1,538–3,538 Euros). Ongoing education from the Danish Society for Patient Safety and the Ministry of Health and National Association of Municipalities and focussing on medication errors in the primary sector are insufficient as medication errors persist. Medication errors imposes a resource and financial burden on the healthcare system, and furthermore hospitalization may be considered a serious consequence for the already vulnerable citizen. We investigated how to prevent future medication errors in Danish residential institutions.
**Methods:** A Danish Poison Information Center (DPIC) quality project (2018–2019) on medication errors in nursing homes and other residential institutions with 24/7 staff attendance included 295 reports. DPIC provided risk assessment leading to either observation at home or hospitalization and the staff was given specific advice about symptoms and observation. Data about how the medication error occurred were collected.
**Results:** The medication errors were often complex with multidrug exposures. Wrong patient identification and exchanged medicine was involved in 48% of the cases. Most exposures involved neuroleptics. Hospital admission was recommended in one of six patients. Types of other medication errors included: Double dose for 7 days, lack of documentation that lead to double doses, citizens with same first name had their medicine exchanged, ten times double dose administered and administration of medicine provided by an unskilled employee.
**Conclusion:** The study points to substantial room for improvement in medication administration in Danish residential institutions. To reduce the number of medication errors and increase patient safety, it is necessary to implement work procedures for staff. E-learning as a learning tool has a low cost and provides the possibility of organizing flexible learning and is usable to create learning and change of habits in the individual workplaces and may secure a procedure when medication error occurs. E-learning reaches large numbers of employees in different workplaces and learning material is easy to keep updated and valid. It accommodates varying didactic needs in terms of material presentation like images, video, text and audio. It should include case-based assignment from practice on how to identify the right person, medication calculation and administration, the procedure regarding correct documentation and a multiple-choice exercise. The E-learning program must be mandatory once a year.

## 148. Collaboration between a poisons information centre and a national authority to protect consumer safety

Patricia Casey[a], Edel Duggan[a] and Sinead McMickan[b]

[a]National Poisons Information Centre of Ireland, Dublin, Republic of Ireland; [b]Health and Safety Authority, Athlone, Republic of Ireland

**Objective:** In June 2021 the National Poisons Information Centre (NPIC) of Ireland alerted the Health and Safety Authority (HSA) to an increasing number of children exposed to reed diffuser (fragrance sticks) products and to a lack of information on the final packaging of these products. The HSA is the national competent authority for the REACH and CLP regulations. The Authority subsequently conducted a targeted enforcement campaign inspecting reed diffuser products and refills sold to the general public, to check compliance with the chemicals legislation [1]. This abstract describes the demographics of the cases reported to the NPIC and the outcome of the HSA enforcement campaign.
**Methods:** We identified retrospectively all enquiries to the NPIC about human cases of exposure to reed diffuser products received between 1 January 2020 and 31 December 2021 inclusive. We extracted data on the patient's age, routes of exposure

and Poisoning Severity Score (PSS) at the time of the call. The HSA inspections were undertaken between November 2021 and March 2022.
**Results:** The NPIC answered 243 calls about 204 patients exposed to reed diffuser products in 2020–2021. In total 198 patients were children aged 0–6 years (97%); 180 patients ingested or were exposed to the reed diffuser liquid. Of these, 127 (71%) had no symptoms, 50 (28%) had minor features and 2 (1%) had moderate features of poisoning. No patients required follow up. Information on the brand name of the reed diffuser or on its chemical constituents was recorded by NPIC staff in 121 calls (50%). The HSA inspected 20 companies and 71 products; 87% of products were not compliant with the requirements of the REACH and CLP Regulations. In addition, 44% of products either had no hazard label or incorrect hazard labels and 48% of products did not display a hazard label on all layers of packaging as required. For 46% of the non-compliant products, inspectors instructed their removal from the market due to incorrect or missing hazard labelling.
**Conclusion:** Collaboration between the NPIC and the HSA identified significant non-compliance with the chemicals legislation and led to the removal of a number of reed diffuser products from the market. The enforcement action taken will help ensure that reed diffuser products can be identified accurately if a poisoning incident occurs, enabling NPIC staff to provide specific management advice.

## Reference

[1] Health and Safety Authority (HSA). Findings of the inspection campaign of hazardous reed diffusers for sale on the Irish market. HSA Newsletter; June 2022 [cited 2022 Aug 1]. Available from https://hsa.newsweaver.co.uk/newsletter/1diflbzgnm2-umbr0d2y35?email=true&lang=en&a=2&p=61827076&t=24949965.

# 149. Repeated poisonings in Denmark: a nationwide study

Thomas Leth Jensen[a], Kim P. Dalhoff[b], Mathilde Tejlbo Frost[b] and Tonny Studsgaard Petersen[b]

[a]Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark; [b]Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark

**Objective:** Accidental and intentional poisonings contribute significantly to morbidity and mortality of patients. Some patients have numerous contacts to a poison information center (PIC) over time, indicating repeated poison exposures. This patient population is of particular concern. Information of the involved poisoning substances are lacking, but necessary, to explore methods to prevent self-harm and reduce mortality. The objective of this study was to characterize the patient population with repeated poison exposures (defined as >5 contacts to a PIC within 12 months) in Denmark regarding gender, age, type of exposure, risk classification, cause (accident, suicide attempt etc.), psychiatric comorbidity, and death, and to identify the substances involved in the poisoning episodes.
**Methods:** This study was a retrospective cohort study of enquiries to the nationwide Danish Poison and Information Centre (DPIC) and the Danish National Patient Registry (DNPR). The databases were used to identify patients with >5 contacts (i.e., individual poisoning episodes) within a 12-month-period over a 5-year study period (1 January 2013 to 31 December 2017). When data from the DPIC registry and the nationwide DNPR were merged, we were able to analyze patient outcomes, diagnoses, hospital admissions and deaths dating back to 1980.
**Results:** We identified 137 patients (with a combined 1752 episodes) meeting the inclusion criteria in the DPIC. The majority were women (82.5%). The mean age at the time of the first contact to the DPIC was 28 years (median 25 years). Psychiatric comorbidities were frequent with 74.5% suffering from personality disorder and 70.1% from affective disorders. In total 1752 poisonings were identified, and the most common types of substance were pharmaceuticals (1,420 episodes) followed by "other" (290), recreational substances (79) and alcohol (64). The most common medical drugs ingested were quetiapine, paracetamol and cyclizine. Median number of contacts to the DPIC was 10, and most contacts to the DPIC for a single patient was 49. Patients with at least one poisoning episode involving cyclizine had on average 11.4 poisoning episodes involving cyclizine, while no such pattern was shown with other drugs. In total 80.9% of patients were alive after 10 years compared to 97.7% in the background population.
**Conclusion:** Most poisonings were intentional and occurred among younger women. Psychiatric comorbidity was frequent. Most often, pharmaceuticals were used as the toxic substance, mainly quetiapine, paracetamol and cyclizine. Changing the status of cyclizine from over-the-counter medication to prescription only medication, as well as implementing more strict rules for the prescription of quetiapine, could limit future poisoning incidences.

# 150. A review of general information requests to the Finnish Poison Information Centre (FPIC)

Terhi Lampinen

Department of Emergency Medicine and Services, Poison Information Centre, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

**Objective:** General information requests are not related to poisoning and they are redirected by FPIC to another specialist. The aim of this study is to review these wrongly targeted requests.
**Methods:** Telephone calls between 2012 and September 2022 related to general information requests were retrospectively retrieved from the FPIC database and analyzed.
**Results:** During the study period, the FPIC received 53,118 general information requests (13.4% of all received calls). Annually, the percentage of these calls ranged between 12.5 and 13.9% of all received calls. The main subcategories were pharmaceutical counselling 38.7% ($n = 20{,}564$), healthcare advice 20.7% ($n = 10{,}984$), animal exposures 16.9% ($n = 8968$), food-related 10.8% ($n = 5737$), pregnancy and lactation 4.5% ($n = 2407$), miscellaneous substances 4.4% ($n = 2324$), contact details of other operators 2.0% ($n = 1088$) and unknown substance/circumstance 2.0% ($n = 1046$). Only slight variations of the annual numbers of most subcategories were observed. In recent years, enquiries concerning animal exposures have decreased 26% over the decade. Instead, especially in the last few months the healthcare advice requests have increased. Healthcare advice requests have also occurred in busy times, between June-August and during evening hours.
**Conclusion:** Although, the Internet had probably directed a good portion of general information requests to the right specialist, the total number of these enquiries has remained the same in recent years. The fear is that the number of healthcare advice requests may continue to increase in the future. Emergency services in Finland are severely congested because of the shortage of healthcare personnel and callers cannot get through to the primary specialist. Some of these requests may

be directed to FPIC. FPIC should continue its work on traditional and social media to increase visibility and awareness of its role. This could help the public to choose the right specialist at once. We will never be able to prevent all the general information requests, but it would be helpful if callers could avoiding inappropriate contacts with the Poison Centre allowing the Poison Centre to focus on its essential task.

## 151. Ethnic diversity of patients discussed with the UK National Poisons Information Service (Birmingham Unit): a short-term pilot study

Pardeep S. Jagpal, Hayley A. Williams and Sally M. Bradberry

National Poisons Information Service, Birmingham, United Kingdom

**Objective:** In 2021, 14% of the UK population was from an ethnic minority background of which Asian/Asian British (6.9%) and Black/Caribbean/African/Black British were most common (3.4%) [1]. We undertook a short-term pilot study of enquiries to the NPIS Birmingham Unit to better understand the demographics of poisoning by ethnicity.
**Methods:** Ethnicity data was explicitly requested during all calls received by NPIS Birmingham between 18 July and 7 August 2022. Ethnicity was recorded as either "White", "Asian", "Black", "Mixed" or "Other.
**Results:** During the study period, the Birmingham Unit manned the NPIS telephone line for 168 hours handling 616 patient related enquiries. Ethnicity was recorded for 360 patients (252 adults; 102 children <18 years; age unknown in 6) and the demographics were closely aligned to that of the UK population ("White" $n = 296$, 82%; "Asian" $n = 27$, 7.5% and "Black" $n = 16$, 4.4%). Eight patients (2%) were recorded as having "Mixed" ethnicity and 13 patients (3.6%) were recorded as being of "Other" ethnicity. Female patients outnumbered males in all ethnic groups other than those considered of "Mixed" ethnicity (ratio 3:1). Accidental, medical or therapeutic error was the most common circumstance for all ethnicities. Intentional deliberate self-harm was more prevalent (32%) in the "White" population than in other ethnic groups (range 15–25%). The nature of exposure differed between ethnic groups. In patients of "White" and "Black" ethnicity, single pharmaceutical exposure was most common, accounting for 39 and 50%, respectively, while in those of "Asian" and "Other" ethnicity, non-pharmaceutical exposure was most common, accounting for 56 and 62%, respectively. There was a higher prevalence ($n = 4$, 25%) of moderate or severe poisoning [2] in those of "Black" ethnicity compared to the other ethnic groups (range 0–13%). Two cases involved a single pharmaceutical exposure, one case of polypharmacy overdose and the circumstance of exposure was unknown in the remaining case.
**Conclusion:** The sample size in this study is too small for any meaningful conclusions to be drawn. However, the data demonstrate that poison centres are uniquely placed to prospectively capture ethnodemographic epidemiological data for cases of poisoning. Understanding differences in patterns of poisoning by ethnicity may support public health officials in tailoring public health messaging.

### References

[1] Uberoi E, Tunnicliffe R. Ethnic diversity in politics and public life. House of Commons Library. Number 01156; 2021 November 15 [cited 2022 Oct 10]. Available from: https://researchbriefings.files.parliament.uk/documents/SN01156/SN01156.pdf.
[2] Persson HE, Sjoberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol. 1998;36: 205–213.

## 152. Potentially inappropriate medication in the elderly: data from a poison centre

Uwe Stedtler[a], Undine Burmeister[b], Johannes Nadler[a] and Maren Hermanns-Clausen[a]

[a]Department of General Pediatrics, Adolescent Medicine and Neonatology, Center for Pediatrics, Poisons Information Center, Medical Center – University of Freiburg, Freiburg, Germany; [b]Universitätsinstitut für Medizinische Mikrobiologie und Virologie, Universitätsmedizin, Oldenburg, Germany

**Objective:** A list of potentially inappropriate medications (PIM) for the elderly, the German PRISCUS list, was published in 2010 as expert recommendations with the aim of improving drug safety for this patient group [1]. In this study, we analysed PIM-exposures in the elderly reported to a German PCC before and after publication of the PRISCUS list.
**Methods:** Human exposure data collected by a German PC between 2006 and 2010 (before publication of the PRISCUS list, period A and between 2016 and 2020 (≥5 years after publication, period B were retrospectively analysed. Only elderly patients (≥65 years old) exposed to medication drugs were included. The number of cases of moderate and major poisonings per 100 exposures (MMP) was determined for PIMs and other medication drugs from the exposure. Statistical analyses included $\chi 2$ analysis.
**Results:** Overall, 5894 patients in the age of 65–101 (median 76) years were included (period A: $n = 2015$, period B: $n = 3879$). Monointoxications accounted for 3911 (66.4%) cases, 2 or 3 drugs for 969 (16.4%) and 451 (7.7%) cases, respectively. The intake of at least 1 PIM was reported in 2086 cases. The proportion of PIM-exposures declined from 40.5% ($n = 816$) in period A to 32.7% ($n = 1270$) in period B ($p < 0.01$). In total 34.6% of PIM-cases (723) showed MMP, but only 22.3% of non-PIM cases ($n = 849$). Unintentional exposures dominated ($n = 3301$); exposures were intentional in 2396 cases, and the cause of exposure was unknown in 197 cases. Overall, 661 PIM-exposures were noted as unintentional exposures. Of these 26.5% ($n = 175$) were classified as MMP. MMP of exposures to other drugs was 16.4% ($n = 434$). PIMs were reported in 1338 intentional poisonings, and of these 38.3% were MMPs (513). Also, 35.4% MMPs (375) were identified in 1058 intentional non-PIM-cases.
**Conclusion:** The relative frequency of PIM intake decreased in the second period. This is in line with the observation that PIM prescriptions have been declining in Germany over the past 10 years. In 2009, the elderly received at least 1 drug from the PRISCUS-list in 25% of all prescriptions, in 2019 in 16% [2]. The intake of PIMs was associated with a higher proportion of MMP than the intake of other medication drugs. The majority of PIM-exposures were noted in cases of intentional poisoning.

## References

[1] Holt S, Schmiedl S, Thürmann PA. Potentially inappropriate medications in the elderly: the PRISCUS list. Dtsch Arztebl Int. 2010; 107:543–551.

[2] Central Institute for Statutory Health Insurance Physician Care. PRISCUS list increasingly taken into account [cited 2022 Oct 15]. Available from: https://www.zi.de/presse/archiv/grafik-des-monats/2021(German).


# 153. A 10-year retrospective analysis of therapeutic errors involving prednisolone reported to the UK's National Poisons Information Service


Talan A. Parnell[a], Sally M. Bradberry[b], Euan A. Sandilands[c], Ruben H. K. Thanacoody[d] and Laurence A. Gray[a]

[a]National Poisons Information Service, Cardiff, United Kingdom; [b]National Poisons Information Service, Birmingham, United Kingdom; [c]National Poisons Information Service, Edinburgh, United Kingdom; [d]National Poisons Information Service, Newcastle, United Kingdom



**Objective:** Oral prednisolone therapy is indicated for use in UK patients for a number of conditions [1]. Recipients commonly require additional pharmacotherapy for significant comorbidities. Prednisolone 5 mg tablets are the commonest formulation due to low adjusted mg/£ cost and prescription flexibility, prescribed at dosages between 10 and 60 mg (2–12 tablets) for therapeutic effect. We retrospectively reviewed enquiry data to determine the risk of toxicity in therapeutic errors where multiple tablets of prednisolone were intended and a separate medication was taken.

**Methods:** The NPIS' poisons information database was queried for 10 years (2012–2021) of enquiries recorded as therapeutic errors, with keywords "steroid" or "prednisolone" entered into either the "medical history" or "comments" fields. In total, 1413 enquiries were received; entries that did not conclusively involve a prednisolone error as described were excluded, resulting in 603 enquiries for analysis.

Table 1. Commonest medications ($n \geq 10$) taken in error, number of enquiries where 6 or 8 tablets were ingested, number of enquiries where further medical treatment or assessment was advised.

| Agent | Count | 6 or 8 Tablets | Treatment |
|---|---|---|---|
| Doxycycline | 56 | 50 | 5 |
| Codeine | 43 | 36 | 24 |
| Thyroxine | 32 | 23 | 3 |
| Bendroflumethiazide | 30 | 24 | 10 |
| Cetirizine | 29 | 27 | 5 |
| Citalopram | 27 | 25 | 11 |
| Prochlorperazine | 24 | 21 | 10 |
| Furosemide | 23 | 17 | 22 |
| Chlorphenamine | 19 | 18 | 4 |
| Amlodipine | 18 | 13 | 15 |
| Digoxin | 16 | 10 | 16 |
| Loratadine | 15 | 15 | 1 |
| Zopiclone | 14 | 11 | 6 |
| Colchicine | 13 | 9 | 13 |
| Indapamide | 11 | 9 | 2 |
| Amoxicillin | 11 | 10 | 0 |
| Amitriptyline | 10 | 7 | 5 |
| Cyclizine | 10 | 6 | 8 |

**Results:** In most cases, 6 ($n = 312$) or 8 ($n = 155$) tablets of a separate pharmacotherapy were ingested. Table 1 illustrates the commonest medications taken erroneously, the frequency of either 6 or 8 tablets ingested and how many patients were advised to obtain further medical treatment or assessment. The majority of exposures occurred in the community ($n = 591$) with some patients being referred to hospital ($n = 173$, 28%) or their General Practitioner (GP) ($n = 40$, 6%) for management. The median age of patients was 68 years with nearly twice as many females ($n = 395$, 66%) as males ($n = 208$, 34%). Most patients were asymptomatic ($n = 463$, 76%) but some exhibited minor symptoms ($n = 125$, 20%). Fourteen enquiries of mixed severity were referred for further discussion with an NPIS toxicologist.

**Conclusion:** Prednisolone errors can result in vulnerable patients with comorbidities taking clinically significant overdoses of a separate pharmacotherapy. As a retrospective analysis of enquiry data, we expect these results to be an under-representation of the true quantity of prednisolone errors.



## Reference

[1] British National Formulary (BNF). Online [cited 2022 Sep 13]. Available from: https://bnf.nice.org.uk/drugs/prednisolone/.


# 154. Retrospective study of serotonin syndrome enquiries to UK National Poisons Information Service in 2021


Arran McKinty[a], Sally M. Bradberry[b], Euan A. Sandilands[c], Ruben H. K. Thanacoody[d], Laurence A. Gray[a] and James M. Coulson[a]

[a]National Poisons Information Service, Cardiff, United Kingdom; [b]National Poisons Information Service, Birmingham, United Kingdom; [c]National Poisons Information Service, Edinburgh, United Kingdom; [d]National Poisons Information Service, Newcastle, United Kingdom



**Objective:** We conducted a retrospective review of hospitalised patients referred to the National Poisons Information Service (NPIS) to identify drugs associated with serotonin syndrome.

**Methods:** A retrospective study from 1 January 2021 to 31 December 2021 of hospital enquiries to the NPIS that mentioned serotonin. Data was extracted from the UK Poisons Information Database. Clinical features were examined to see whether they met either the Sternbach or Hunter criteria for serotonin syndrome. The frequency of drugs associated with serotonin syndrome was analysed.

**Results:** In total 128 enquiries were identified which met the criteria for serotonin syndrome. The sex distribution was 52% ($n = 67$) female, 47% ($n = 60$) male, and 1% ($n = 1$) unknown. Overall, 56% ($n = 72$) of cases were intentional, 19% ($n = 24$) were recreational use, 21% ($n = 27$) were unknown, and 4% ($n = 5$) were classed as other. The age distributions were 30% ($n = 38$) aged 10–19 years, 27% ($n = 35$) 20–29 years, 16% ($n = 20$) 30–39 years, 16% ($n = 20$) 40–49 years, 9% (n = 12) for 50+ years, and 2% ($n = 3$) unknown. Poison Severity Score (PSS) was minor in 15% ($n = 19$), moderate in 41% ($n = 53$), 41% ($n = 52$) severe, and 3% ($n = 4$) were unknown. Thirty-nine medications already associated with serotonin syndrome were identified. The ten most frequently identified drugs identified are listed in Table 1. Excluding the unknown overdoses, where multiple drugs may have been ingested, 70% ($n = 90$) of enquiries were multi-drug overdoses.

Table 1. Top 10 drugs associated with serotonin syndrome diagnosis, the broader classification of drugs, and the occurrences that each one appeared in 128 identified enquiries.

| Agents | Frequency |
|---|---|
| Sertraline | 29 |
| Amphetamines | 22 |
| Drug not known | 20 |
| Venlafaxine | 14 |
| Mirtazapine | 12 |
| Olanzapine | 11 |
| Citalopram | 11 |
| Promethazine | 7 |
| Lamotrigine | 7 |
| Cocaine | 6 |

**Conclusion:** The vast majority of enquiries of serotonin syndrome, which met either the Sternbach or Hunter criteria, were mixed overdoses associated with either antidepressants or drugs of abuse and had moderate or severe clinical features.

## 155. A case of laboratory confirmed diphtheria: migratory flows, infectious diseases and the role of Poison Control Centres (PCC)

Giulia Scaravaggi, Davide Lonati, Azzurra Schicchi, Valeria M. Petrolini, Lucia Bernasconi, Monica Carnovale and Carlo A. Locatelli

Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy

**Objective:** Diphtheria is an infection caused by *Corynebacterium diphtheriae* that produce a toxin. It is a vaccine-preventable disease, but recently, increased cases were detected in Europe linked to migratory flows [1]. We describe a case of laboratory confirmed diphtheria and the role of PCC in its management.
**Case report:** In August 2022 our PCC was called from an infectious diseases specialist of a hospital in northern Italy who was treating a 35-year-old man admitted for suspected diphtheria. The patient arrived in Italy 1-week before after 5-months imprisonment in Libya. The history was positive for skin lesions and fever and because of the concomitant presence of monolateral tonsillitis, diphtheria was suspected. Throat and skin swab test were positive for *Corynebacterium diphtheria*. Antibiotic treatment was started (piperacillin/tazobactam + doxycycline + linezolid) together with attempts to obtain the diphtheria antitoxin (DAT) and the contact tracing procedure. Meanwhile clinical evolution was characterized by seizure (computerised tomography (CT) scan normal) and myocarditis. Our PCC was involved in supplying DAT and providing advice on appropriate administration. Ten vials (100,000 UI) of DAT where immediately provided by the PCC and administered without adverse effects. The patient's clinical manifestations improved and he was finally discharged asymptomatic after 17 days after hospitalisation. The 19 subjects identified as at risk contacts were treated with vaccine and preventive antibiotic treatment. They never developed clinical manifestations and their swab tests remained negative.
**Conclusion:** The movement of migrants means physicians have to face old diseases. The prompt administration of DAT is a fundamental step in the management of diphtheria. The Pavia Poison Centre has held DAT as an essential antidote in its stockpile for 5 years (actual availability enough for 10 adult patients). This may also be helpful for similar emergencies in other European countries [2]. Poison Control Centres can play an important role in storage and emergency supply of antitoxins. Improving diphtheria vaccination in migrants is a current important public health issue.

### References

[1] European Centre for Disease Prevention and Control. Increased diphtheria cases in migrant centres in Europe [cited 2022 Oct 10]. Available from: https://www.ecdc.europa.eu/en/news-events/increased-diphtheria-cases-among-migrants-europe.
[2] Scaravaggi G, Buscaglia E, Petrolini VM, et al. Diphtheria: two cases treated with antitoxin. Clin Toxicol. 2020,58:593.

## 156. Involuntarily drugging: increasing numbers of inquiries about suspected drink spiking reported to the Danish Poison Information Center

Dorte F. Palmqvist[a,b] and Lisbeth Bringgaard[a,b]

[a]Danish Poison Information Center, Copenhagen, Denmark; [b]Department of Anaesthesia and Intensive Care, Bispebjerg – and Frederiksberg University Hospital of Copenhagen, Copenhagen, Denmark

**Objective:** Since 2016 the Danish Poison Information Center (DPIC) has experienced an increase in enquiries from citizens, who suspected they had been involuntarily drugged. We analyzed these cases.
**Methods:** The profile of callers suspecting drugging was investigated by a retrospective review of all enquiries to DPIC from 1 January to 31 December 2021. The following categories were reviewed: geography, gender, age, month, intention of drugging. Data on time span from the incident to DPIC contact and advice given from DPIC was also extracted. Comments from enquirers were implemented in the study as anecdotal data. There was no laboratory confirmation of exposure with urine or blood samples.
**Results:** In 2021, the DPIC received 314 calls (enquiry total 38,098) from citizens suspecting drugging; 52% were from the Capital Region. The gender distribution was 66% women, 31% men and 3% not recorded. Allocation by age groups were: 13–19 years 34%, 20–29 years 39%, 30–39 years 8%, 40–49 years 3%, 50–59 years 1% and not recorded 15%. Overall, 4.2% of victims had experienced robbery, and/or 3.5% suspected sexual abuse. A majority were no longer poisoned or could be observed at home. In 8% of the cases hospitalization was recommended. In 74% of the cases the enquiries were made 1 day or more after the incident. The allocation between callers were 52% self-referrals, 36% relatives and 12% healthcare professionals. Months with COVID-19 lockdowns resulted in a decrease in enquiries followed by an increase in calls when society reopened. The majority of callers suspected being drugged at a club or bar. Some expressed fear and/or frustration due to their unusual behavior and/or amnesia associated with the incident. Several victims stated they were not taken seriously, when contacting authorities.
**Conclusion:** We found a correlation between COVID-19 lockdown and the number of enquiries, which we associated with nightlife activity. The following findings were unexpected: A third of enquirers were men, and the victims age span ranged from 13 to 59 years. When initiating preventive strategies, it is essential to appreciate that all citizens are potential victims of drugging. Enquirers are recommended to report the event to the police. Many of the cases indicated intoxication with drugs, but alcohol

intoxication could not be excluded. Some victims/relatives requested drug testing, which we think is a good idea but is challenging to accommodate due to 74% of calls occuring one or more days after the incident. The quantitative and anecdotal findings indicate there is a need of preventing drugging and providing the victims with support and help.

## 157. How can we help you? Collaboration between Poisons Information Centre and ambulance services in Estonia

Ruth Kastanje and Mare Oder
Estonian Health Board, Tallinn, Estonia

**Objective:** Every year the treatment of patients with poisoning costs approximately 1.5 million euros from Estonia's Health Insurance budget. Timely consultation with a Poison Centre is known to be an efficient measure to cut the costs and help the patient obtain the most appropriate care. In Estonia most of ambulance brigade team leaders are nurses and specialist consultation should be especially valuable to them. This study examines what sort of help the ambulance service requests from the Poisons Information Centre and which patients worry them most.
**Methods:** Calls from ambulance teams in the Estonian Poisons Information Centre (EPIC) database were analysed from 1 January 2021 to 31 December 2021. Calls about accidents and suicide attempts were analysed separately by age group and causative agents; the Toxscore for the patients was evaluated. Data were also collected on the response provided by EPIC e.g., the need to hospitalise, treatment measures advised to be taken.
**Results:** The most frequently asked question related to immediate treatment measures needed (32.4%), followed by possible symptoms (24.6%), the need to hospitalise (17.2%) and toxic dose (17.7%). Overall, 98% of the inquiries were about oral exposures and 18% of calls were made when the ambulance was on its way to the patient. In the accidental poisonings group most patients were children aged 1-3 years. In this group, 46.8% of patients were recommended observation at home and 38% did not need any medical intervention. Overall, 56% of children had Toxscore 0. In the accidental group, 52% of patients were referred to hospital and 48% recommended to stay at home. In the attempted suicide group, 98% of patients were referred to hospital for psychiatric evaluation. In this group, most patients were children (28%) followed by young adults 20–29 years (19%). Information most commonly related to different medications (mainly psychotropic drugs, 52%). At the same time we noticed, that there were several calls from hospital doctors about patient with serious poisonings about whom there has been no inquiry from the ambulance.
**Conclusion:** The ambulance service uses EPIC mainly to decide immediate treatment measures, be ready for possible symptoms and decide whether to take the patient to hospital. They should be encouraged to call more often to ensure all patients receive appropriate prehospital treatment. Fortunately, in half the cases involving accidental exposure half the patients did not actually need an ambulance. To improve this situation EPIC plans courses for dispatch staff, to encourage them to consult us for any case.

## 158. Patterns of fentanyl exposures reported to the U.S. Poison Centers

Saumitra Rege, Ryan J. Cole and Christopher Holstege
University of Virginia, Charlottesville, VA, USA

**Objective:** Misuse of opioids continues to be a significant public health crisis globally. According to the Centers for Disease Control and Prevention (CDC), there were more than 108,000 overdose deaths in the United States (US) in 2021, with over 75% of those involving an opioid – a 15% increase from the prior year. The present study sought to evaluate the recent trends in fentanyl exposures, both prescription and non-prescription, reported to the US poison centers (PCs).
**Methods:** The national poison data system (NPDS) was queried for fentanyl exposures that were reported to the US PCs from 2017 to 2021. We identified and descriptively assessed the relevant demographic and clinical characteristics. Poisson regression models were used to evaluate the trends in the number and rates (per 100,000 human exposures) of fentanyl exposures. Percent changes from the first year of the study (2017) were reported with the corresponding 95% confidence intervals (95% CI).
**Results:** Overall, there were 18,591 fentanyl cases reported to the US PCs during the study period. Among these 60.6% cases were reported from acute care hospitals and 46.2% were single substance exposures. Among cases, ages between 20 and 29 years (27.3%) constituted the most common age group. The proportion of such cases (24.1–27.1%) increased during the study period. Males accounted for 64.9% cases. Most exposures occurred in a residence. Prescription fentanyl was the most commonly reported fentanyl type (73.4%) but non-prescription fentanyl exposures increased significantly during the study period. The most frequently co-occurring substances observed with the cases were benzodiazepines (11.5%). Intentional abuse (55.8%) and suspected suicides (12%) were the most common reasons for exposure. Among the sample, approximately 19% of the cases were admitted to the critical care unit. Major effects were seen in 25.1% of cases with the case fatality rate being 17.1%. Naloxone was the most frequently used therapy and in most cases was used prior to the PC recommendation. Tachycardia, respiratory depression and drowsiness were the commonly seen clinical effects. The frequency of fentanyl exposures increased by 264.1% (95% CI: 253.7%, 277.5%, $p < 0.001$) while the rate increased by 270.1% (95% CI: 255.2%, 289.4%, $p < 0.001$).
**Conclusion:** The number of fentanyl exposure cases handled by the PCs increased significantly. Personalized evidence-based strategies, population level interventions, creation of protective environments, and better screening of patients are some key measure to limit this trend.

## 159. Trends in calls to the National Poisons Information Centre of Ireland following the introduction of a phone number for the general public

Niamh English and Patricia Casey
National Poisons information Centre, Dublin, Republic of Ireland

**Objective:** The National Poisons Information Centre (NPIC) in Ireland introduced a specific phone line for calls for members of the public in January 2011. This was accompanied by an ongoing

awareness campaign, mainly using social media platforms and a variety of outreach programs to promote the service to the general public. The aim of this study was to examine call patterns in the years following the introduction of the public poisons line.
**Methods:** This retrospective study examines calls received by the NPIC from 1 January 2010 to 31 December 2021, inclusive.
**Results:** The average number of calls per month from members of the public increased from 185 calls in 2010 to 475 calls in 2021. Calls from hospitals and General Practitioners (GPs) decreased over the same period. Other healthcare professional calls increased slightly most months. The results have not been straight gradients every month. We have looked at potential reasons for the rise and fall in the histograms. This includes the introduction of Facebook, Instagram and Twitter along with outreach initiatives. We looked at call numbers and dates to determine if there is a link in the fluctuations.
**Conclusion:** Calls from members of the public have increased by over 150% since the public poisons line was introduced in 2011. Hospital and GP calls decreased by approximately 30% each, while calls from healthcare professionals increased by over 20% during the same period. Social media and awareness campaigns have more recently been introduced to our service. There has been an increase of almost 15% in the total number of calls to our service from January 2010 to December 2021. This is most likely a reflection of the increase in member of public calls.

## 160. Comparison of poisoning patterns during COVID-19 pandemic with the trend analysis-predicted models

Zanina Pereska, Niko Bekjarovski, Natasha Simonovska, Aleksandra Babulovska, Afrodita Berat-Huseini, Kiril Naumoski and Kristin Kostadinoski

University Clinic of Toxicology, Ss Cyril and Methodius University, Skopje, North Macedonia

**Objective:** The COVID-19 pandemic was associated with a reduced number of acute poisonings and changes in poisoning pattern in some countries. The aim of our study is to compare the profile of acute poisonings in 2020–2021 with the registered poisoning pattern in the previous 10-year period (2010–2019).
**Methods:** Data from the Poisons Information Centre (PIC), University Clinic of Toxicology, Skopje, North Macedonia were analysed in a two-year retrospective study including data of 2212 acutely poisoned patients compared to the data from the trend analysis of registered poisonings in the past 10-year period (2010–2019).
**Results:** During 2020 and 2021, a continuous decrease in poisonings was registered (23.6 and 25.7%, respectively), with a more significant decrease in females (30.5 and 26.8%, respectively) than in males (17.5 and 24.8%, respectively) compared to the predicted values. Beside the increased poisoning in males, there was no significant difference in gender distribution between the two observed years ($\chi^2$=2.304, df =1, $p$ = 0.129). There was significant partial association of females and recovery outcome in the last two years ($\chi^2$= 5.743, df =1, $p$ = 0.017). The smallest decrease expressed in percentage change for 2020 and 2021 was registered for alcohol poisoning (17.8 and 15.7%, respectively), and psychoactive substance (PAS) use (22.4 and 23.3%) while the largest decrease was observed in drug poisoning (26.4 and 28.7%) followed by poisoning with chemicals (24.0 and 26.3%). During 2020, the biggest decrease compared to the predicted values was observed among adolescents (27.7%), then among the elderly (25.6%) and the smallest among adults (18.8%). In 2021, adolescents and the elderly had a smaller decrease compared to the predicted values (22.7 and 22.0%, respectively) and to the previous year.
**Conclusion:** During the COVID-19 pandemic in 2020 and 2021, acute poisonings maintained a decreasing trend in comparison with predicated values according to the trend line statistic based on data from the previous 10 years. We registered a smaller decrease in the number of acute alcohol intoxications and use of PAS comparing to other types of poisoning, and an increase in poisonings in men. All of this indicates a changed intoxication pattern and an increased need to direct more medical attention to the treatment of PAS and alcohol abuse.

## 161. SARS-CoV-2 infection is not predictive for renal function impairment after non-steroidal anti-inflammatory drug use – a case-control study

Aurélie Pahud De Mortanges[a], Verena Schöning[b], Evangelia Liakoni[b] and Felix Hammann[b]

[a]Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital, Bern University Hospital and Graduate School for Health Sciences, University of Bern, Bern, Switzerland; [b]Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

**Objective:** In early 2020, expert and social media debate arose about the safety of non-steroidal anti-inflammatory drugs (NSAID) in Coronavirus disease 2019 (COVID-19). By now, consensus has been reached that NSAID use does not increase disease severity [1]. Nevertheless, both NSAID and COVID-19 may have detrimental effects on the kidneys [2]. This retrospective case-control study aims to investigate whether severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) test status combined with demographic and laboratory data is predictive for impairment of renal function following NSAID intake.
**Methods:** The study population consisted of patients tested for SARS-CoV-2 by reverse transcription polymerase chain reaction (PCR) nasopharyngeal swab test between February and November 2020 at the Insel Hospital Group (Bern, Switzerland). We included patients with an estimated glomerular filtration rate (eGFR) $\geq$ 75 mL/min before NSAID treatment. We defined cases as subjects with a $\geq$20% decrease in eGFR during or up to 3 days after NSAID treatment. Controls had an eGFR of $\geq$75 mL/min during and after NSAID treatment. Cases and controls were matched in a 1:3 ratio. We applied different statistical models (multivariate logistic regression, decision trees, random forest, and k-nearest neighbor) to identify features, including demographics, laboratory values, and SARS-CoV-2 test status, predictive for the development of renal impairment. We selected features for biological plausibility and high data availability, and removed one feature out of every pair with a Spearman correlation coefficient $|>0.2|$.
**Results:** Overall, 78 cases and 234 matched controls were included and 11 features were modeled. The resulting decision tree is exemplary for our findings, with a very high sensitivity (97.4%), low specificity (56.4%), and an overall balanced accuracy of 76.9%. Laboratory values mainly contributed to the classification (potassium, eGFR, aspartate aminotransferase in descending order), whereas SARS-CoV-2 test status was not represented in the final tree. The performance of the decision tree remained unchanged when SARS-CoV-2 test status was removed from the set of predictors.
**Conclusion:** The results of this matched case-control study indicate that SARS-CoV-2 test status does not predict renal

impairment after NSAID treatment, but rather laboratory measurements as indicators of overall clinical status may be helpful.

## References

[1] Drake TM, Fairfield CJ, Pius R, et al. Non-steroidal anti-inflammatory drug use and outcomes of COVID-19 in the ISARIC clinical characterisation protocol UK cohort: a matched, prospective cohort study. Lancet Rheumatol. 2021;3:e498–e506.

[2] Liakopoulos V, Roumeliotis S, Papachristou S, et al. COVID-19 and the kidney: time to take a closer look. Int Urol Nephrol. 2022;54: 1053–1057.

# 162. Accidental subcutaneous injection of isopropyl alcohol to hallux during digital block resulting in necrosis

Shireen Banerji and Christopher Pitotti

Rocky Mountain Poison Center, Denver, CO, USA

**Objective:** Iatrogenic events cause significant morbidity and mortality to millions of patients globally and severity can range from no effect to death. We describe a case involving accidental administration of isopropyl alcohol (IPA) instead of lidocaine during a routine outpatient podiatric procedure.

**Case report:** A 57-year-old female with no significant past medical history presented to her podiatrist for an outpatient elective removal of the toenail of her right hallux. To administer a right hallux digital block the provider infiltrated 4 mL of isopropyl alcohol 70% instead, mistakenly, for an equivalent volume of lidocaine. She immediately complained of pain in the affected site which appeared blanched and described the taste of rubbing alcohol in her mouth. Her vital signs remained normal. Following poison center (PC) consultation, she was transferred to an Emergency Department for further evaluation and care. She reported her pain as a 10/10 ("the worst pain of my life") on Hospital Day 1. Her toe developed swelling and surrounding tissue discoloration. All labs remained normal. The PC advised warm water to improve circulation, surgical consultation for possible debriding, pain control and wound care. On Hospital Day 2 she developed blisters on the affected toe but was well enough to be discharged with instructions to follow up with her podiatrist in 5 days or return if pain worsened. Upon follow up by the PC on Day 3, she reported pain to be 5/10 and able to walk despite edema and ongoing blistering. At 1-week, she reported pain as 6/10 and her foot "feeling like it was on fire". She was prescribed opioid analgesics and antibiotics. She described blisters and feeling like the blisters were "strangling" her toe, possibly needing to be lanced off and that the layers of her skin were separating. At 8 weeks, she reported persistent pain (7/10) requiring tramadol and gabapentin and a walking boot for ambulation. She completed a 3-week course of clindamycin. She described her toe as appearing black. Plastic surgery was consulted and tissue debridement was performed prior to skin grafting due to tissue loss and tendon exposure.

**Conclusion:** Accidental subcutaneous injection of 4 mL of IPA resulted in severe morbidity in this otherwise healthy patient. IPA is both hyperosmolar and can penetrate cell membranes and denature proteins making it an ideal topical disinfectant but with toxicity like vesicant chemotherapeutic infiltration. This case illustrates that providers and staff must remain vigilant to ensure patient safety is maintained.

# 163. Prolonged effect of chlordiazepoxide more than a month after intake, requiring treatment with flumazenil

Nanna Reiter[a], Christian A. Wamberg[a], Kim P. Dalhoff[b] and Tonny S. Petersen[b]

[a]Department of Anaesthesiology and Intensive Care, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark; [b]Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark

**Objective:** Chlordiazepoxide is used as first line medical treatment of alcohol withdrawal symptoms in Denmark. It is a long-acting benzodiazepine with active metabolites. The aim of this case report was to raise awareness of the prolonged sedative effect of chlordiazepoxide, and the possibility of antidote reversion even weeks after chlordiazepoxide administration.

**Case report:** A 56-year-old man with compensated alcoholic liver cirrhosis was admitted to hospital due to confusion. He was treated for 7 days in an alcohol ambulatory unit with a total dose of 420 mg chlordiazepoxide and an unknown dose of acamprosate for alcohol withdrawal symptoms. During and after the treatment, he experienced fatigue and unsteadiness and his relatives were worried about overmedication. Eleven days post-outpatient treatment with chlordiazepoxide, he was admitted to hospital after being found in a state of confusion. At admission alanine aminotransferase (ALT) was normal, lactate dehydrogenase (LDH) slightly elevated. Plasma ammonia was 81 μmol/L, spontaneous International Normalized Ratio (INR) 1.6, albumin 22 g/L and ethanol was not detectable in blood samples. Lactulose and isotonic glucose solution were given due to suspected hepatic encephalopathy, and 100 mg chlordiazepoxide and 2.5 mg diazepam were administrated to treat possible alcohol withdrawal symptoms. During the next 3 days a total of 217.5 mg diazepam and 600 mg phenobarbital were administered. Cerebrospinal fluid and transthoracic echocardiogram were within normal ranges, brain computerised tomography (CT) scan was normal, but electroencephalogram (EEG) showed encephalopathy. Flumazenil was not administrated due to risk of convulsions. On day 4 of hospitalization the patient was intubated due to respiratory distress, and on days 7–13 propofol and remifentanil sedation was supplemented with midazolam-infusion. On day 17 the patient was unconscious. Brain CT was still normal. The clinical course was complicated by *Staphylococcus aureus* pneumonia. On day 14, he was transferred to another hospital due to capacity issues. After flumazenil administration the patient regained consciousness. He was treated with an infusion as well as bolus flumazenil over the next 12 days, discharged to the ward at Day 36 and still hospitalized on day 56 due to confusion and unsteadiness. On day 25 the blood concentration of chlordiazepoxide was 0.012 mg/kg. The nordazepam concentration (0.47 mg/kg) was high enough to cause altered consciousness.

**Conclusion:** Prolonged and reversible effects of chlordiazepoxide and other sedative agents must be suspected in patients with otherwise unexplained altered consciousness after treatment for alcohol withdrawal symptoms, and in patients given relatively low doses with known liver-disease and possible impaired metabolism.

## 164. Myeloneuropathy in a patient receiving treatment with Entonox© for recurrent shoulder dislocations: a case report

Gurpreet S. Jutley, Rehman Crisp and Mark Pucci

University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

**Objective:** Myeloneuropathy secondary to chronic non-medical use of nitrous oxide ($N_2O$) is well recognised and becoming increasingly common [1]. We present a case of myeloneuropathy secondary to repeated therapeutic use of Entonox©, a medical gas mixture consisting of 50% $N_2O$ and 50% oxygen, for recurrent shoulder dislocations.
**Case report:** A 27-year-old female presented with a 2-month history of paraesthesia in the hands and feet that progressed to involve the lower limbs and trunk. She had a background of Ehlers-Danlos syndrome and suffered recurrent shoulder dislocations requiring on average twice-weekly reductions over the prior 12 months. The patient reported being administered Entonox© as analgesia, typically for 30 minutes, during shoulder relocation procedures. On examination the patient had a positive Romberg's test, impaired light touch and pinprick sensation up to T8 sensory level. Proprioception was impaired bilaterally at the toes and ankles. Blood tests revealed a vitamin B1402 concentration of 200 pg/mL (200–900 pg/mL), raised homocysteine concentration of 31 μmol/L (6.7–15.2 μmol/L) and raised methylmalonic acid concentration of 2722 nmol/L (0–280 nmol/L). Magnetic resonance imaging (MRI) of the whole spine was reported as unremarkable. A diagnosis of myeloneuropathy secondary to functional vitamin B1402 deficiency caused by $N_2O$ was made and treatment with 1 mg intramuscular hydroxocobalamin was commenced, initially on alternate days for 2 weeks, followed by every 4 weeks. Despite this, the patient's neurological symptoms had not significantly improved at follow-up at 4 months.
**Conclusion:** Myeloneuropathy secondary to therapeutic use of $N_2O$ has rarely been reported [2,3]. Repeated inhalation of $N_2O$ can result in functional inactivation of vitamin B1402 by oxidation of the cobalt atom in the B1402 moiety. The optimal dose regimen of vitamin B1402 treatment is unknown. One third of patients with subacute combined degeneration of the cord have complete resolution following treatment with B1402, on average in 36 weeks [1]. Clinicians should be aware of this potential life-changing adverse effect of repeated use of Entonox©, particularly in frequent attenders to the Emergency Department.

### References

[1] Patel KK, Mejia Munne JC, Gunness VRN, et al. Subacute combined degeneration of the spinal cord following nitrous oxide anesthesia: a systematic review of cases. Clin Neurol Neurosurg. 2018;173:163–168 (Erratum in: Clin Neurol Neurosurg. 2019;177:123–124).
[2] Wijesekera NT, Davagnanam I, Miszkiel K. Subacute combined cord degeneration: a rare complication of nitrous oxide misuse. A case report. Neuroradiol J. 2009;22:194–197.
[3] Doran M, Rassam SS, Jones LM, et al. Toxicity after intermittent inhalation of nitrous oxide for analgesia. BMJ. 2004;328:1364–1365.

## 165. Adverse reactions of oral methylprednisolone therapy in children with multisystem inflammatory syndrome associated with COVID-19

Viorela Nitescu[a], Diana Usurelu[b], Ana-Maria Mihalcea[b], Teodora Turcu[b], Andra Postelnicu[b], Ruxandra Stejeroiu[b], Stefania Ionescu[b], Dorina Craciun[c] and Coriolan Ulmeanu[a]

[a]Pediatric Poisoning Centre, "Grigore Alexandrescu " Hospital, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania; [b]Pediatric Poisoning Centre, "Grigore Alexandrescu " Hospital, Bucharest, Romania; [c]University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

**Objective:** To analyze the adverse reactions of oral methylprednisolone therapy in children with multisystem inflammatory syndrome associated with COVID-19 (MIS-C).
**Methods:** We conducted a prospective study over 2 years related to children with MIS-C who received oral methylprednisolone as a consolidation treatment at home. The dose was of 1 mg/kg for 2 weeks followed by its progressive decrease over another 2 weeks. Patients with preexisting pathology, clinical or paraclinical abnormalities at the time of treatment initiation were excluded. The following variables were analyzed: age, sex, clinical signs and biological parameters: complete blood count, liver function tests, amylase, glucose, electrolytes, blood urea nitrogen, creatinine, lipid profile, and urine test. The patients were evaluated at the end of the treatment and then 2, 5, 8 and 11 months after.
**Results:** Overall, 29 patients were studied between 2020 and 2022; mean age 9.9 years and male:female ratio 1:1. At the end of the treatment 24 children (82.75%) showed signs of cortisone impregnation: cushingoid appearance 80% ("full moon" face; redistribution of body fat tissue, obesity, stretch marks, facial and palmo-plantar hyperemia), myopathy 3.5%, excessive hairiness 20.8%; arterial hypertension 20.8%, leukocytosis 62.5%, hepatic cytolysis 13.8%, hyperglycemia 17.2%, hypercholesterolemia 34.7%, hypertriglyceridemia 31.0%. Two months after stopping the treatment, 11 patients (34.7%) still had clinical signs of cortisone impregnation, one patient had hepatic cytolysis, and 4 (13.8%) presented hyperglycemia. Five months after stopping the treatment, only 3 patients (9.8%) still had cushingoid appearance and none had biological abnormalities. At the last two follow-up visits (8 months and 11 months after stopping the treatment) no patient had any side effects of corticosteroid treatment.
**Conclusion:** The most frequent adverse reactions of oral methylprednisolone therapy in our MIS-C patients were: cushingoid appearance followed by leukocytosis, hypercholesterolemia, hypertriglyceridemia and hyperglycemia [1]. Adverse reactions of oral methylprednisolone therapy completely disappeared 8 months after stopping the treatment in all patients, the most difficult to reverse being clinical signs of cortisone impregnation.

### Reference

[1] Jain MK, Sahu SK, Behera JR, et al. Multisystem inflammatory syndrome in children associated with COVID 19 treated with oral steroid. Indian J Pediatr. 2021;88:106.

## 166. Stuck: challenges in the management of clozapine-induced gastrointestinal hypomotility (CIGH)

Joshua Bloom[a], Mark L. Abroms[b] and Mark K. Su[c]

[a]Ronald O. Perelman Department of Emergency Medicine, NYU Grossman School of Medicine, New York, NY, USA; [b]Department of Psychiatry, NYU Grossman School of Medicine, New York, NY, USA; [c]Department of Health and Mental Hygiene, New York City Poison Control Center, New York, NY, USA

**Objective:** Clozapine-induced gastrointestinal hypomotility (CIGH) is an underappreciated adverse event seen in up to 80% of patients taking clozapine and can range in severity from constipation to life-threatening adynamic ileus (up to 0.9%) [1]. We present a case of a patient with schizoaffective disorder who developed CIGH after months of inpatient clozapine administration. This patient had a prolonged hospital course and developed multiple complications, but he remained adamant about continuing on clozapine. We also describe the treatment regimen used to improve bowel function.
**Case report:** A 41-year-old man with a history of treatment-resistant schizoaffective disorder, bipolar type, was admitted to an inpatient psychiatric unit. In the unit, he was receiving lamotrigine 200 mg daily, escitalopram 20 mg daily, and clozapine 100 mg daily in the morning and 350 mg daily at night. Therapeutic drug monitoring during this time consistently showed clozapine concentrations over 1000 ng/mL (suggested therapeutic range, 100–700 ng/mL). On hospital day 105, he developed acute abdominal pain and computed tomography findings suggestive of a small-bowel obstruction. No mechanical obstruction was identified by laparotomy, and CIGH was diagnosed. The patient and his healthcare proxy were opposed to discontinuing clozapine due to the severe refractory nature of his psychosis. He was monitored on the surgical service, placed on total parenteral nutrition, and started on promotility therapies; clozapine was reintroduced as an oral disintegrating tablet on hospital day 121. His bowel function remained compromised for 33 days and he experienced multiple infectious complications including infectious gastritis and *Clostridium difficile* colitis. He eventually regained bowel function after initiation of bethanechol and tegaserod and was stabilized for transfer to psychiatry after 38 days on the surgical service. He was discharged on clozapine 100 mg daily in the morning, 200 mg daily at night. He was readmitted to psychiatry later that month; his bowel function remained intact during this admission, and clozapine dose was unchanged.
**Conclusion:** CIGH can be life-threatening; providers should be aware of the potential for this adverse event and discontinue clozapine if it occurs. If drug discontinuation is not possible, alternative approaches to managing CIGH include dose reduction, bowel rest, and promotility medications, especially those acting via muscarinic or serotonergic mechanisms. A multidisciplinary approach is likely necessary to determine the optimum treatment for these patients.

### Reference

[1] Palmer SE, McLean RM, Ellis PM, et al. Life-threatening clozapine-induced gastrointestinal hypomotility: an analysis of 102 cases. J Clin Psychiatry. 2008;69:759–768.

## 167. Serotonin toxicity secondary to drug interactions involving selegiline, 5-hydroxytryptophan, carbidopa/levodopa, and tetrahydrobiopterin in a patient with dopa-responsive dystonia

Brian G. Wiener[a], Sarah G. Mahonski[b], Mary Ann Howland[c], Mark K. Su[d] and Robert S. Hoffman[a]

[a]Division of Medical Toxicology, Ronald O. Perelman Department of Emergency Medicine, New York University Grossman School of Medicine, New York, NY, USA; [b]Department of Emergency Medicine, SUNY Upstate Medical University, Syracuse, NY, USA; [c]College of Pharmacy and Health Sciences, St. John's University, New York, NY, USA; [d]New York City Poison Control Center, New York, NY, USA

**Objective:** Dopa-responsive dystonia (DRD), a genetic condition of impaired dopamine synthesis, is characterized by movement disorders that are responsive to levodopa. Patients are at risk for serotonin toxicity when treated with multiple dopaminergic and serotonergic medications. We present an interesting and rare case to illustrate the risks of polypharmacy.
**Case report:** A 30-year-old man with DRD presented with syncope, confusion, and abnormal extremity movements after his smartwatch notified him of tachycardia. During the past three weeks prior to presentation, he had increased his selegiline dose from 5 to 15 mg secondary to worsening dystonic movements. He was also prescribed tetrahydrobiopterin, 5-hydroxytryptophan, and carbidopa/levodopa. His initial vital signs were: blood pressure 153/92 mmHg; heart rate 157 beats/minute; respiratory rate 22 breaths/minute; temperature 37.1 °C; oxygen saturations 96%. Physical examination was notable for confusion, diaphoresis, dilated and reactive 8 mm pupils, 6 beats of ankle clonus bilaterally, and 4+ bilateral patellar and Achilles tendon reflexes. A non-contrast head computerised tomography (CT) scan was normal. Toxicology diagnosed the patient with serotonin toxicity and treatment with benzodiazepines was initiated. His clinical status improved rapidly and he was discharged home 36 hours later with complete resolution of symptoms.
**Conclusion:** DRD is a rare disease that often requires polypharmaceutical treatment. Selegiline is a selective and irreversible monoamine oxidase (MAO) B inhibitor used in patients with DRD. In larger doses, selegiline loses specificity and inhibits both MAO A and B. This patient was taking oral 5-hydroxytryptophan, a serotonin precursor, and tetrahydrobiopterin, a cofactor for serotonin synthesis, as well as carbidopa/levodopa which has been reported to occasionally cause dysregulation of striatal serotonin activity. These medications taken together, along with an increase in dose of selegiline likely contributed to serotonin toxicity in our patient. This case highlights the risk of serotonergic polypharmacy.

## 169. Spontaneous opioid detoxification: report of two cases

Norbertas Pašukonis[a], Gabija Valauskaitė[b] and Robertas Badaras[c]

[a]Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [b]Department of Intensive Care Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [c]Toxicology Centre of Republic Vilnius University Hospital, Vilnius, Lithuania

**Objective:** Opioid overdose is a life-threatening condition, which has become an increasing problem in Europe. About 1 million citizens of the European Union are opioid users, of which 28% requested medical treatment [1]. Usually, patients are treated with a standard detoxification protocol and methadone. We present two clinical cases of opioid overdose with spontaneous detoxification after stabilizing patients' vital conditions. These patients, who used opioids for many years and suffered acute pain episodes, reported no pain after a month of hospitalization following acute overdose.
**Case reports:** Case 1. A 47-year-old female presented to the emergency department in deep somnolence. She had taken a large, unspecified number of drugs orally about 6 hours previously for suicidal purposes, a mix of escitalopram, codeine, and levothyroxine. Chronic pain was the only reason for a suicide attempt. Vital functions were: blood pressure 162/112 mmHg, heart rate 96 bpm, oxygen saturation 87%, and Glasgow Coma Score (GCS) 8. Mechanical ventilation was provided for 28 days due to respiratory depression with 21 days of continuous veno-venous hemodiafiltration to support acute kidney injury. After 40 days of hospitalization in the intensive care unit with somatic complications (infection, sepsis and systemic inflammatory response syndrome) her condition stabilized. After long-term sedation and naloxone therapy spontaneous opioid detoxification was reached. Case 2. A 48-year-old female was found at home unconscious. Many empty drug packages were found around her, including tramadol, fentanyl, alprazolam, quetiapine, and mirtazapine. On admission to the emergency department, massive vomiting, dysphagia, somnolence, miosis, stupor, cyanosis, and respiratory insufficiency were noted. Vital functions were: blood pressure 113/78 mmHg, heart rate 98 bpm, oxygen saturation 80%, and GCS 10. For 11 days in the intensive care department, mechanical ventilation was provided, with continuing naloxone therapy and sedation. After two more days, she left against medical advice in good general condition.
**Conclusion:** The development of tolerance and reduced pain threshold is frequently associated with chronic opioid users. After long-term sedation and opioid weaning, the pain threshold increases. Patients with opioid-induced hyperalgesia can tolerate higher pain stimuli and their opioid addiction is reversed. As an outcome, such patients achieve a better quality of life, which leads to reduced risk of suicide attempts. Both patients who took various prescribed opioids for many years, required no painkillers after successful therapy for overdose, demonstrating that general sedation and long-term patient intensive care can result in spontaneous opioid detoxification.

## Reference

[1] European drug report: trends and developments. Luxembourg: Publications office of the European Union; 2021 [cited 2022 Oct 10]. Available from: https://www.emcdda.europa.eu/publications/edr/trends-developments/2021.

# 170. QT prolongation and Torsade de Pointes in a 13-year-old transgender adolescent in treatment with bicalutamide and tacrolimus

Ferran Gómez-Aguilar[a], Lidia Martínez-Sánchez[a], Vanessa Arias-Constantí[a], David Muñoz-Santanach[a] and Georgia Sarquella-Brugada[b]

[a]Pediatric Emergency Department, SJD Barcelona Children's Hospital, Esplugues de Llobregat, Spain; [b]Cardiology Department, SJD Barcelona Children's Hospital, Esplugues de Llobregat, Spain

**Objective:** To describe a case of ventricular tachycardia in an adolescent with a history of syncope and long QT identified in the emergency department (ED). The patient was being treated with bicalutamide and tacrolimus, both on the list of drugs with possible risk of Torsade de Pointes (TdP) and drugs to avoid in patients with congenital Long QT Syndrome [1].
**Case report:** A 13-year-old transgender girl arrived to the ED due to two episodes of sudden loss of consciousness lasting 2 minutes, preceded by palpitations and dizziness. She had a spontaneous and *ad integrum* recovery, with no post-critical period. Upon arrival at the ED, the patient had a stable pediatric assessment, with normal vital signs and physical examination. She was receiving bicalutamide and estradiol plus dienogest as she was in the process of sexual transition, and topical tacrolimus for atopic dermatitis. She had a familiar history of sudden death. An electrocardiogram was performed, which showed a prolonged QTc interval of 560 ms (manual method), and continuous monitoring was started. During observation, she presented a sudden episode of loss of consciousness, hemodynamic instability and respiratory depression coinciding with wide QRS (160 ms) polymorphic tachycardia (280 bpm). Initial stabilization was performed, the tachycardia resolved spontaneously with complete recovery in less than 3 minutes. She was transferred to the intensive care unit, where she had two new episodes compatible with TdP, and was started on beta-blocker treatment and magnesium sulfate. Investigations continued with an echocardiogram and laboratory tests, including electrolytes, which showed no abnormalities. The patient did not present any more episodes, so she was transferred to an internal ward, withdrawing her usual medication (probably related to QT interval prolongation), and maintaining beta-blocker treatment with nadolol. Genetic tests showed an abnormal gene variant [KCNH2 p.(His177Pro)], the clinical significance of which remains to be established. It has not been reported previously but may be related to the patient's pathology.
**Conclusion:** We present a case that demonstrates how important it is to verify that there are no possible drug-drug interactions, especially in pediatric patients taking unusual medications [2]. In this case, bicalutamide (off-label and novel drug in pediatrics, in use for the induction of feminization in transgender adolescent girls) combined with tacrolimus, could cause a prolongation of the QT interval and trigger life-threatening arrhythmias, particularly in patients with congenital long QT.

## References

[1] Woosley RL, Heise CW, Gallo T, et al. QTDrugs list. AZCERT Scientific Publications, Inc. [cited 2022 Oct 10]. Available from: www.crediblemeds.org.
[2] Berling I, Hatten BW, Hoffman RS, et al. Guidelines for reporting case studies and series on drug-induced QT interval prolongation and its complications following acute overdose. Clin Toxicol. 2020;58:20–28.

## 171. Hiccough like symptoms, global amnesia, confusion and neuro-motor denervation after inadvertent subarachnoid injection of high dose clindamycin: a case report

Andrea Giampreti[a], Marco Cirronis[a], Mariapina Gallo[a], Georgios Eleftheriou[a], Raffaella Butera[a], Lorella Faraoni[a], Maria Gioia Contessa[a], Elisa Seghelini[b] and Giuseppe Bacis[a]

[a]Poison Control Center, ASST Papa Giovanni XXIII, Bergamo, Italy;; [b]Institute of Anesthesia, Intensive Care and Emergency Medicine, University of Brescia, Brescia, Italy

**Objective:** At present, no data concerning the effects of injection of high-dose lincosamides into subarachnoid-space are available. We describe a case of erroneous cerebrospinal fluid (CSF) injection of 600 mg clindamycin that resulted in neurological disorders and coxalgia.
**Case report:** A 32-year-old man hospitalized for surgical treatment of patellar tendinopathy received 600 mg of clindamycin instead of bupivacaine through the subarachnoid lumbar space. After 3 hours "hiccough-like" movements, confusion, time-space disorientation, memory-loss and inability to recall the recent past appeared. The Poison Control Center was consulted and CSF lavage was suggested. During the following 24-36 hours he presented a progressive neurological improvement. Brain nuclear magnetic resonance spectroscopy (NMR), laboratory tests and CSF culture were negative. CSF clindamycin concentrations were 270 and 780 mg/L, 8 and 15 hours after injection, respectively. He was discharged with persistent mild headache and new onset of pain in the right inferior limb on day 6. After 1 month the patient presented a clinical picture of muscle weakness of the lower right limb, neuro-motor deficit with denervation findings at electromyography (EMG). At 5 months follow-up the patient presented in good general condition with a resolution of headache and a good muscle performance testing at dynamometer.
**Conclusion:** Clindamycin is a lincosamide mainly used orally or intravenously but not by direct CSF injection. Clindamycin is not known to have major neurotoxic effects, but has well established potential effects on neuro-transmission and neuromuscular conduction. In our patient the high CSF concentration of clindamycin (about 600–2000 fold higher than therapeutic) may have played a critical role in determining either central effects (probably due to cholinergic disequilibrium) either peripheral effects as hiccough-like-movements and neuro-motor deficit (due to neuromuscular-conduction disorders). Clinical manifestations started after 3 hours; this may be related to the physiological CSF turnover in humans (about 5 hours). CSF clindamycin concentration were higher at 15 hours compared to 8 hours. The reason may be twofold. Firstly, clindamycin may have been administered partially in the subarachnoid space and partially in the epidural region (the latter could determine a slower absorption into the CSF/intrathecal compartment). Secondly, it is possible that, during the CSF drainage, clindamycin redistributed from deep compartments to the intrathecal one. Undesired/inadvertent intrathecal injection is a preventable medical error and, also although rare, fatal cases have been reported. Emergency CSF lavage remains the principal management based on the literature; it should be considered and carried out as soon as possible, to alleviate potential complications and nerve damage.

## 172. Diffuse alveolar hemorrhage as an adverse effect of ticagrelor after percutaneous coronary intervention

Rixt E. Smit[a], Fellery de Lange[a], Steef J. Sinkeler[b], Annette L. van Ojik[c] and Carina Bethlehem[d]

[a]Department of Intensive Care Medicine, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [b]Department of Cardiology, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [c]Department of Clinical Pharmacy and Pharmacology, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [d]Department of Intensive Care Medicine and Department of Clinical Pharmacy and Pharmacology, Medical Center Leeuwarden, Leeuwarden, Netherlands

**Objective:** We describe the case of a patient with out of hospital cardiac arrest (OHCA) who developed diffuse alveolar hemorrhage (DAH) after use of ticagrelor as part of dual antiplatelet therapy.
**Case report:** A 33-year old male with no prior history was admitted to the Intensive Care Unit (ICU) after an OHCA due to ventricular fibrillation caused by anterior myocardial infarction. Two drug-eluting stents were placed in the proximal left coronary artery. Before coronary angiography acetylsalicylic acid (ASA) 500 mg was given intravenously together with 5000 IU of heparin. Periprocedural cangrelor was administered intravenously, followed by a loading dose of 180 mg ticagrelor. Dual antiplatelet therapy (DAPT) was continued per protocol with ticagrelor 90 mg bid and ASA 80 mg qd. The next day his pulmonary situation worsened with decreased pulmonary compliance and increased oxygen requirement. Hemoglobin levels dropped and there were constant bloody secretions in the endotracheal tube. A bronchoscopy was performed which revealed large quantities of diffuse free blood in both inferior pulmonary lobes without a visible bleeding source. Additional computerised tomography (CT) imaging showed findings consistent with DAH. Since DAH is not a known complication of cardiopulmonary resuscitation and no other cause of DAH could be identified, we hypothesized that ticagrelor might be the culprit as it is reported in literature [1,2]. Therefore, ticagrelor was discontinued on the fourth day of ICU admission and replaced by prasugrel the next day. Therapy with ASA and venous thromboembolism prophylaxis with low molecular weight heparin was continued without interruption. Follow-up bronchoscopy the day after a loading dose of prasugrel was given showed no remaining signs of active bleeding. Aside from the switch from ticagrelor to prasugrel no other interventions were performed.
**Conclusion:** In this patient, ticagrelor probably led to severe DAH which resolved quickly after switching to prasugrel. We considered the pulmonary hemorrhage to be an adverse effect of ticagrelor.

### References

[1] Yilmaz S, Kiliç O, Tolga Yaylila Y. Diffuse alveolar hemorrhage associated with ticagrelor therapy after percutaneous coronary intervention. Anatol J Cardiol. 2018;20:60–61.
[2] Yıldırım F, Kara İ, Okuyan H, et al. Diffuse alveolar hemorrhage associated with low molecular weight heparin and dual antiplatelet therapy after percutaneous coronary intervention. Clin Respir J. 2017;11:1071–1073.

## 173. A new challenge in the toxicology department: euglycemic diabetic ketoacidosis

Ágnes Bakos, Ildikó Urbán and István Elek
Péterfy Sándor Hospital, Budapest, Hungary

**Objective:** Euglycemic diabetic ketoacidosis (EDKA) is a rare, but serious complication of sodium-glucose cotransporter-2 (SGLT2) inhibitor treatment [1]. We present two diabetic alcohol poisoned patients with EDKA.
**Case series:** Case 1. A 53-year-old woman with past medical history of type 2 diabetes mellitus, hypertension, epilepsy, and hypothyroidism was brought to our department. Upon arrival the patient was alert and confused, but other neurological abnormalities were not detectable. She had hypotension (85/34 mmHg) and tachycardia (113/min). Venous blood gas showed glucose 13.6 mmol/L, metabolic acidosis (pH 7.143) with high anion gap, elevated potassium and lactate concentration. According to her relatives, she had been on a diet, lost 15 kg in 2.5 months and had given herself insulin and liraglutide regularly. Her cerebral computed tomography scan was negative. Laboratory results detected abnormal renal function, significant glucosuria and acetonuria. Her electrocardiogram (ECG) revealed no pathology. Toxicology testing confirmed a blood ethanol concentration 274.01 mg/dL but negative methanol and ethylene glycol. She received supportive therapy and insulin. Her metabolic abnormalities and altered mental status improved within 24 hours. After her confusion resolved, she admitted also taking empagliflozin regularly. Case 2. A 63-year-old man was admitted to our department because of drinking alcohol for three days and taking some alprazolam tablets. In his medical history was diabetes mellitus, hypertension, and ischaemic heart disease. On admission he was heavily drunk, with hypertension and tachycardia. Venous blood gas showed normal glucose (4.6 mmol/L), metabolic acidosis (pH 7.12) with high anion gap, elevated lactate concentration (5.2 mmol/L) and haemoconcentration. Toxicology testing confirmed blood ethanol concentration 175.41 mg/dL and serum benzodiazepine 100.4 ng/mL; ethylene glycol and methanol were not detected. Laboratory results showed slightly elevated urea and moderately elevated hepatic enzymes, acetonuria and glucosuria. He was treated with supportive therapy and later insulin. Despite being dehydrated on admission his diuresis was copious. After 36 hours his metabolic status settled. It was revealed that his diabetes was treated with metformin and empagliflozin. Based on the history and symptoms, EDKA caused by empagliflozin was assumed in both patients.
**Conclusion:** EDKA should be considered in diabetic patients taking a SGLT2 inhibitor with metabolic acidosis of unclear aetiology. Alcohol intoxication, restricted food intake and hypovolemia are important risk factors of EDKA.

### Reference

[1] Sampani E, Sarafidis P, Papagianni A. Euglycemic diabetic ketoacidosis as a complication of SGLT-2 inhibitors: epidemiology, pathophysiology, and treatment. Expert Opin Drug Saf. 2020;19:673–682.

## 174. Addictive potential of recreational nitrous oxide use

Lot van der Ben[a], Johanna J. Nugteren-Van Lonkhuyzen[a], Irma S. van den Hengel-Koot[a], Dylan W. de Lange[a,b], Antoinette J. H. P. van Riel[a] and Laura Hondebrink[a]
[a]Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands; [b]Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands

**Objective:** Since the change in European legislation of nitrous oxide ($N_2O$) in 2014, the number of $N_2O$ intoxications reported to the Dutch Poisons Information Center (DPIC) has increased exponentially [1]. Most patients reported excessive $N_2O$ use, indicating addictive potential. Until recently, $N_2O$ was presumed non-addictive. Studies investigating the addictive potential of $N_2O$ are slowly emerging. We therefore investigated the presence of $N_2O$-related substance use disorder (SUD) in patients with $N_2O$ intoxication.
**Methods:** Patients $\geq$16 years with $N_2O$ intoxication reported to the DPIC, who reported excessive $N_2O$ use (>50 balloons/>200 L/>450 g $N_2O$) or experienced signs of neuropathy, were included in a prospective study in 2021. With consent, participants received an online survey within one week after DPIC consultation. The survey included a validated questionnaire on SUD according to DSM-IV-TR criteria [2] and questions on neuropathy-related symptoms and pattern of use. If agreed, participants received the same survey one and three months later.
**Results:** Overall, 75 participants were included, of whom ten participants completed the first survey. Their median age was 23 years (IQR; 18–24) and the majority was female ($n = 8$, 80%). All met SUD criteria for substance dependence, i.e., 80% ($n = 8$) used more $N_2O$ to experience the same effects, 90% ($n = 9$) used $N_2O$ for a longer period than intended, and 80% ($n = 8$) tried but failed to quit using $N_2O$. All participants used $N_2O$ from tanks to fill balloons and 70% ($n = 7$) used on a weekly basis; 90% ($n = 9$) experienced signs of neuropathy, including paresthesia ($n = 9$, 90%), sensory loss ($n = 9$, 90%), muscle weakness ($n = 9$, 90%), ataxia ($n = 7$, 70%) and fine motor difficulties ($n = 6$, 60%). During follow-up after one ($n = 7$) and three months ($n = 1$), all participants continued to meet SUD criteria and still experienced neurological symptoms.
**Conclusion:** This study demonstrates the addictive potential of $N_2O$. Therefore, screening for dependence is indicated when treating patients with acute or chronic $N_2O$-induced toxicity. Legal measurements restricting easy access to large amounts could reduce excessive use and accompanying health issues.

### References

[1] van Riel AJHP, Hunault CC, van den Hengel-Koot IS, et al. Alarming increase in poisonings from recreational nitrous oxide use after a change in EU-legislation, inquiries to the Dutch Poisons Information Center. Int J Drug Policy. 2022;100:103519.
[2] Scherer M, Furr-Holden CD, Voas RB. Drug use disorder (DUD) questionnaire: scale development and validation. Eval Rev. 2013;37:35–58.

## 175. Gamma-hydroxybutyrate (GHB) withdrawal syndrome treated with GHB: the use of oral sodium oxybate in GHB-dependence

Søren Bøgevig, Mathies M. Jepsen and Tonny S. Petersen

Department of Clinical Pharmacology, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** In many European countries the use of gamma-hydroxybutyric acid (GHB) as a drug of abuse is widespread. Regular use of GHB can lead to a use disorder. Due to the short effect of the drug, the GBH use disorder is associated with very frequent intakes of GHB, i.e., approximately 2 hourly (also at night). The GHB withdrawal syndrome is characterized by rapid onset of symptoms (e.g., tremor, nausea, tachycardia, insomnia, anxiety) and swift progression of severity, including severe agitation, delirium and epileptic seizures. Benzodiazepines (BZDs) or/and barbiturates, often in very high doses, have been used to treat GHB withdrawal, but BZD resistance commonly occurs. In the Netherlands GHB dependence has been studied systematically and treated with GHB tapering. The Danish Poisons Information Centre has, by tradition, been involved in GHB-dependence and in 2016 the first patient was treated with sodium oxybate (SO) for severe withdrawal. In 2021 SO was introduced as an "off label" treatment in GHB dependence, using a "titrate and taper"-protocol in nine hospitals in the Capital Region of Denmark. The aim of this data monitoring project was to investigate the use of the treatment protocol and see if SO was effective and safe.
**Methods:** Data was continuously collected in a 12-month period (1 May 2021 – 30 April 2022). All patients treated with SO (for GHB-withdrawal) were identified in the electronic prescription module (Sundhedsplatformen, Epic). Data included: demographics, amount of "street"-GHB use and concomitant use of other drugs and ethanol, the use of SO (time to 1 dose, duration and amount used during titration and tapering), symptoms, intensive therapy, use of BZDs and adverse effects of SO.
**Results:** In total, 41 patients were included. The average age was 30 (±6) years. The amount of daily "street" GHB was 143 mL. Overall 29/41 were treated with oral SO within 5 hours of admission. The optimal titration dose (=symptom control) of SO was found after 6 (±5) hours and an average treatment duration with SO was 8.5 (±5) days. SO provided symptom control in cases where large doses of BZDs (>1000 mg diazepam) had already been tried and in patients already intubated due to severe withdrawal. No severe adverse effects of SO were recorded.
**Conclusion:** The use of SO to treat the GHB-withdrawal in a "titrate and taper" protocol has so far proven to be both safe and effective in a Danish hospital setting and has markedly changed patient care in GHB withdrawal syndrome.

## 176. Co-exposure to gamma-hydroxybutyrate (GHB) attenuates stimulant effects of methamphetamine to a greater degree than co-exposure to benzodiazepines

Shaun Greene[a], Rebekka Syrjanen[a], Sarah Hodgson[a], Rachelle Abouchedid[a] and Jennifer Schumann[b]

[a]Victorian Poisons Information Centre, Melbourne, Australia; [b]Victorian Institute of Forensic Medicine, Melbourne, Australia

**Objective:** Acute methamphetamine toxicity is associated with sympathomimetic stimulation and neuropsychiatric disturbance, including agitation [1]. First line management interventions include benzodiazepine administration. Co-ingestion of benzodiazepines with methamphetamine may attenuate stimulatory-induced sympathomimetic stimulation, including agitation. Other central nervous system (CNS) depressants including GHB are commonly co-used with methamphetamine [2]. We examined the effect of co-exposure to benzodiazepines versus co-exposure to GHB in patients presenting to emergency departments with analytically confirmed methamphetamine exposure.
**Methods:** Data was extracted from a human research ethics committee approved clinical registry collecting de-identified clinical and analytical data on a convenience sample of illicit drug presentations to emergency departments (ED) in Victoria, Australia [3]. Blood samples are analysed using combined liquid chromatography/mass spectrometry/time of flight mass spectrometry for 575 common pharmaceutical psychoactive substances (including 324 novel psychoactive substances). Methamphetamine (Meth-Lone), methamphetamine with benzodiazepine co-detection (Meth-BZD) and methamphetamine with GHB co-detection (Meth-GHB) were compared. Cases were excluded if any stimulant or CNS depressant other than methamphetamine, GHB, or a benzodiazepine was also detected.
**Results:** Median methamphetamine blood concentration (0.2 mg/L) was significantly higher ($p < 0.0001$) in Meth-GHB cases ($n = 78$) versus Meth-BZD cases ($n = 83$, 0.07 mg/L) and Meth-Lone cases ($n = 105$, 0.1 mg/L). Percentage of patients presenting with agitation was significantly lower in Meth-BZD cases and Meth-GHB (36 and 39%, respectively) compared to Meth-Lone cases (58%, $p = 0.01$). Presentation median heart rate in Meth-GHB cases (76 beats per min) was significantly lower than in Meth-Lone cases (110 beats per minute, $p < 0.0001$), and in Meth-BZD cases (96 beats per minute, $p = 0.008$). Median presenting systolic blood pressure was 130 mmHg for both Meth-Lone cases and Meth-GHB cases. Presenting systolic blood pressure was significantly lower (120 mmHg) in Meth-BZD cases ($p < 0.0003$). Presenting temperature for Meth-GHB cases was significantly lower (35.7°C) compared to Meth-Lone cases (36.4°C, $p < 0.0001$) and Meth-BZD cases (36.2°C, $p < 0.0001$).
**Conclusion:** Despite significantly higher methamphetamine blood concentrations, patients with methamphetamine-GHB co-exposure had significantly reduced levels of sympathomimetic stimulation, including agitation. GHB analogues may be beneficial for management of acute methamphetamine toxicity.

### References

[1] Harnett JT, Dargan PI, Dines AM, et al. Increasing emergency department attendances in Central London with methamphetamine toxicity and associated harms. Emerg Med J. 2022;39:463–466.
[2] Wodarz N, Krampe-Scheidler A, Christ M, et al. Evidence-based guidelines for the pharmacological management of acute methamphetamine-related disorders and toxicity. Pharmacopsychiatry. 2017;50:87–95.
[3] Syrjanen R, Schumann J, Fitzgerald J, et al. The Emerging Drugs Network of Australia-Victoria Clinical Registry: a state-wide illicit substance surveillance and alert network. Emerg Med Australas. 2023;35:82–88.

## 177. Investigation of differences in the neurorespiratory effects after oral administration of γ-hydroxybutyrate versus γ-butyrolactone with a pharmacokinetic modelling approach in the rat

Tannina Bellil[a], Lucie Chevillard[a], Jean-Michel Gaulier[b] and Bruno Mégarbane[a]

[a]INSERM UMRS-1144, Paris Cité University, Paris, France; [b]ULR 4483, Lille University, Lille, France

**Objective:** γ-hydroxybutyrate (GHB) and its more easily available precursor γ-butyrolactone (GBL), marketed for legal industrial applications, are increasingly used as recreational drugs and have been involved in cases of sexual assaults. Our aim was to compare the neurorespiratory effects and blood GHB pharmacokinetics obtained after the oral administration of GHB or GBL in a rat model mimicking human poisonings.
**Methods:** The neurorespiratory effects of orally administered GHB and GBL were investigated in comparison to saline in rats (n = 6/group), using clinical sedation scale, body temperature, plethysmography, arterial blood gas, and blood lactate measurements. A preliminary approach allowed us to determine the following doses to use to obtain comparable clinically evaluated sedation and bradypnea: 18.5 mmol/kg GHB (corresponding to 110% of its reported lethal dose-50%) and 9.1 mmol/kg GBL (corresponding to 50% of its lethal dose-50%). The areas under the curve of each measured parameter versus time were determined. Comparisons were performed using Student t-tests and two-way ANOVA followed by Dunnett's test for multiple comparisons. Blood was sampled using dried blood spots (10μL) and GHB concentrations determined using supercritical fluid chromatography. Plasma GHB concentration versus time profile after oral GHB or GBL administration were modeled using a one-compartment model with linear elimination and non-linear or linear absorption, respectively (WinNonlin-Phoenix®, Certara, NJ).
**Results:** Rats exhibited significant sedation ($p < 0.05$ with GHB and $p < 0.01$ with GBL), bradypnea and hypothermia in comparison to saline ($p < 0.05$). Hypoxemia ($p < 0.05$) with mixed (respiratory and metabolic with non-lactic increased anion gap) acidosis (arterial pH, $p < 0.01$) was obtained with GBL administration. However, GBL did not significantly alter the minute volume although it significantly increased the inspiratory time ($p < 0.01$), the expiratory time ($p < 0.01$), and the tidal volume ($p < 0.001$). GHB was responsible for non-significant trends in all these parameters, however without acidosis. After oral administration of 18.5 mmol/kg GHB versus 9.1 mmol/kg GBL, blood GHB peaked at 2 h ($C_{max}$, 16.5 ± 3.2 mmol/L) versus 40 min ($C_{max}$, 12 ± 3.1 mmol/L). GHB absorption was characterized by a nonlinear mechanism (Tabs = 1.84 h) after GHB administration but a linear mechanism (rate constant, 2.46h$^{-}$) after GBL administration. Blood GHB followed first-order pharmacokinetics with an apparent distribution volume of 1.3 versus 0.41 L/kg and an apparent clearance of 0.21 versus 0.10 L/kg.h, respectively.
**Conclusion:** Both GHB and GBL are responsible for neurorespiratory effects in our rat model, but those following oral GBL administration are more marked despite the use of lower doses. Differences in toxicity between GHB and GBL seem related to differences in pharmacokinetic profiles, at least partly explained by the higher GHB bioavailability after oral GBL administration than after GHB administration.

## 178. Insulin kinetics in high dose insulin therapy – a human randomized controlled trial

Søren Bøgevig[a], Tonny S. Petersen[a], Troels Riis[a], Andreas Brønden[a], Louis Praeger-Jahnsen[b], Lennart Friis-Hansen[b], Lotte C. G. Høgberg[c] and Mikkel B. Christensen[d]

[a]Department of Clinical Pharmacology, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [b]Department of Clinical Biochemistry, Center for Translational Research, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [c]Department of Anaesthesia and Intensive Care, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [d]Department of Clinical Pharmacology, Center for Translational Research, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** High dose insulin/glucose therapy (HIT) has gained much attention as a treatment modality in severe overdoses with calcium channel blockers and/or beta-adrenergic antagonists. Evidence for HIT stems mainly from animal studies and human case reports, whereas randomized human trials investigating the effectiveness and adverse events of HIT are scarce. Elimination of insulin in these extreme supraphysiological (and unlabelled) doses has never been systematically studied but is important during and especially after termination of HIT, where glucose infusions are still necessary. We investigated HIT in a randomized controlled trial, and, as a secondary endpoint, measured insulin concentrations prior, during and after 2 hours of HIT.
**Methods:** We randomized 10 healthy male participants (age 18–38, BMI 20–28), to a 2-hour infusion of high dose insulin (10 IE/kg/h as infusion) or placebo on top of an intravenously administered beta-adrenergic antagonist (esmolol infusion 0.25 mg/kg/min) or placebo on four separate days. We measured hemodynamics and sampled blood at prespecified timepoints prior, during, and after the infusion for measurements of plasma insulin (electrochemiluminescence immunoassay Cobas 801e, Roche Diagnostics GmbH, Mannheim, Germany).
**Results:** Maximal concentration ($C_{max}$) of insulin at the end of insulin infusion was (mean ± SEM) 347 ± 33.3 nmol/L on insulin-placebo days and 341 ± 56.6 nmol/L on insulin-esmolol days. Insulin elimination followed first order kinetics and half-life was 71 ± 4.7 minutes and 63 ± 2.5 minutes on insulin-placebo and insulin-esmolol days, respectively. Normal (physiological) levels of insulin (picomolar range) were reached around 10 hours after the end of the infusion.
**Conclusion:** After two hours of HIT in healthy individuals, insulin concentrations were roughly a thousand times higher than normal physiological concentrations around 0.340 nmol/L. The elimination of insulin after termination of HIT followed first-order kinetics, with insulin half-life just above one hour on average reaching physiological levels after 10 hours.

## 179. A prospective validation study of a clinical decision instrument for head computed tomography in intoxicated patients presenting to the emergency department

Richard McNulty[a,b], Maiana Hegh[c], Elena Xu[b], Earl Butler[a] and Naren Gunja[a]

[a]Western Sydney Toxicology Service, Sydney, Australia; [b]Emergency Department, Blacktown-Mt Druitt Hospitals, Sydney, Australia; [c]School of Medicine, Western Sydney University, Sydney, Australia;

**Objective:** Head computed tomography (CT) in intoxicated patients is a common, resource intensive and low yield investigation. Our recent retrospective study suggested that acute pathology was only found on head CT if the intoxicated patient had at least one of the following clinical features: intubation, head injury, seizures, focal neurological deficits or headache [1]. We hypothesised that the absence of these key features could be used as a decision instrument to rule out the need for head CT.
**Methods:** We prospectively collected data for all adult intoxicated patients with Glasgow Coma Score (GCS) < 15 between March 2021 and May 2022 attending the four emergency departments (ED) covered by our toxicology service. We also included intoxicated patients discharged from the ED and neurosurgical admissions. Head CT was ordered at the ED clinicians' discretion. We recorded clinical presentation features, agents and head CT results.
**Results:** During the 15-month study period, there were 219,273 ED attendances. There were 1,315 patients with GCS <15 due to intoxication; mean age 38 years. Common ingestions were ethanol (468), stimulants (134), GABA-ergics (128) and opioids (66). In total 407 patients had head CT (31%), of which 31 patients (8%) had acute head CT findings: 19 intracranial haemorrhages, 2 skull fractures, 6 nose fractures, 2 oedema/hypoxia ischaemic injuries and 7 scalp haematomas. All acute findings on head CT were associated with at least one of the key features above. All had a history of fall or signs of head injury. In addition, 8 had headache, 6 were intubated, 3 seizures and 1 focal neurological deficit (arm weakness). Thirteen patients had 2 features and 3 had 3 features. Absence of the key features gave 100% negative predictive value for acute head CT findings. In patients that were not scanned, there were no representations because of deterioration.
**Conclusion:** Our prospective internal study is further evidence that acute findings on head CT of intoxicated patients in the ED are only found in those who had one of the key features above. There is potential for development of a rule-out clinical decision instrument for head CT in intoxicated patients.

### Reference

[1] McNulty R, Bandaranayake L, Wong T, et al. Utility of non-contrast head computed tomography in poisoned patients. Emerg Med Australas. 2021;33:888–892.

## 180. Reversible and transient thrombocytopenia induced by snake C-type lectin-like proteins (snaclecs) from nose-horned viper venom

Mojca Dobaja Borak[a], Kity Požek[b], Damjan Grenc[a], Adrijana Leonardi[b], Tihana Kurtović[c], Katarina Reberšek[d], Helena Podgornik[d,e], Alenka Trampuš Bakija[f], Beata Halassy[c], Igor Križaj[b] and Miran Brvar[g]

[a]Centre for Clinical Toxicology and Pharmacology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [b]Department of Molecular and Biomedical Sciences, Jožef Stefan Institute, Ljubljana, Slovenia; [c]Centre for Research and Knowledge Transfer in Biotechnology, University of Zagreb, Zagreb, Croatia; [d]Department of Haematology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [e]Department of Clinical Biochemistry, Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia; [f]Division of Pediatrics, University Medical Centre Ljubljana, Ljubljana, Slovenia; [g]Centre for Clinical Toxicology and Pharmacology, Faculty of Medicine, University Medical Centre Ljubljana and Centre for Clinical Physiology, University of Ljubljana, Ljubljana, Slovenia

**Objective:** In Slovenia, the nose-horned viper (*Vipera ammodytes ammodytes*, *Vaa*) is the most medically important venomous snake, and a *Vaa* snakebite can result in severe thrombocytopenia. Since no agonists of platelet aggregation have been detected in Vaa venom, snake C-type lectin-like proteins (snaclecs) could be responsible for the occurrence of thrombocytopenia. The aim was to evaluate platelet count and function by thromboelastometry in Vaa-envenomed patients, to isolate snaclecs from *Vaa* venom and to investigate their ability to bind platelet receptors and trigger agglutination/aggregation.
**Methods:** In this clinical study, we evaluated platelet function in *Vaa*-envenomed patients with thrombocytopenia by rotational thromboelastometry (ROTEM) before and after antivenom therapy. Standard coagulation measurements and ROTEM indicators such as clot formation time (CFT) and maximum clot firmness (MCF) for extrinsic (EXTEM) and intrinsic (INTEM) ROTEM were obtained. In the biochemical part of this study, we isolated snaclecs from crude *Vaa* venom using a combination of different liquid chromatography techniques, and identified *Vaa*-snaclecs in pure fractions by liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS). In *ex vivo* studies, we investigated snaclecs binding to platelet receptors and platelet activation by flow cytometry. The ability *of Vaa* snaclecs to cause thrombocytopenia was assessed *ex vivo* with platelet aggregation/agglutination assays.
**Results:** Eight *Vaa*-bitten patients with thrombocytopenia on admission were included. *Vaa*-envenomation was confirmed by determination of *Vaa* venom in serum (66 ± 53 ng/mL). A profound thrombocytopenia ($42 \pm 32 \times 10^9$/L) was observed in all patients. On admission, CFT for EXTEM and INTEM were abnormally prolonged (316 ± 140 and 329 ± 156 seconds) and MCF for EXTEM and INTEM were abnormally low (40 ± 6 and 39 ± 7 mm). All patients were treated with $F(ab')_2$ fragments raised against the whole viper venom, and thrombocytopenia was reversed in all patients within one hour ($158 \pm 27 \times 10^9$/L). The CFT for EXTEM and INTEM (93 ± 24 and 112 ± 17 seconds) and MCF for EXTEM and INTEM (58 ± 4 and 56 ± 5 mm) returned to within normal limits after administration of $F(ab')_2$ fragments, indicating preserved platelet function after profound and transient/reversed thrombocytopenia. *Ex vivo* studies showed that the isolated dimeric *Vaa*-snaclec-3&2 binds to the platelet GPIb receptor and causes platelet agglutination with a drop in platelet count without platelet activation, as the expression of GPIIb/IIIa and P-selectin, markers of platelet activation, remained unchanged in comparison to control.
**Conclusion:** *Vaa*-envenomation causes profound and transient thrombocytopenia of functional platelets. *Vaa*-snaclec-3&2 binds to the GPIb receptors and causes a transient decrease in platelet count without activation and impairment of platelet function.

## 181. Investigation of oxycodone-induced neuro-respiratory effects in a rat model using a PK/PD approach

Maria Tannous[a], Lucie Chevillard[a], Jean-Michel Gaulier[b] and Bruno Mégarbane[a]

[a]INSERM UMRS-1144, Paris Cité University, Paris, France; [b]ULR 4483, Lille University, Lille, France

**Objective:** Oxycodone is a potent mu-opioid receptor agonist, however, one-and-a-half time less powerful than morphine. Oxycodone has played a major role in the opioid overdose crisis that resulted in about half a million of deaths in the US since the early 2000s. We aimed to characterize oxycodone-induced neuro-respiratory effects using a pharmacokinetic (PK)/pharmacodynamic (PD) approach.
**Methods:** The neuro-respiratory effects of oxycodone injected intravenously at 50% of its lethal dose (22.8 mg/kg) were investigated in comparison to saline in catheterized rats ($n = 9$/group) using clinical sedation scale, body temperature, plethysmography, arterial blood gas, and blood lactate measurements. Naloxone-related effects were tested. The areas under the curve of each parameter versus time were determined. Comparisons were performed using Student *t*-tests and one-way ANOVA followed by Dunn's test for multiple comparisons. Plasma concentrations of oxycodone and its main metabolite noroxycodone were measured using liquid chromatography coupled to mass spectrometry in tandem. Concentrations versus time profiles were modeled using a two-compartment and a one-compartment model with linear elimination, respectively (WinNonlin-Phoenix®, Certara, NJ).
**Results:** Oxycodone induced rigidity ($N = 9/9$), seizures ($N = 4/9$), and death ($N = 1/9$). Significant sedation (using $AUC_{0\text{-}150}$, $p < 0.05$) but only mild decrease in temperature (at 4 h, $p < 0.05$ and 5 h, $p < 0.01$) were observed. Oxycodone induced significant hypoxemia ($p < 0.05$) and mixed respiratory/lactic acidosis with elevation in arterial partial pressure of carbon dioxide ($PaCO_2$, $p < 0.05$), decrease in blood bicarbonate ($p < 0.05$) and increase in lactate ($p < 0.001$). Despite no significant alterations in the minute volume, tidal volume, and respiratory rate, there was a significant increase in inspiratory time ($p < 0.05$) but a decrease in expiratory time 4 hours post-injection ($p < 0.05$). Subcutaneous 1.6 mg/kg naloxone administration 5 min after oxycodone significantly reduced sedation ($p < 0.01$), increased temperature ($p < 0.05$), and minute volume ($p < 0.05$). Oxycodone followed a first-order PK with a steady-state distribution volume of 4.8 L/kg, an elimination half-life of 1.3 h, and a clearance of 4.1 L/h/kg. Noroxycodone followed a first-order elimination-dependent PK with a longer elimination half-life (1.44 h). PK/PD models for each tested effect showed concentration-dependent alterations, starting with sedation and increase in inspiratory time before seizures.
**Conclusion:** Despite its relatively limited potency, oxycodone is responsible for concentration-dependent opioid receptor-related neuro-respiratory toxicity including seizures and lactic acidosis.

## 182. Untargeted liquid chromatography-mass spectrometry (LC-MS) to identify toxic exposures can reduce unnecessary testing: a case of guanfacine poisoning

David H. Schaffer, Abigail Kerns, Lindsay A. L. Bazydlo and Christopher Holstege

University of Virginia, Charlottesville, VA, USA

**Objective:** Patients frequently present with a suspected toxic exposure but no readily available clinical test can confirm the diagnosis, often resulting in extensive testing for non-toxicologic pathology. We report a case of a 12-month old presenting with guanfacine poisoning, first identified by liquid chromatography-mass spectrometry (LC-MS), which prevented invasive and unnecessary testing and follow-up.
**Case report:** A 12-month old female with no past medical history was found to be persistently somnolent after her parents attempted to awake her from a nap. Emergency medical services (EMS) transported her to the emergency department. Initial vital signs were temperature 36.5 °C, heart rate 96 beats/min, respiratory rate 28 breaths/min, blood pressure 102/42 mmHg. Exam was remarkable for a lethargic infant with miotic pupils, normal tone, and moist mucus membranes. Laboratory studies were remarkable for a serum bicarbonate of 14 mEq/L and anion gap of 17 mEq/L. Serum ethanol, salicylates, and acetaminophen were all undetectable, and a urine drug screen was negative. The patient was admitted for further evaluation and monitoring. Brain magnetic resonance imaging (MRI) was unremarkable. Altered mental status persisted and untargeted liquid chromatography quantitative time-of-flight mass spectrometry (LC-QTOF MS) testing of urine was performed for suspected poisoning. The data was collected using information-dependent acquisition (IDA) method and matched to a library, where guanfacine was identified using accurate mass and product ion ($MS^2$) spectra data. The sample was then sent out to a CLIA-certified reference lab for confirmation of the guanfacine in the urine at a concentration of 25 ng/mL. The hospitalist caring for the patient had been prepared to perform a lumbar puncture to test for other causes of encephalopathy and genetics consultation was considered, both of which were canceled after urine MS testing resulted. Further history revealed that guanfacine was prescribed to an older sibling and was present in the home. The primary care pediatrician was informed and a report was filed to the local authorities.
**Conclusion:** In this era of designer drugs and novel drug analogs, there is a paucity of clinically available rapid testing which can confirm diagnosis of a toxic exposure. Supportive care and testing for alternative causes are the mainstay of management. This case demonstrates that use of untargeted LC-QTOF MS has potential to confirm diagnosis and reduce invasive, lengthy, and expensive testing for non-toxicologic pathologies in the pediatric population.

## 183. Ketamine intoxication mimicking catatonia

Abigail Kerns, Lindsay A. L. Bazydlo and Christopher Holstege

University of Virginia, Charlottesville, VA, USA

**Objective:** Ketamine is a dissociative anesthetic that antagonizes N-methyl-D-aspartate (NMDA) receptors. It has been recently advocated for treatment-resistant depression and catatonia [1]. We report a case of ketamine intoxication due to abuse that was initially misdiagnosed with catatonia.
**Case report:** A 34-year-old male with history of alcohol use disorder presented to the emergency department with altered mentation. Two days prior he suddenly developed mutism with frequent pacing around the house. His mother reported recent misuse of oxycodone and alprazolam. Vital signs were: blood pressure 173/105 mmHg, pulse 80 beats/minute, respiratory rate

19 breaths/minute, temperature 36.8 °C. Exam was notable for a male pacing around the room who would not answer questions or engage with staff. He was able to say the word "ketamine". He had bilateral horizontal nystagmus. Laboratory testing was significant for a white blood cell count of $13 \times 10^9$/L, bicarbonate 20 mEq/L, and anion gap of 17 mEq/L. Urine immunoassay screen was positive for marijuana. Psychiatry was consulted, catatonia was diagnosed, and lorazepam was recommended. Over the course of five hours mental status improved, and he was able to provide additional history. He reported snorting ketamine over the preceding months with recent escalation in doses. His mother subsequently brought in a bag of white powder which he was able to identify as ketamine that he purchased on the Internet's dark web. His clinical status remained stable, and he was discharged 18 hours after presentation. The patient presented again that afternoon for abdominal pain and gross hematuria. Urinalysis was positive for hematuria, which was attributed to recent use of ketamine. Analysis using liquid chromatography with high resolution tandem mass spectrometry was positive for ketamine.

**Conclusion:** The dissociative effects of ketamine lead to misuse. Diverted ketamine and its analogs can be purchased from the Internet. Ketamine intoxication can present with diverse neuropsychiatric manifestations. Patients may present with inebriation and may be agitated or violent. Stupor or coma can occur. Ketamine use has also been associated with ulcerative cystitis that can present with gross hematuria [2]. This case report details a patient with neurological signs hematuria who was initially misdiagnosed with catatonia and later admitted to escalating doses of intranasal ketamine.

## References

[1] Iserson KV, Durga D. Catatonia-like syndrome treated with low-dose ketamine. J Emerg Med. 2020;58:771–774.

[2] Shahani R, Dickson B, Stewart RJ, et al. Ketamine-associated ulcerative cystitis: a new clinical entity. Urology. 2007;69:810–812.

# 184. Influence of age on clinical outcome following corrosive ingestion in adults

Blanka Caganova[a], Silvia Plackova[a], Erik Puchon[a] and Igor Batora[b]

[a]National Toxicological Information Centre, University Hospital Bratislava, Bratislava, Slovakia; [b]Department of Occupational Medicine and Toxicology, Faculty of Medicine, Comenius University Bratislava, Bratislava, Slovakia

**Objective:** Corrosive poisoning is still associated with many fatalities. The purpose of the present study was to compare the clinical outcomes of corrosive ingestion injury in elderly and non-elderly adults with regard to severity of mucosal injury, complications, and mortality.

**Methods:** Corrosive substance exposures reported to the National Toxicological Information Centre in Slovakia during 2000–2020 were reviewed retrospectively. Only patients who underwent an endoscopic evaluation within 24 hours were included in the study. The patients were divided into two groups: the non-elderly (<60 years) and elderly adults (≥60 years). Data were evaluated for demographic and clinical factors. Endoscopic findings were classified according to Zargaŕs classification [1].

**Results:** We retrospectively analyzed medical reports of 176 adult patients with acute corrosive ingestion. The non-elderly group comprised 115 (65.3%) patients younger than 60 years whereas in the elderly group there were 61 (34.7%) patients 60 years of age or older. The mortality rate in the elderly was significantly higher (elderly 23.0% versus non-elderly 11.3%). The incidence of respiratory complications was almost two times higher in the elderly (31.1% versus 17.4% for the non-elderly). Patients in the elderly group developed respiratory failure (27.9%) more often compared to younger adults (15.7%). Respiratory complications significantly correlated with an increased mortality rate in the elderly whereas there was no association between gastrointestinal complications and mortality in the elderly. Leukocytosis developed more frequently in the elderly group (34.4 versus 9.6%). Antibiotic usage was significantly more frequent in the elderly group compared to younger adults (63.9 versus 48.7%). The difference in the mean length of hospital stay between the non-elderly and elderly groups was significant (4.8 versus 8.2 days). The highest risk of complications and fatalities was observed in patients after hydrochloric acid ingestion.

**Conclusion:** Our 20-year study confirmed that mortality after corrosive ingestion is significantly higher in patients aged ≥60 years. Elderly patients with respiratory complications had the poorest clinical outcomes.

## Reference

[1] Zargar SA, Kochhar R, Mehta S, et al. The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. Gastrointest Endosc. 1991;37:165–169.

# 185. Caustic accidents due to ingestion of industrial products in public places: a case series

Valentina Negrini[a], Cristina Grazioli[a], Davide Lonati[b], Benedetta Brolli[a], Lucia Bernasconi[a], Azzurra Schicchi[b], Valeria M. Petrolini[b], Olha Maystrova[b], Francesca Crema[c] and Carlo A. Locatelli[b]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS. Postgraduate School of Pharmacology and Clinical Toxicology, University of Pavia, Pavia, Italy; [b]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy; [c]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy

**Objective:** Ingestion of a caustic product may cause serious damage to the tissue of the gastro-enteric tract. One of the principal causes of accidents is the liquid transfer from the original container to an anonymous bottle (often smaller and easier to handle but without a proper label) that may be easily mistaken for a drink. In public places (e.g., bars or restaurants) caustic liquid may be served to the clients or drunk by the staff.

**Methods:** A retrospective analysis of caustic ingestions in public places and referred to our PCC between 2010 and 2022 was performed. We included cases in which an industrial product was involved and the esophagogastroduodenoscopy (EGDS) report was available.

**Results:** Thirty cases were evaluated (M/F: 22/8; median age 31.5 ± 30.5 years). Five were paediatric patients. Dishwasher detergent was the substance principally involved (18/30; 60%), containing high concentrations of sodium/potassium hydroxide. The symptoms commonly reported (immediately after ingestion)

Table 1. Results of esophagogastroduodenoscopy in 30 patients drinking a caustic product in a public place (e.g., bar or restaurant).

| Zargar classification | Oesophagus | Stomach |
|---|---|---|
| Grade 0 | 6/30 (20%) | 8/30 (26.7%) |
| Grade 1 | 0 | 0 |
| Grade 2A | 20/30 (66.7%) | 12/30 (40%) |
| Grade 2B | 1/30 (3.3%) | 4/30 (13.3%) |
| Grade 3A | 3/30 (10%) | 3/30 (10%) |
| Grade 3B | 1/30 (3.3%) | 3/30 (10%) |
| Grade 4 | 0 | 0 |

were vomiting (60%), throat/epigastric pain (43.3%), lip/tongue/oral oedema (36.7%), oral ulcers/de-epithelialisation (23.3%), sialorrhea (16.6%), and hematemesis (13.3%). EGDS (according to the Zargar classification) was negative only in 2 cases (Table 1). All patients were treated with intravenous proton pump inhibitors, fasting and antiemetics. In one patient cranial computerised tomography (CT) scan was also performed. One patient underwent surgical treatment. One patient died due to respiratory complications.

**Conclusion:** In case of ingestion even of minimal quantities, caustic products may cause severe damage (Grade 2A oesophagus 66.7%; stomach 40%) and potentially be life-threatening. The safe handling of these products is fundamental to avoid accidents with potentially lethal consequences. Transfer of products should be prohibited and the label with the information of toxicity should always be available to permit rapid intervention in case of accident.

## 186. Biological features of laundry detergent capsule poisoning in children: a 7 year study

Viorela Nitescu[a], Andreea Lescaie[b], Ioana Alexandra Ilisei[b], Alexandru Ulmeanu[a] and Coriolan Ulmeanu[a]

[a]Pediatric Poisoning Centre, University of Medicine and Pharmacy "Carol Davila". Bucharest, Romania; [b]Pediatric Poisoning Centre, Bucharest, Romania

**Objective:** To present biological changes and their correlation with the severity score in laundry detergent capsules poisoning in children.

**Methods:** A retrospective study of children with laundry detergent capsule poisoning admitted to our unit over a 7-year period (2015–2021). Demographic and epidemiological data, clinical features, biological parameters and Poisoning Severity Score (PSS) were analyzed using Excel-Analysis-ToolPak.

**Results:** Overall 157 children were included; median age of 1.92 years (SD: 1.18, IQR: 0.5–6.67) and a 1.24 male-to-female ratio. PSS was 0 in 8.9%, 1 in 78.3%, 2 in 11.5% and 3 in 1.3% of cases. After exclusion of infection, leukocytosis was present in 51 (32.7%); median leukocyte count was 12.595/mm$^3$ (SD: 4289, IQR: 6200–25,700) and was positively correlated with the PSS ($p = 0.04$). Median blood pH was 7.38 (SD:0.04, IQR: 7.27–7.51). Mild acidosis was noted in 37.9% and slightly increase of pH in 4.6% There was no correlation between pH and PSS ($p = 0.28$). Median base deficit was −5.1 mmol/L (SD: 2.48, IQR: 0.3 to −12.7) and 85% of cases had a lower base deficit. Base deficit was positively correlated with PSS ($p = 0.01$). Median lactate was 1.92 mmol/L (SD: 0.74, IQR: 1–4.9) and increased values were noted in 31.9% of cases. Lactate concentration was not correlated with PSS ($p = 0.1$). pH did not vary depending on the base deficit value (Pearson correlation 0.32) or on the lactate concentration (Pearson correlation −0.11). Electrolyte analysis showed all children had normal sodium concentration, 4 had an increased potassium concentration, 5 had a chlorine concentration of 1–2 mmol/L above upper limit of normal (ULN), and 3 children had a chlorine value below the lower limit of normal (LLN). Liver transaminase analysis showed 3 children with elevated alanine aminotransferase (ALT) and 50 (32.2%) with elevated aspartate aminotransferase (AST) (below 2× ULN). Thirteen children (8.7%) presented increased urea concentration, all below 2× ULN. Creatinine was normal in all cases.

**Conclusion:** The severity of poisoning was positively correlated with leukocyte count and base deficit value, but was not correlated with pH and lactate concentration. The pH was generally within normal limits, although children had increased values of base deficit and lactate concentration [1,2].

### References

[1] Davis MG, Casavant MJ, Spiller HA, et al. Pediatric exposures to laundry and dishwasher detergents in the United States: 2013–2014. Pediatrics. 2016;13:e20154529.

[2] Day R, Bradberry SM, Thomas SHL, et al. Liquid laundry detergent capsules (PODS): a review of their composition and mechanisms of toxicity, and of the circumstances, routes, features, and management of exposure. Clin Toxicol. 2019;57:1053–1063.

## 187. Fatal methanol poisoning: case report

Julia V. Radenkova-Saeva[a] and Dijana Angelov[b]

[a]Toxicology Clinic, University Hospital for Emergency Medicine "NI Pirogov", Sofia, Bulgaria; [b]Clinic of Toxicology, University Hospital for Emergency Medicine "N.I. Pirogov", Sofia, Bulgaria

**Objective:** Methanol poisoning is responsible for high morbidity and mortality all around the world. We report a case of fatal methanol poisoning.

**Case report:** A 58-year-old man was admitted to the emergency department after ingesting half a bottle of fluid with suspected methanol. The patient was found unconscious on the street without accompanying documentation. On arrival, he was intubated and mechanically ventilated due to a low Glasgow Coma Score of 3/15. Physical examination showed the following: pupils were not reactive to light on both sides. Initial blood pressure was 60/40 mmHg with a regular heartbeat of 91 beats/min. Respiratory rate was 11, and oxygen saturation 93.8%. Auscultation of the lungs was normal. The heart sounds showed no abnormalities. The remaining physical examination was normal. Initial laboratory testing identified severe metabolic acidosis. Arterial blood gases revealed a pH 6.88, $pO_2$ 107.22 mmHg, $pCO_2$ 25.37 mmHg, bicarbonate 4.6 mmol/L, and base excess −28.5. Blood tests showed a methanol concentration of 2.16 g/L; ethanol was not detected. Treatment included supportive care, administration of sodium bicarbonate for correction of acidosis, administration of 95% ethanol solution as antidote. Hemodialysis is considered effective in clearing methanol, but due to severe hemodynamic instability hemodialysis was not an option in this case. The patient's general condition continued to rapidly deteriorate and approximately 2 hours after admission he died, despite emergency medical personnel resuscitation efforts. It is likely the patient ingested a large amount of methanol over a long period of time, without concomitant ethanol use, and the methanol was metabolized into its toxic metabolite, formic acid.

**Conclusion:** Poisoning with methanol is life-threatening and needs rapid recognition and early treatment. Morbidity and mortality depends on the interval between ingestion and initiation of therapy. Patient outcomes can be improved if methanol

poisoning is recognized and treated promptly, before the methanol is metabolized into formic acid.

## 188. An unexpected case of fatal detergent ingestion

Amy Thomson, Rachel Khoury-Harb and Genevieve Adamo

NSW Poisons Information Centre, Sydney, Australia

**Objective:** To describe a fatal outcome from a "low concentration" detergent. Benzalkonium chloride (BZK) is a quaternary ammonia compound disinfectant. Accepted evidence suggests severe injury is rare unless the concentration is greater than 7.5%. In this case an 89-year-old inadvertently ingested 200 mL of BZK 5% leading to a fatal outcome.
**Case report:** An 89-year-old male living in a nursing home, was found leaning over his bathroom sink coughing and salivating, and unable to say what had occurred. A bottle of a cleaning product containing BZK was found half empty with the lid missing in his room. At 14:39, a nurse contacted the Poisons Information Centre (PIC) stating 10–15 mL of dilute product had been ingested, describing the patient as asymptomatic. Between 15:40 and 16:45 he deteriorated, persistently coughing, with dysphagia, impaired breathing and haemoptysis prompting ambulance retrieval. At 18:00, the Emergency Department called the PIC reporting he had haematemesis, was unable to lie flat and had ingested 200 mL of BZK. He was subsequently intubated and endoscopy revealed excessive bleeding and friability of necrotic appearing muscosa. At 04:20, he developed ventricular tachycardia followed by cardiac asystole.
**Conclusion:** This is a case of an unexpected death due to a BZK ingestion. BZK disrupts lipid bilayers, and the effects of ingestion include mucosal and tissue irritation, with gastritis, and more serious adverse reactions include corrosive injury, circulatory failure, and death. The risk of toxicity was thought to be related to concentration as exposure to products more than 7.5% are known to cause corrosive injury [1]. This case demonstrates that the concentration of the product and total dose ingested must be considered together to make an appropriate risk assessment. Thorough history taking is vital to ascertain specific patient risk factors including dilution factors, volume ingested, and symptoms exhibited which contribute to seeking early medical attention and may prevent harm. In humans, an oral dose of BZK 100–400 mg/kg is thought to be fatal [2]. This patient ingested approximately 139 mg/kg, lack of symptom recognition and assumptions around size of ingestion, and dilution of the product all contributed to delayed access to definitive care and a fatal outcome.

### References

[1] Detergents-Cationic. In: In Depth Answers [database on the Internet]. Greenwood Village (CO): IBM Corporation; 2020 [cited 2021 Mar 12]. Available from: www.micromedexsolutions.com.
[2] Benzalkonium chloride used as an excipient. Report published in support of the 'Questions and answers on benzalkonium chloride used as an excipient in medicinal products for human use'. European Medicines Agency; 09/10/2017 [cited 2021 Mar 12]. Available from: https://www.ema.europa.eu/en/documents/report/benzalkonium-chloride-used-excipient-report-published-support-questions-answers-benzalkonium_en.pdf.

## 189. Household hazard due to hygiene products – a whole new form of "nappy rash"

Mandy Gollmann[a], Anja Michel[b] and Anne Stürzebecher[a]

[a]Poison Information Centre Erfurt, Erfurt, Germany; [b]Poison Information Centre Freiburg, Freiburg, Germany

**Objective:** It is known that quaternary ammonium compounds are corrosive to the skin in higher concentrations (>7.5%). However, prolonged exposure to the skin may cause severe chemical burns even in lower concentrations. We report on a case of a child that suffered severe corrosive injury after long exposure to a laundry sanitiser under occlusion.
**Case report:** At around 7 p.m., a mother put a nappy on her 2-year-old daughter that had been contaminated by a spill of laundry sanitiser in the shopping bag earlier in the day. The sanitizer contained, among others, 2–3% of quaternary ammonium compounds. The nappy was not wet, nor did it smell significantly of the product when the child put it on. Only a stain on the outside of the nappy indicated contamination. The girl was then put to bed. After 2–3 hours, she woke up screaming and crying in pain. At this time, a patch of erythema of approximately $5 \times 10$ cm was visible on her left inner thigh. The mother initially applied an antihistaminic to the site suspecting an insect bite, as well as oral acetaminophen for the pain. Additionally, the child was bathed to remove possible remaining laundry sanitiser. The Poison Information Center was then contacted, who recommended seeing a physician the following day in case of no improvement. Around 1 a.m., the girl was presented to the emergency department due to increasing discomfort. The clinical manifestation developed to the full extent around 10 a.m. the following morning with extensive blistering and third-degree chemical burns. Surgical debridement became necessary to remove the blisters, and the wound dressing was changed daily. Over the next 4 weeks, however, wound healing was protracted and deficient. Because of presumed deeper extension into the tissue, it was discussed whether a compression stocking was necessary.
**Conclusion:** Quaternary ammonium compounds are believed to disrupt cell membranes by acting similarly to phospholipids and integrate in the membrane. Due to these properties, prolonged exposure even in low concentrations may lead to severe injury. Therefore, immediate and thorough decontamination after exposure to skin (and likewise eyes) is imperative to avoid corrosive injury.

## 190. Disinfectant ingestion – a real danger in children

Viorela Nitescu[a], Andreea Lescaie[b], Dora Boghitoiu[a] and Coriolan Ulmeanu[a]

[a]Pediatric Poisoning Centre, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania; [b]Pediatric Poisoning Centre, Bucharest, Romania

**Objective:** To present a severe case of Gigasept® disinfectant exposure in a child.
**Case report:** An 18-month-old boy was admitted to our clinic 5 hours after ingestion of an unknown quantity of Gigasept®, a professional disinfectant that contains coco propylenediamine guanidine diacetate 15.6 g, phenoxypropanol 35 g, benzalkonium

chloride 2.5 g per 100 g solution. He drank the disinfectant from a juice bottle stored at home. He vomited immediately after ingestion and within a few minutes developed glottal edema and severe acute respiratory failure that required intubation and artificial ventilation. On admission he was comatose, febrile (38.1 °C), intubated with mechanical ventilation, with intense oropharyngeal edema and hyperemia and massive swelling of the uvula. Blood tests revealed severe metabolic acidosis (pH 7.25, base excess −7.7 mmol/L). Chest X-ray showed bilateral perihilar alveolar infiltrates. Upper digestive endoscopy performed 24 hours after ingestion revealed esophageal and gastric caustic lesions classified as grade 2 and 3 according to Zargar's classification. Treatment included antibiotics (meropenem and gentamicin), corticoid therapy with methylprednisolone, omeprazole, a nasogastric tube for calibration and nutrition. He initially had progressively worsening of lung damage and developed a pneumothorax that required pipe drainage on the 7th day. Thereafter he began to improve. On the 10th day mechanical ventilation was stopped. The pneumothorax resolved (thoracic drainage was stopped on day 12). The nasogastric tube was removed on the 18th day. The second endoscopy performed on the 21st day revealed minimal lesions of the esophagus with ulcerations <0.5 cm and punctiform necrosis and diffuse discrete hyperemia of the gastric mucosa. He was discharged on the 25th day in good condition. At follow up evaluation one month after presentation he had a normal physical examination, blood tests and chest X-ray. Upper digestive endoscopy revealed normal esophageal and gastric mucosa with no signs of stricture.
**Conclusion:** Ingestion of Gigasept®, a very common and potent disinfectant, can cause very complex and severe damage which includes neurologic and respiratory involvement due to the glycol ether (phenoxypropanol) and gastrointestinal caustic lesions due to a quaternary ammonium compound (benzalkonium chloride).

## 191. Risk/benefit ratios of a new opioid peptide, its nociceptin-linked hybrid and their sustained-release hydrogel-based formulations: an experimental study in mice

Clara Bianchi[a], Lucie Chevillard[a], Charlotte Martin[b], Steven Ballet[b] and Bruno Mégarbane[a]

[a]INSERM UMRS-1144, Paris Cité University, Paris, France; [b]Research Group of Organic Chemistry, Vrije Universiteit Brussel, Brussels, France

**Objective:** Pain is a major public health issue. Opioid analgesic prescription is increasing, despite possible adverse effects, dependence, overdoses and even fatalities attributed to central respiratory depression. Fundamental research is focusing on the development of synthetic opioids with increased safety and sustained-release formulations allowing improving analgesia management with reduced risk of toxicity. Our aim was to evaluate the analgesic and neuro-respiratory effects of an opioid peptide (KGOP01) and its hybrid form associated to a nociceptin antagonist (KGNOP01) formulated alone or in co-formulation with a hydrogel.
**Methods:** The antinociceptive (using hot-plate method) and respiratory effects (using whole-body plethysmography) of these four compounds in comparison to saline were studied in mice after a unique subcutaneous administration (*N*=six mice/group). The areas under the curve (AUC from 0 to 24 hours) of each parameter versus time were determined. Comparisons were performed using Student t-tests and two-way ANOVAs followed by Dunnett's tests for multiple comparisons. The benefit/risk ratio was calculated by dividing the AUCs of analgesia and inspiratory time.
**Results:** Prolonged analgesia was observed up to 8 hours post-injection with all formulations ($p < 0.05$). KGOP01 was less potent than the hybrid form. Hydrogels allowed a prolonged and strengthened analgesia up to 24 hours ($p < 0.01$). Although no significant alteration in the minute volume was observed, all compounds except KGOP01 induced a significant increase in inspiratory time ($p < 0.05$). Interestingly, the formulations only induced a limited transient respiratory depression, with a better benefit/risk ratio for hydrogels compared to solutions.
**Conclusion:** Opioid hybrids and co-formulations represent encouraging solutions to reduce opioid-related toxicity while prolonging their analgesic effectiveness.

## 192. Lead poisoning in a family – plastic manufacturing or herbal powder?

Dong-Zong Hung

Division of Toxicology, China Medical University Hospital, Taichung City, Taiwan

**Objective:** Lead is a common toxic metal that contaminates the environment and is a concern because of its detrimental effects on the development of cognitive function in children [1]. Lead has been used for a long time in plastic production as a cost-effective stabilizer for polyvinyl chloride (PVC). We report a case of lead poisoning in a family where the cause was not immediately obvious.
**Case report:** A daughter of a family, 23 years old, suffered from lead poisoning (blood lead level (BLL) 70.05 μg/dL) with unstable gait. She complained of gastrointestinal upset and lower limb weakness for months. Hypertension, anemia, liver injury with jaundice, and decreased muscle power in both legs were also found at examination in the emergency room. The other three members of the family were subsequently found to have high BLLs (Table 1). They reported they had operated a family factory for plastic pellet manufacturing for more than 10 years. We performed a field investigation and only minimal lead was identified in samples taken from the factory, but a high lead content (105,500 μg/g) was detected in a bottle of herbal powder that was found on the table and had frequently been taken by the family for years. All the family were advised to stop taking the herbal powder and received chelation therapy. Their BLLs declined and the daughter improved clinically and was able to walk with minimal assistance after 6-months' treatment.
**Conclusion:** Herbal medicine adulterated with lead had been prohibited by the Chinese government for several years. There are still traditional Chinese medicine (TCM) practitioners who use it illegally, and clinicians must always pay attention to the patient's history of herbal medicine usage.

Table 1. Blood lead levels in a family with lead poisoning.

| | Father (45 years) | Mother (45 years) | Son (25 years) | Daughter (23 years) |
|---|---|---|---|---|
| Blood lead level (μg/dL) | 71.35 | 61.18 | 54.32 | 70.05 |

## Reference

[1] World Health Organization (WHO). Lead poisoning fact sheet [cited 2022 Oct 4]. Available from: https://www.who.int/news-room/fact-sheets/detail/lead-poisoning-and-health.

# 193. The effect of mercury on children

Olga Otrubova[a], Silvia Plackova[b], Blanka Caganova[b], Erik Puchon[b] and Igor Batora[c]

[a]Department of Occupational Medicine and Toxicology, Faculty of Medicine, National Toxicological Information Centre, Comenius University, Bratislava, Slovakia; [b]Department of Occupational Medicine and Toxicology, National Toxicological Information Centre, University Hospital Bratislava, Bratislava, Slovakia; [c]Department of Occupational Medicine and Toxicology, Faculty of Medicine, University Hospital Bratislava, Comenius University, Bratislava, Slovakia

**Objective:** The National Toxicological Information Centre (NTIC) was consulted on two cases with a similar course. In both cases the mother brought the youngest child to the physician because of fatigue or pain persisting for several weeks. Initial tests did not determine the cause of the symptoms. Older children in the families also had signs of illness and initially no-one connected them. Finally, consultation with NTIC and toxicology examination confirmed mercury exposure. Increased mercury concentrations were confirmed in other family members.
**Case reports:** Case 1: A 10-month-old male presented with a history of fatigue, weight loss, sweating, and inability to sit. Examination showed: tachycardia 160/min, hypertension, dehydration, muscle hypotonia, depigmentation, chest papules, and desquamation on the palms. The free thyroxine (fT4) was at the upper limit, and catecholamines were increased. The father occasionally worked in garbage collection, which along with the clinical picture triggered investigation for heavy metal poisoning. The initial blood mercury concentration was 36.93 μg/L. Treatment with 5 cycles of intravenous unithiol was well tolerated (blood mercury concentration 4.7 μg/L by day 144). Two years after the event, the boy was symptom-free. Independently the older sibling had chest pain and palpitations and was also treated with unithiol. Case 2: A 5-year-old female was suffering from pain in the waist area and the popliteal fossa subjectively so strong that she refused to walk, was fatigued and inappetent. Examination showed: tachycardia 130/min, hypertension, subfebrile temperature (below 38 °C), positional tremor of the upper limbs, and elevated fT4. The mother admitted later that the children found an unmarked container of mercury in the garage and played with it. The initial blood mercury concentration was 24.9 μg/L. Treatment with 4 cycles of intravenous unithiol was well tolerated, with progressive resolution of symptoms (blood mercury concentration was 4.32 μg/L by day 127). The older sibling had chest and abdominal pain, petechiae, and insomnia and also received unithiol.
**Conclusion:** Sensitivity to mercury in our cases depended on the age – the youngest children of these families had the most pronounced clinical signs. The initial picture of intoxication varied: Patient 1 – failure to gain weight, muscle weakness, skin manifestations, and sweating. Patient 2 was without skin manifestations (although her sibling had them), and had musculoskeletal pain, fatigue, reduced appetite, and tremor. In both cases, treatment with unithiol was well tolerated and difficulties improved. Behavioral changes, sweating, tremor as well as skin manifestations, cardiac problems, changes in thyroid parameters, and shifts in catecholamines may indicate mercury intoxication in children. The path to a correct diagnosis is difficult, so it is beneficial to contact a toxicologist in suspected cases.

# 194. Barium chloride poisoning

Kai-Ju Lee[a], Jou-Fang Deng[a] and Daniel Spyker[b]

[a]National Poison Center, Taipei Veterans General Hospital, Taipei City, Taiwan; [b]Emergency Medicine, Oregon Health & Science University, Portland, OR, USA

**Objective:** Though uncommon, barium poisoning can be life-threatening. Administration of magnesium sulfate or sodium sulfate can precipitate ingested barium to an insoluble sulfate salt and reduce barium absorption [1]. Given the rapid absorption of soluble barium salt, such intervention should be as early as possible [2]. Absorbed barium blocks passive efflux potassium channels, resulting in increased intracellular and decreased extracellular potassium, thus, aggressive correction of hypokalemia in the first 24 hours can lead to successful treatment. We report a case of intentional barium poisoning.
**Case report:** A 22-year-old female attempted suicide by ingesting 9 self-filled barium chloride capsules obtained from the Internet, approximately 4.5 g. She developed nausea, vomiting, abdominal pain, and chest tightness about 10 minutes after ingestion. Upon arrival in the emergency department, she was alert and vital signs were normal. Electrocardiogram (ECG) showed sinus rhythm with prolonged PR interval (229 ms), and QTc prolongation (653 ms). She also had hypokalemia (2.6 mmol/L) and elevated serum barium concentration (2806 mcg/L). Her gastrointestinal symptoms resolved after one dose of prochlorperazine and metoclopramide. With the diagnosis of barium chloride intoxication, she received magnesium sulfate orally, potassium supplement (60 mEq orally and 20 mEq intravenously) two hours after ingestion. Six hours after ingestion, her serum barium concentration was 1091 mcg/L and potassium was 4.5 mmol/L with normal ECG rhythm. Sequential serum barium concentrations were 0.577, 0.547, and 0.315 mcg/L respectively at 14, 20, and 32 hours after the ingestion. The patient was discharged with no further discomfort 2 days after ingestion. The pharmacokinetic profile suggests a two compartment distribution with first-order absorption. The model fit here was for an absorption half-life of 6.81 min and alpha and beta (initial and final) half-lives of 1.45 and 19.8 hours.
**Conclusion:** Our experience supports the treatment of barium-intoxicated patients with magnesium sulfate orally, antiemetic agents as needed, and aggressive management of potassium. Moreover, monitoring of ECG continuously until all laboratory data normalized and the toxidrome subsided. Patients usually recover within 24–48 hours.

## References

[1] Minns AB. Barium. In: Olson KR, Smollin CG, Anderson IB, et al., editors. Poisoning & drug overdose. 8th ed. New York: McGraw Hill; 2022.
[2] Zhang Q, Wang Y, Li X, et al. Metabolism of barium in the human body after suicidal ingestion: a CARE-compliant case report. Medicine. 2022;101:e30571.

## 195. Lead encephalopathy with fatal outcome in pediatric patients: a case series

Cinthia D. Gigliotti, Ana P. Voitzuk and Vanina Greco

National Poison Center (CNI), Profesor Alejandro Posadas National Hospital, Buenos Aires, Argentina

**Objective:** Lead is one of the ten chemicals that causes the greatest damage to global public health, used as raw material in different industries; 75% is destined for the manufacture of motor vehicle batteries [1]. The main sources of pollution in Argentina are industrial waste and foundries [2]. Children are more at risk of exposure due to genetic, nutritional and socioeconomic factors. Chronic exposure to low levels of lead produces irreversible neurocognitive-behavioral disorders. Lead encephalopathy is the worst manifestation of lead neurotoxicity [3]. We report 3 pediatric cases of encephalopathy due to environmental exposure to lead, consulted at our Poison Center.
**Case series:** We present three patients under two years old who developed lead encephalopathy after environmental exposure to lead. Two cases presented in status epilepticus and the third presented a meningeal syndrome. Laboratory studies ruled out metabolic-infectious aetiologies. A history of exposure to lead was revealed by anamnesis and they received chelating treatment with dimercaprol and sodium calcium edetate. Two patients passed away after five days of hospitalization, while the third evolved with loss of acquired maturational patterns, spastic quadriparesis and died at two months. The confirmation of poisoning was retrospective by blood lead concentrations (29–198 μg/dL). The socio-environmental survey confirmed that the source of exposure was contaminated home soil with lead from batteries. The inhabitants were unaware of the health hazards inherent in lead exposure and handling, and also presented high blood lead concentrations and manifestations of neurotoxicity.
**Conclusion:** Lead poisoning is a preventable environmental disease in childhood, without a safe threshold of exposure and direct correlation between dose and neurotoxicity [4]. Lead encephalopathy should be considered as a differential diagnosis in pediatric patients due to the worldwide distribution, multiple uses and environmental persistence of lead.

### References

[1] WHO guideline for the clinical management of exposure to lead. Geneva: World Health Organization; 2022. Available from: https://www.who.int/publications/i/item/9789240037045
[2] García SI. Guidance on prevention, diagnosis, treatment and epidemiological surveillance of childhood environmental lead poisoning. Buenos Aires, Argentina: Ministerio de Salud de la Nación. Programa Nacional de Prevención y Control de las Intoxicaciones; 2014 (Spanish).
[3] Calello DP, Henretig FM. Lead. In: Lewis NS, Howland MA, Lewin NA, editors. Goldfrank's toxicologic emergencies. 11th ed. New York: McGraw-Hill Education; 2019. p. 1292–1308.
[4] Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for lead. US Department of Health and Human Service; 2020. p. 133–200. Available from: https://www.atsdr.cdc.gov/toxprofiles/tp13.pdf

## 196. Acute lead poisoning from drinking tea with "lead-sugar"

Erik Lindeman[a] and Per Leanderson[b]

[a]Swedish Poisons Information Centre, Stockholm, Sweden; [b]Department of Health, Medicine and Caring Sciences, Occupational and Environmental Medicine Center in Linköping, Linköping University, Linköping, Sweden

**Objective:** To describe a case of acute lead self-poisoning caused by the ingestion of lead acetate purchased over the Internet.
**Case report:** A 31-year-old man with a chronic psychotic disorder was admitted for deteriorating psychiatric symptoms and suspected self-poisoning with a chemical substance. A few months earlier he had been treated for liver damage following the ingestion of the solvent dimethyl formamide (DMF), and DMF poisoning was again suspected on the current admission due to moderately elevated liver enzymes. The diagnosis was re-evaluated when the patient's mother brought a jar marked "lead acetate" to the hospital late on day 1, when it suddenly seemed obvious how well the clinical picture fitted with lead poisoning. The patient was withdrawn and lethargic (encephalopathy), he had a blackish discoloration of gums and teeth ("Burton's line"), he suffered extreme thirst and had bouts of vomiting and diarrhoea (lead colic) and he was anaemic (hemoglobin 90 g/L). Blood lead analysis on day 2 was 112 μg/dL and he was treated with unithiol (DMPS) 250 mg q4h and sodium calcium edetate 3 g/day for 5 days (Table 1). His mental status and his blood concentrations improved markedly after the first days of chelation therapy. He then admitted to taking lead acetate in his tea "off and on" for the past month, although he would or could not say why. From day 15–21 he received a second period of chelation with unithiol (DMPS) monotherapy 250 mg b.i.d for seven days (he refused succimer/DMSA). This had no effect on his blood lead concentration, which remained stationary at 46 μg/dL throughout the second chelation attempt. After this the patient refused all further testing and was transferred to psychiatry.
**Conclusion:** Chelation therapy was associated with the initial excretion of large amounts of lead to the urine, albeit with rapidly diminishing yields. The patient made an apparent good recovery.

Table 1. Lead concentrations and treatment in a patient who intentionally drank lead acetate over the period of a month.

| Hospital day | Blood lead μmol/L | Blood lead μg/dl | 24 h Urine lead μmol/L | 24 h Urine lead μg/dl | 24 h Urine volume | Total lead excreted to urine/24h | Chelation therapy Unithiol (DMPS) 250 mg q4h Sodium calcium edetate 3 g/24 h |
|---|---|---|---|---|---|---|---|
| 2 | 5.4 | 112 | | | | | Unithiol (two doses) |
| 3 | 5.2 | 108 | 90 | 1869 | 6250 | 117 mg | Yes |
| 4 | 2.0 | 41 | 19 | 385 | 6600 | 25 mg | Yes |
| 5 | 1.5 | 31 | 5.8 | 120 | 6700 | 8.1 mg | Yes |
| 7 | 1.0 | 21 | 2.4 | 51 | 5600 | 2.8 mg | Yes |
| 8 | 1.0 | 21 | | | | | No |

Blood samples were taken in the morning. Urine was collected for 24 h between 06:00 and 06:00 am.

## 197. Successful organ transplantation after fatal yew ingestion

Anne Stürzebecher[a], Michael Deters[a], Monika Scholle[b] and Svitlana Ziganshyna[c]

[a]Poisons Information Centre Erfurt, Erfurt, Germany; [b]Deutsche Stiftung Organtransplantation, Leipzig, Germany; [c]University of Leipzig Medical Center, Leipzig, Germany

**Objective:** Giving advice on the use of organs for transplantation after brain death of intoxicated patients is not a common request to poison centres, and data is limited. In these cases, blood screening for toxic substances is essential for a reliable diagnosis of brain death and potential organ donation. We report a case of fatal *Taxus baccata* (European yew) poisoning where blood concentrations were determined prior to organ donation.
**Case report:** A middle-aged woman of slight stature ingested 50 shredded yew leaves in a suicide attempt. Despite extensive therapeutic measures, she deteriorated rapidly. Within six hours, cardiogenic shock occurred. Cardiopulmonary reanimation and attempts to treat arrhythmias with digitalis antidote and lidocaine proved unsuccessful. Venous-arterial extracorporeal membrane oxygenation (VA-ECMO) was implemented about seven hours after cardiogenic shock first occurred. A sufficient circulation could finally be re-established, and function of most organs slowly returned to normal. However, she failed to wake up after termination of sedation, and imaging revealed severe brain oedema. Subsequently, organ donation was considered due to concern for progression to brain death. Blood concentrations of taxines were determined. On day one, qualitative detection of taxine B, other pseudoalkaloids, and the specific marker 3,5-dimethoxyphenole confirmed exposure. On day two, only traces of taxine B could be found, and was undetectable in serum on day 3. Consequently, brain death determination was completed, and organ donation could proceed. A post-mortem organ donation of two kidneys was implemented with good postoperative results. Liver donation was not possible due to hypoxic liver injury resulting from prolonged reanimation, and donation of the lungs could not be performed because of severe oedema.
**Conclusion:** Case reports [1,2] have shown the efficacy of VA-ECMO in yew-intoxicated patients. Myocardial function can return to normal without sequelae if circulation is bridged by VA-ECMO until the toxin is eliminated. Our data confirmed these findings: cardiac sonography on day three after intoxication showed a significantly improved myocardial function. Despite extensive therapeutic measures, a fatal outcome in this case could not be prevented as the patient had already developed severe cerebral damage before VA-ECMO was implemented. Successful organ transplantation was nonetheless possible.

### References

[1] Baum C, Bohnen S, Sill B, et al. Prolonged resuscitation and cardiogenic shock after intoxication with European yew (*Taxus baccata*): complete recovery after intermittent mechanical circulatory support. Int J Cardiol. 2015;181:176–178.
[2] Holzer A, Bartecka-Minoa K, Arif T, et al. Two cases of severe *Taxus baccata* poisoning treated with extracorporeal membrane oxygenation (ECMO). Clin Toxicol. 2022;60(S1):29.

## 198. Paediatric exposure to concentrated chlorophene (clorofene) solutions

Jonas Moens, Heleen Van Melckebeke, Jonas Van Baelen, Lieve Stammen, Karolien De Leener, Dominique Vandijck and Anne-Marie Descamps

Antigifcentrum, Neder-Over-Heembeek, Belgium

**Objective:** To present a series of paediatric exposures to concentrated chlorophene (clorofene) solutions. Chlorophene is a halogenated phenolic compound generally used in antiseptic solutions (0.8%) that should be diluted to a maximum concentration of 0.08% before application [1].
**Case series:** Case 1. A 2-year-old boy swallowed 10–15 ml of a 0.8% chlorophene solution following confusion with an oral drug. Upon ingestion, the child presented with epigastric pains which spontaneously disappeared after 24 hours of hospital observation. No further symptoms were reported. Case 2. A 3-year-old boy was given a teaspoon of a 0.8% chlorophene solution following confusion with an oral drug. During the 24-hour hospital observation period no significant symptoms were reported. Case 3. A 10-year-old girl was administered a teaspoon of a 0.8% chlorophene solution following confusion with an oral drug. Immediately afterwards she developed nausea and oropharyngeal irritation. Symptoms had resolved after one hour and having drunk one litre of water. Case 4. A 3-year-old girl was given a teaspoon of a 0.8% chlorophene solution following confusion with an oral drug. During the overnight observation at the hospital no significant symptoms were reported. Case 5. A 2-year-old girl presented nasal irritation after nasal irrigation with a chlorophene solution with an unknown concentration.
**Conclusion:** Symptoms potentially appearing after exposures to concentrated halogenated phenolic compounds such as chlorophene solution can be explained by their irritant potential, aspiration potential and their probable effects on the central nervous and cardiovascular system. Signs of irritation are particularly important, especially in case of exposure to mucous membranes. No central nervous system, cardiovascular or aspiration symptoms were reported in any of our cases. Therefore, in our opinion, it seems that children can be monitored at home by a dependable observer after ingestion of a small quantity of chlorophene solutions up to 0.8%. In four cases the cause of the exposures was confusion with a liquid oral medicine. Another case was caused by a wrong dilution method. Though these exposures provoked minor symptoms, the use of concentrated chlorophene solutions should be avoided if liquid oral medicines are used or if preparation of the correct dilution is too complicated for the user. Users should be advised not to store concentrated chlorophene solutions together with oral medication.

### Reference

[1] Summary of product characteristics: Neo-Sabenyl®, 0.8 g/100 ml, concentrate, Qualiphar S.A., Bornem, Belgium, 2022. Available from: https://qualiphar.be/wp-content/uploads/2020/05/Bijsluiter-Neo-Sabenyl.pdf

## 199. Fatal pediatric colchicine overdose: role for early initiation of granulocyte colony stimulating factor?

Courtney Granter[a], Caitlin E. Wolfe[b], Jill Duncan[b], Marnie J. Wood[c] and Nancy Murphy[b]

[a]IWK Pharmacy Department, Halifax, Canada; [b]Atlantic Canada Poison Centre, Halifax, Canada; [c]Nova Scotia Medical Examiner Service, Dartmouth, Canada

**Objective:** Describe a fatal pediatric case of intentional colchicine ingestion, and explore timing of granulocyte colony stimulating factor (GCSF) for toxicant induced myelosuppression.
**Case report:** A 14-year-old female presented following intentional overdose of 29 tablets of 0.6 mg colchicine (0.2 mg/kg total). By 36 hours post-ingestion she became tachypneic, tachycardic with altered mental status, and required intubation and vasopressors. She developed a fever, and coagulopathy of liver dysfunction resistant to vitamin K. By 76 hours post-ingestion she had profound leukopenia ($1.12 \times 10^9$/L), with low neutrophil count ($0.07 \times 10^9$/L). GCSF was administered at 97 hours post-ingestion. Unfortunately, at 125 hours she had a profound deterioration of neurological function, and care was withdrawn. No rebound in cell counts was observed prior to death. A post-mortem examination revealed a detectable colchicine concentration of 19 ng/mL in an undated ante-mortem sample.
**Conclusion:** Colchicine in overdose produces cytopenias due to arresting mitosis through its actions on microtubules, typically beginning by day 3 post-overdose [1]. A dose of 0.8 mg/kg is anticipated to be lethal, while our case describes a rapidly fatal outcome at a considerably lower dose in a pediatric patient with no risk factors for enhanced toxicity [2]. Our ante-mortem concentration is not time stamped, but a similar fatal ingestion of 0.25 mg/kg was recently described with a level of 14 ng/mL at 18.5 hours after ingestion [3]. Multiple case reports describe successful use of GCSF to encourage proliferation and maturation of new neutrophils after colchicine overdose, mostly initiating around day 5 when cytopenias have fully developed [1,4]. We suggest that earlier, prophylactic administration might be considered in similar cases once toxicity is clinically established, as the projected trajectory is so poor and other available care is only supportive. Given that the cytopenia follows a stereotyped course once severe toxicity begins, initiating GCSF prior to the nadir may be of clinical utility.

### References

[1] Harris R, Marx G, Gillett M, et al. Colchicine-induced bone marrow suppression: treatment with granulocyte colony-stimulating factor. J Emerg Med. 2000;18:435–440.
[2] Fu M, Zhao J, Li Z, et al. Clinical outcomes after colchicine overdose: a case report. Medicine. 2019;98:e16580.
[3] McCabe DJ, Wilson BZ, Radke JB, et al. A fatal colchicine ingestion with antemortem blood concentration. Am J Forensic Med Pathol. 2022;43(3):253–255.
[4] Critchley J, Critchley L, Young R, et al. Granulocyte-colony stimulating factor in the treatment of colchicine poisoning. Hum Exp Toxicol. 1997;16:229–232.

Table 1. Attributed causative agents in fatal poisoning in childhood in England and Wales in two study periods.

| | Time period | |
|---|---|---|
| Agent | 2006–2020* | 1968–2000** |
| Opioids (methadone) | 23 (18) | 47 (NS) |
| Hydantoin | 3 | NS |
| Insulin | 2 | NS |
| Antidepressants | 2 | 78 |
| Synthetic narcotics | 2 | NS |
| Barbiturates | 0 | 33 |
| Salicylates | 0 | 40 |
| Other drugs | 15 | 195 |
| Other gases | 133 | 740 |
| Carbon monoxide | 30 | 1691 |
| Corrosives | 2 | NS |
| Lead | 1 | 19 |
| Other non-drugs | 7 | 64 |

*2006–2020 data: ICD10 code; **1968–2000 data: ICD8 & 9 code; NS: not specified.

## 200. Fatal poisoning in childhood in England and Wales, 2006–2020

Mark Anderson

National Poisons Information Service, Newcastle, United Kingdom

**Objective:** To analyse trends in fatal poisoning in children aged <10 years in England and Wales, 2006–2020, and compare with previously published data.
**Methods:** Annual England and Wales mortality datasets published by the Office of National Statistics (ONS) between 2006 and 2020 were obtained. Data were extracted for deaths in children aged <10 years due to poisoning (ICD10 code T36–T39) and analysed by calendar year, age band, sex, and agents involved. Age-specific mortality rates were calculated using ONS mid-year population estimates. These data were compared to previously published data [1].
**Results:** The mortality rate in children aged <10 years attributed to poisoning in England and Wales fell from 7.5 to 1.4 deaths per million in boys and 3.9 to 1.2 deaths per million in girls between 2006 and 2020, continuing a downward trend from the 1968–2000 data.
**Conclusion:** Analysis of mortality statistics show a continued downward trend in deaths attributed to poisoning in children aged under 10 years in England and Wales. This includes deaths due to inhalation (carbon monoxide and other gases), many of which will be due to house fires. The cause of this reduction is likely to be multifactorial, including a continued emphasis on fire safety precautions, improved access to poisons information and treatment, and a trend towards prescribing medications with lower acute toxicity in children. Methadone remains the most significant medication risk for children in England and Wales [2].

### References

[1] Flanagan RJ, Rooney C, Griffiths C. Fatal poisoning in childhood, England & Wales 1968–2000. Forensic Sci Int. 2005;148:121–129.
[2] Anderson M, Hawkins L, Eddleston M, et al. Severe and fatal pharmaceutical poisoning in young children in the UK. Arch Dis Child. 2016;101:653–656.

## 201. Alcohol intoxication in adolescence can affect the behavior of young people in the future

Juan Ortega Pérez[a], Laura Riera López[a], Jordi Puiguriguer Ferrando[a], Catalina Homar Amengual[a], Meritxell Vidal Borràs[b], Maria Codinach Martín[c], Bernardino Barceló Martín[d,e] and Bernardino Comas Díaz[a]

[a]Hospital Universitario Son Espases, Palma de Mallorca, Spain; [b]Institut Català d'Oncologia Girona, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [c]Servicio de Urgencias, Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [d]Clinical Analysis Department, Clinical Toxicology Unit, Hospital Universitari Son Espases, Palma de Mallorca, Spain; [e]Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain

**Objective:** Adolescence is a transition stage with important physical and mental changes and growing autonomy is related to experimentation and impulsiveness that can lead to risk behaviors such as alcohol abuse [1]. This abuse becomes a clinical, social and public health problem related to various short- and long-term problems [2]. We analyze whether having experienced acute alcohol intoxication (IAA) is a risk factor for presenting psychopathological problems and risk behaviors in the two years following the visit to the hospital emergency department and to assess gender differences.
**Methods:** The computerized medical records of 197 adolescents aged 13–17 years who attended the emergency room between 2014 and 2017 were retrospectively reviewed in a tertiary hospital. Of these, 95 presented for IAA and 102 for another reason (control group). Epidemiological variables (age and sex) were analyzed and the outcome variables (reintoxication, psychopathological problems, accident rate, risky sexual behavior and psychopathological follow-up) were compared between both groups in the two years after intoxication.
**Results:** The year 2017 had the highest number of admissions due to IAA registered (16.8% in 2014; 25.3% in 2015; 22.1% in 2016; 35.8% in 2017). The age group with the highest intoxication was 16 years. Regarding problematic behaviors, the most frequent were psychological and/or psychiatric follow-up with 25.6% in patients with IAA and 25.4% in the control group, and the presence of accidents with 53.7% in patients with IAA and 43.1% in the control group. Regarding the differences between gender, of the variables analyzed, in re-intoxication 6.9% in women and 1% in men and in risky sexual behavior 8.9% in women and 1% in men were detected.
**Conclusion:** The results did not identify significant differences between the group of patients with IAA and the control group in any of the variables studied in the two years after alcohol poisoning. In relation to gender, women presented a higher number of re-intoxications and risky sexual behavior.

### References

[1] de Veld L, van Hoof JJ, Wolberink IM, et al. The co-occurrence of mental disorders among Dutch adolescents admitted for acute alcohol intoxication. Eur J Pediatr. 2021;180:937–947.
[2] Bousoño Serrano M, Al-Halabí S, Burón P, et al. Substance use or abuse, internet use, psychopathology and suicidal ideation in adolescents. Adicciones. 2017;29:97–104.

## 202. Relationship of suicide attempts with reopening of schools after their long-term closure due to COVID-19

Katerina Kotikova[a], Daniela Pelclova[a] and Tomas Navratil[b]

[a]Department of Occupational Medicine, Toxicological Information Centre; Charles University, and General University Hospital, Prague, Czech Republic; [b]Department of Electrochemistry at the Nanoscale, J. Heyrovsky Institute of Physical Chemistry of the Czech Academy of Sciences, Prague, Czech Republic

**Objective:** Self-poisoning is a common method of suicide even in children and adolescents. We compared the number of suicide attempts by self-poisoning in children and adolescents before and during the COVID-19 pandemic to analyse the impact of the reopening of schools after their long-term closure on the rate of reported self-poisonings. The most common substances involved in self-poisonings were analysed in both age groups.
**Methods:** Data from the Czech Toxicological Information Centre in Prague were analysed retrospectively for trends in the frequency of child (0–15 years) and adolescent (16–19 years) self-poisonings between 2018 and 2021. Data collected included age group, sex, date of the call, and toxic substance.
**Results:** In 2020, a significant decrease in reported child and adolescent self-poisonings was found compared to 2018 and 2019. In contrast, in 2021, a significant increase was registered, especially from April 2021, when elementary schools (education up to 15 years) were gradually reopened after almost one-year of online teaching. In April, May, and June 2021, the total number of child self-poisonings increased to 140.7, 187.6 and 298.0% comparing the same months in 2018, 2019, and 2020, respectively. Females prevailed in all years. In adolescents, no significant increase was registered. In a total 2182 subjects, 987 children (females 858, males 129) and 1195 adolescents (females 889, males 306) with intentional self-poisonings caused by a known drug(s) were analysed. In children, the three most common substances reported were paracetamol (22.2%), antidepressants (20.6%), and ibuprofen (18.8%); in adolescents, antidepressants (25.7%), benzodiazepines (19.7%), and paracetamol (18.8%) were most common.
**Conclusion:** The rate of self-poisonings in Czech children and adolescents significantly increased in 2021, especially in the spring months when educational institutions were reopened. In children, the most common drug used for self-poisoning was paracetamol and in adolescents, antidepressants.

### Acknowledgement

Cooperatio 207041-3 Pharmacology.

Table 1 Self-poisoning in children 2018–2021 before and during COVID-19.

| Year | 2018 | 2019 | 2020 | 2021 | 2018-2021 | Comparison of the years | | |
|---|---|---|---|---|---|---|---|---|
| Age (years) | Total (F/M) | Total (F/M) | Total (F/M) | Total (F/M) | Total (F/M) | 2020/2018 | 2020/2019 | 2021/2020 |
| 0-15 | 354 (302/52) | 289 (238/51) | 248 (211/37) | 454 (399/55) | 1345 (1150/195) | 70.1% | 85.8% | 183.0% |
| 16-19 | 403 (284/119) | 414 (315/99) | 329 (243/86) | 452 (334/118) | 1598 (1176/422) | 81.6% | 79.5% | 137.4% |
| Total | 757 (586/171) | 703 (553/150) | 577 (454/123) | 906 (733/173) | 2943 (2326/617) | – | – | – |

## 203. Dimetindene – too strict toxic dose?

Michal Cecrle[a] and Daniela Pelclova[b]

[a]Department of Occupational Medicine, Toxicological Information Centre, First Medical Faculty of the Charles University, Institute of Pharmacology, General University Hospital in Prague, Prague, Czech Republic; [b]Department of Occupational Medicine, Toxicological Information Centre, First Medical Faculty of the Charles University, General University Hospital in Prague, Prague, Czech Republic

**Objective:** Dimetindene maleate is a sedating antihistamine indicated for symptomatic treatment of coughs, common cold and urticaria in children. Data concerning toxicity is very limited and there is no agreement on the dose necessitating hospital admission in children. A recent recommendation is 2 mg for children aged 0–6 years and 5 mg for children aged >6 years [1]. Earlier literature recommended admission after ingestion of 0.5 mg/kg [2]. We aimed to ascertain the potentially toxic dose when the child should be admitted for observation and/or treatment.
**Methods:** Discharge reports from hospitals were requested in the period from August 2019 to August 2022. Dose ingested, age, body weight, latency from ingestion to admission to the hospital, symptoms, Poisoning Severity Score (PSS), length of hospital stay, and treatment were searched.
**Results:** From 218 discharge reports requested, 77 reports arrived, concerning 32 boys and 45 girls (mean age 2 years 8 months). The average dose ingested was 0.74 mg/kg (range 0.026–1.63 mg/kg). The latency from ingestion to admission was 1.6 hours (range 0.5–5.3 hours); 37 children received activated charcoal in hospital. Most children (93.5%) were asymptomatic (PSS 0) up to the dose of 1.63 mg/kg. Only 4 children (5.3%) developed mild and transient symptoms (PSS1) (3× drowsiness and 1× mydriasis responsive to light), with latency 1.35 hour after an average dose 0.38 (range 0.25–0.50) mg/kg. One child (1.3%) who ingested 1.03 mg/kg, had PSS 2 (stumbles, weakness). In 28 children, electrocardiography with normal physiological result was performed. The length of hospitalization did not exceed 24 hours in 75 children (97.4%), 2 children stayed in the hospital for 2 days for symptoms unrelated to dimetindene maleate ingestion. Overall, 27 children had mild symptoms of acute upper respiratory tract infection potentially mistaken for symptoms of intoxication. Also, the latency and timing of ingestion (bedtime, lunchtime) could intensify fatigue and sleepiness.
**Conclusion:** The children very rarely developed minor symptoms after accidental ingestion of dimetindene maleate and were usually asymptomatic after ingestion of up to 1.63 mg/kg. According to these data, the potentially toxic dose of dimetindene is 0.5 mg/kg and above, and to prevent unnecessary hospitalizations children that have ingested less than 0.5 mg/kg can be observed at home.

### Acknowledgement

Project Cooperatio 207041-3

### References

[1] TOXINZ. Dimethindene maleate [cited 2022 Oct 10]. Available from: https://www.toxinz.com/Spec/2191188/235311.
[2] Lübke G. Dimetindenmaleat. In: Mühlendahl KE, Oberdisse U, Bunjes R, Brockstedt M, editors. Vergiftungen im Kindesalter. 4th ed. Germany: Thieme, 2003. p. 175.

## 204. Accidental poisoning at home in children aged 10 years and younger in the UK during the COVID-19 pandemic

Eleri Thomas[a], Stephen Jones[a], Sally M. Bradberry[b], Euan A. Sandilands[c], Ruben H. K. Thanacoody[d] and Laurence A. Gray[a]

[a]National Poisons Information Service, Cardiff, United Kingdom; [b]National Poisons Information Service, Birmingham, United Kingdom; [c]National Poisons Information Service, Edinburgh, United Kingdom; [d]National Poisons Information Service, Newcastle, United Kingdom

**Objective:** Despite poison prevention strategies, accidental poisoning in children at home remains an issue. During the COVID-19 pandemic lockdown interludes, nurseries and schools closed to reduce virus spread. Parents and carers worked and cared for children at home. Additionally, products, such as hand cleaning agents, were commonly used and placed in child-accessible locations. We investigated cases reported to our poison centre.
**Methods:** Enquiries received by the UK National Poisons Information Service (NPIS) concerning accidental poisonings at home, in children aged 10-years-old and younger, between 1 January 2019 and 31 December 2021 were interrogated, retrospectively, focusing on the call volumes, types of agents ingested and poisoning trends. One-way ANOVA and Tukey's Honest Significant Difference (HSD) test compared mean monthly enquiry numbers. Chi-square test examined proportions.
**Results:** Overall, 30,101 enquiries were received during 2019–2021 (2019 $n = 10{,}162$; 2020 $n = 10{,}618$; 2021 $n = 9{,}321$). Of these, 81% of enquiries related to children 0–3 years of age ($n = 24{,}466$). There were 7% more cases involving males compared to females. In March 2020, as the UK entered lockdown, 622 enquiries were received (March 2019 $n = 832$, March 2021 $n = 871$), followed by 5099 enquiries taken during the lockdown interval of April to August 2020 (April–August 2019 $n = 4471$, April–August 2021 $n = 4290$). One-way ANOVA revealed a statistically significant difference among the three years ($p = 0.016$). The mean number of enquiries per month during lockdown was significantly different to the equivalent period in 2021 (1020 versus 858, $p = 0.017$). The difference between mean number of enquiries per month during the lockdown interval and the equivalent period in 2019 was not statistically significant (1020 versus 894, $p = 0.061$). Ingestion of hand cleaners accounted for 1.4% ($n = 143$) of enquiries in 2019, increasing to 4.4% ($n = 471$) in 2020 ($p < 0.001$). Multivitamins were consistently the most commonly ingested product (7.5% of enquiries each year, $p = 0.665$).
**Conclusion:** During March 2020, when the UK entered COVID-19 lockdown, a sudden decrease was observed in poison enquiries to the UK NPIS. Many healthcare services were overwhelmed with COVID-19 related enquiries and were restricted in their ability to take poisoning calls. Subsequently, an increase in the number of enquiries during the lockdown interval was recorded. The lack of child supervision due to concomitant home-working and childcare, and inappropriate storage of agents such as hand gels, are likely to be the cause for the increases in poisonings in children during lockdown intervals.

## 205. Risk factors for deliberate self-poisoning among children and adolescents in the Netherlands: a prospective study

Ilze M. J. Thoonen, Saskia J. Rietjens, Irma S. van den Hengel-Koot, Dylan W. de Lange and Arjen Koppen

Dutch Poisons Information Center, UMC Utrecht, Utrecht, Netherlands

**Objective:** The number of deliberate self-poisonings (DSPs) among young people has increased dramatically worldwide in the past decade. Risk factors associated with such poisonings are not well-defined. The aim of this study was to characterize DSPs among children and adolescents reported to the Dutch Poisons Information Center (DPIC).
**Methods:** A prospective observational study was performed on DSPs among children and adolescents up to 17 years of age, as reported to the DPIC. During DPIC consultation, the following data were collected: age, gender, Body Mass Index (BMI), living situation, toxicant (type, dose, route and way of obtaining) and treatment advice.
**Results:** Between 1 February and 30 April 2022, the DPIC was consulted about 405 (suspected) DSPs among children and adolescents aged 7–17 years. The majority of patients were female (84%). In our study, 25% of the patients had a BMI that was classified as either overweight or obese. Additionally, 17% of the children and adolescents of 12–17 years of age in our study were living in a mental healthcare residence, which is higher compared to the living situation of the general population of children and adolescents in this age group in the Netherlands (approximately 2%). Cases mainly involved pharmaceuticals ($n = 341$, 84%), particularly over-the-counter (OTC) medication ($n = 230$, 67%), such as paracetamol (52%) and ibuprofen (18%). In 31% of the cases ($n = 106$), prescription medication was involved and in 12% ($n = 40$) the medication of someone else was taken. Children and adolescents living at home with parents/caregivers had a higher odds of using pharmaceuticals in DSP, compared to children and adolescents living in a mental healthcare residence (OR =3.387, 95% CI = [1.707, 6.646]). In contrast, those living in a mental healthcare residence had higher odds of being exposed to household products (OR =3.404, 95% CI = [1.036, 10.720]).
**Conclusion:** The female gender, a high BMI and living in a mental healthcare residence are all risk factors for DSPs among adolescents. There is a difference in preferred toxicant between children and adolescents living at home or in mental healthcare residences, possibly related to the availability of toxicants. Prevention of self-poisonings could focus on promoting the awareness of safe storage of pharmaceuticals and household products among caregivers and medical professionals, as well as limiting the sales of OTC medication, especially paracetamol, to this young population.

## 206. Deaths in pediatric patients from suspected suicide attempts by self-poisoning

Will R. Goodrich, Rita Farah and Nathan P. Charlton

Department of Emergency Medicine, Division of Medical Toxicology, University of Virginia Health, Charlottesville, VA, USA

**Objective:** To highlight recent trends in deaths following suspected suicide attempts in the pediatric population, and the agents involved in these exposures.
**Methods:** We conducted a retrospective review of the National Poison Data System (NPDS), the data warehouse for the United States' 55 poison centers (PCs) during 1 January 2015–31 December 2021. PCs submit, in near real time, de-identified data to NPDS after providing poison exposure information and management to callers from the general public and healthcare providers. Cases coded by specialists in poison information as intentional suspected suicide involving pediatric patients aged 6–19 years were included. We conducted a descriptive analysis of the top substances involved in pediatric deaths.
**Results:** There were 628,514 suspected suicide attempts in pediatric patients, 79% being females. There were 342 deaths from suspected suicide attempts. While the majority of deaths occurred among females ($n = 226$, 66%), the death rate was higher among males ($p < 0.001$). The top 5 pharmaceutical substances involved in fatal outcomes were bupropion ($n = 59$), acetaminophen (alone, not in combination; $n = 54$), diphenhydramine ($n = 51$), ethanol ($n = 21$), and fluoxetine ($n = 21$). Non-pharmaceutical products were less commonly involved in pediatric death by suspected suicide, with the top 10 substance categories implicated 13 times. There were 102 deaths among 13–15 year olds. The top 3 substances involved in deaths this age group were bupropion ($n = 19$), diphenhydramine ($n = 18$), and ibuprofen ($n = 8$). There were 226 deaths in 16–19 year-olds. The top 3 agents involved were diphenhydramine ($n = 33$), bupropion ($n = 31$) and acetaminophen ($n = 30$). Single substance exposures were reported in 126 suspected suicide attempts that resulted in death. In the 10–12 year old group, diphenhydramine ($n = 2$), amitriptyline ($n = 1$), and bupropion ($n = 1$) were most common. For the 13–15 years old group, bupropion ($n = 6$) and diphenhydramine ($n = 5$) were most common. In 16–19 year olds, diphenhydramine ($n = 17$), acetaminophen (alone, $n = 12$), and bupropion ($n = 8$) were most common. Interestingly, combining the 13–19 year old groups yielded diphenhydramine ($n = 22$), nitrites and nitrates ($n = 15$), acetaminophen ($n = 14$), and bupropion ($n = 14$) as the most common single substance ingestions leading to death.
**Conclusion:** Unfortunately, suspected suicide attempts and deaths in the pediatric population continue to uptrend. Over-the-counter medications are most implicated in these attempts, alone and in combination with other pharmaceuticals and non-pharmaceuticals. Mental health screening will continue to be key to identifying patients in this population at risk of suicide. Commercially designed medication packaging and home medication safety measures should continue to be emphasized by medical professionals and poison centers.

## 207. Edible cannabis exposures in pediatric patients misdiagnosed as seizures leading to unnecessary and costly medical testing

Will R. Goodrich[a], Ryan J. Cole[a], Lindsay A. L. Bazydlo[b] and Christopher P. Holstege[a]

[a]Department of Emergency Medicine, Division of Medical Toxicology, University of Virginia Health, Charlottesville, VA, USA; [b]Department of Pathology, University of Virginia School of Medicine, Charlottesville, VA, USA

**Objective:** To highlight the potential for harm and cost from unnecessary medical testing in pediatric patients exposed to edible cannabis products misdiagnosed as seizures.

**Case series:** Two pediatric patients with seizure-like activity were evaluated in the emergency department of a tertiary medical center. The first was an 8-year-old male with whole-body "shaking", seeing weird colors, and hearing squeaking noises. Presenting blood testing and a head computerised tomography (CT) scan were negative resulting in discharge home. He had a recurrent episode, and mother administered diphenhydramine, and brought him to a tertiary hospital. Presenting vital signs were heart rate 105 beats/min, blood pressure 97/54 mm Hg, respirations 21 breaths/min, pulse oximetry 100%, temperature 37.2 °C. Pediatric neurology determined his "shaking" while conscious was not a seizure. Urine immunoassay was positive for marijuana. He became asymptomatic 18 hours after symptom onset. Confirmatory urine testing revealed a tetrahydrocannabinol (THC) concentration of 504 ng/mL. The second patient was a 2-year-old female who woke up crying and moaning with 5 reported episodes of body stiffening and twitching. Presenting vital signs were heart rate 83 beats/min, blood pressure 113/65 mm Hg, respirations 22 breaths/min, pulse oximetry 96%, temperature 34.6 °C. Subsequent bloodwork, blood cultures, urinalysis, viral testing, X-rays, and a head CT scan were unremarkable except complete blood count with white blood cells 12 k/uL, and venous blood gas with pH 7.27, $CO_2$ 57.4 mmHg, bicarbonate 25.9 mmol/L. A urine immunoassay was positive for marijuana. She was admitted to the pediatric ward due to altered mentation where her temperature and blood gas normalized. Neurology was consulted and determined the episodes were not seizures. Confirmatory urine testing revealed a THC level of 820 ng/mL. She was asymptomatic approximately 23 hours after symptom onset.
**Conclusion:** Both patients had unnecessary medical costs and risk for potential harm. Decriminalization and legalization of cannabis in the United States places pediatric patients at increased risk of exposure to edible cannabis products. These products often resemble candy or other common commercially available snack foods. Caregivers may not be forthcoming regarding exposures. Cannabis ingestions may result in drowsiness, hallucinations, tremor, palpitations, and numbness. Vital sign abnormalities include tachycardia, tachypnea, and hypotension. Presentation without prompt identification of cannabis exposure leads to unnecessary testing with its increased costs, prolonged hospitalization, and potential harm from diagnostics like radiation, intravenous access, and lumbar puncture. Rapid, more specific, urine toxin immunoassays can help facilitate the correct diagnosis and avoid unnecessary testing and procedures.

## 208. Voluntary intoxications in adolescents during the pandemic period

Arianna Festa[a], Valeria M. Petrolini[a], Federico Fassio[b], Lucia Bernasconia[a], Benedetta Brolli[a], Valentina Negrini[a], Cristina Grazioli[a], Giulia Scaravaggi[a] and Carlo A. Locatelli[a]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [b]Department of Public Health, Experimental and Forensic Medicine, Biostatistics and Clinical Epidemiology Unit, University of Pavia, Pavia, Italy

**Objective:** Measures to limit contagion during the COVID-19 pandemic brought radical changes in lifestyle habits. As of March 2020, Italy has had very restrictive measures including long lockdown periods and distance learning for schoolchildren. The population most affected by this abrupt deprivation of social interaction is adolescents. Different specialists have raised concerns about the increase in adolescents' manifestations of distress, access to neuropsychiatric services, eating disorders, or self-harm. We conducted a study to assess the impact of this phenomenon on voluntary poisonings among older children and teenagers.
**Methods:** We included all cases of voluntary self-injurious intoxication referred to our poison center from 2018 to 2021. Inclusion criteria was age between 10 and19 years. Data on the characteristics of intoxications and the temporal distribution were analyzed.
**Results:** In total 3931 subjects were included: 807 in 2018, 767 in 2019, 859 in 2020 and 1498 in 2021. The increase in intoxication numbers was observed from January 2021 and affected all Italian regions regardless of the pandemic health impact in 2020. Comparing 2021 cases with the mean of the previous three years an 84% increase was observed, higher in females than males (84 versus 74% of total cases). The median age decreased from 17 to 16 years (IQR 15–18, Mann–Whitney test $p < 0.001$) and we noted the highest increase in 13-year-old subjects (2021 to previous year ratio =2.42), 14-year-olds (2.15) and 16-year-olds (2.31). As in 2018–2020, the most commonly used agents were drugs (78% of cases), followed by household products and chemicals (19%). Among drugs, we found significant increase in antidepressant ($p = 0.005$) and neuroleptic ($p < 0.001$) use, with a decrease in antiepileptic drugs ($p = 0.003$); regarding anti-inflammatories and paracetamol we found no significant differences. In 2021, 28% of patients remained asymptomatic and two deaths occurred.
**Conclusion:** Our data confirm what has already been reported with regard to the psychological injury suffered by many adolescents, removed from their natural contexts such as school, friendships, sports and play activities. The effects were observed in the period following the most critical phase of the pandemic, and the trend of the phenomenon does not seem to be downward for now.

## 209. Increasing severity of propranolol poisoning in Edinburgh, UK

Emma E. Morrison, Michal Klatka and Euan A. Sandilands

National Poisons Information Service, Edinburgh, United Kingdom

**Objective:** To describe the trends in propranolol poisoning in a single UK centre from 2018 to 2021 and associated population prescribing changes.
**Methods:** The Royal Infirmary of Edinburgh Toxicology Department serves an adult population of 728,000. Coded Emergency Department poisoning presentations from the 1 September 2018 to 31 August 2021 were retrospectively reviewed. Regional population prescribing data was collected via the Pharmacy Service and the number of community dispensing items was analysed. Data from National Records of Scotland was interrogated to provide regional information on deaths reporting propranolol.
**Results:** The annual hospital presentations and regional prescribing data describe increasing numbers of propranolol presentations annually (Table 1). Most patients are female with a median age of 30 years (IQR 22–40); the majority report poisoning with the intention of harm. The proportion of presentations requiring admission to critical care is increasing annually, demonstrating increasing severity of poisoning. The annual death rate where

Table 1. Annual hospital presentations and regional prescribing data involving propranolol.

| | | | Sept 2018–Aug 2019 | Sept 2019–Aug 2020 | Sept 2020–Aug 2021 |
|---|---|---|---|---|---|
| Emergency department (ED) presentations | Total number | | 84 | 131 | 160 |
| | Male (*n*, %total) | | 26 (31%) | 29 (22%) | 32 (20%) |
| | Female (*n*, %total) | | 58 (69%) | 102 (78%) | 128 (80%) |
| Admissions | Discharged from ED (*n*, %total) | | 50(59.5%) | 70 (53.4%) | 84 (52.5%) |
| | Ward (*n*, %total) | | 31 (36.9%) | 49 (37.4%) | 60 (37.5%) |
| | Critical care (*n*, %total) | | 3 (3.6%) | 12 (9.2%) | 16 (10%) |
| Age | Years (median, IQR) | | 28 (20-41) | 30 (23-43) | 29 (22-36) |
| Intent | Self-harm (*n*, %total) | | 74 (88%) | 118 (90%) | 139 (87%) |
| | Accidental (*n*, %total) | | 5 (6%) | 6 (5%) | 3 (2%) |
| | Recreational (*n*, %total) | | 1 (1%) | 3 (2%) | 4 (2%) |
| | Unknown (*n*, %total) | | 4 (5%) | 4 (3%) | 14 (9%) |
| Deaths (including out of hospital) | Total number (*n*) | | 1 | 2 | 5 |
| Prescriptions | Patient age (years) | 15–24 (*n*, %total) | 102,659 (15.3%) | 102,556 (14.9%) | 102,653 (14.7%) |
| | | 25–44 (*n*, %total) | 256,032 (38.4%) | 265,329 (38.7%) | 272,344 (39.2%) |
| | | 45–64 (*n*, %total) | 189,331 (28.4%) | 193,022 (28.2%) | 194,700 (28.0%) |
| | | 65–74 (*n*, %total) | 65,886 (9.9%) | 68,099 (9.9%) | 68,733 (9.9%) |
| | | 75–84 (*n*, %total) | 37,855 (5.8%) | 38,975 (5.7%) | 40,212 (5.8%) |
| | | 85 + (*n*, %total) | 15,711 (2.4%) | 16,090 (2.4%) | 16,229 (2.3%) |
| | Total prescriptions (*n*) | | 667,474 | 684,071 | 694,871 |

propranolol was named also increased, though the absolute numbers are small. During the same period, the total number of propranolol prescriptions increased each year, with an increase of 2.5% in 2019–2020 and 1.6% in 2020–2021. A small annual increase in the proportion of prescriptions in the 25–44 age group is also reported.

**Conclusion:** Propranolol in Edinburgh is recommended for use in adults for the treatment of tremors associated with anxiety or thyrotoxicosis, and migraine prophylaxis. Increased mental health presentations to primary care during this timeframe have previously been described [1]. We conclude that greater propranolol availability and deteriorating population mental health underpins the increasing severity and presentation rate of propranolol poisoning. Increased prescribing would suggest that prescribing interventions to limit access may be an appropriate intervention.

## Reference

[1] Archer C, Turner K, Kessler D, et al. Trends in the recording of anxiety in UK primary care: a multi-method approach. Soc Psychiatry Psychiatr Epidemiol. 2022;57:375–386.

# 210. Antimuscarinic toxicity presenting as a stroke mimicking hypertensive akinetic mutism with response to physostigmine

Brandtly Yakey[a], Michael Gyory[b], Erik Olsen[b], Varun Vohra[a] and Andrew King[a]

[a]Michigan Poison & Drug Information Center, Wayne State University School of Medicine, Detroit, MI, USA; [b]Detroit Medical Center, Detroit, MI, USA

**Objective:** Diphenhydramine toxicity leading to antimuscarinic toxidrome is commonly encountered by toxicologists and is easily identifiable by experienced clinicians. While alterations in speech patterns including mumbling, hypophonic, and delirious speech are classic findings, frank mutism is infrequently encountered [1].

**Case report:** A 48-year-old male with a past medical history of hypertension was brought to the emergency department by emergency medical services after he was found with altered mentation by a family member approximately one hour prior. His vital signs were: blood pressure 240/120 mm Hg; heart rate 140 beats/min; respiratory rate 16 breaths/min; oxygen saturation 98% on room air. The patient appeared confused and was nonverbal, sitting completely still in bed, and was incontinent of urine. His pupils were 4 mm and reactive bilaterally. His electrocardiogram demonstrated sinus tachycardia with no QRS or QTc interval prolongation. Given his aphasia and hypertension, stroke evaluation was started. Non-contrast computed tomography of the head was unremarkable. Later, the family reported an empty bottle of diphenhydramine in the bathroom. Intravenous (IV) physostigmine 4 mg was administered over 5 minutes with subsequent normalization of his mental status and a self-reported intentional overdose of diphenhydramine after losing a large sum of money gambling. He denied any other co-ingestions. He required subsequent IV physostigmine 1 mg seven hours after the initial dose due to the recurrence of symptoms with resolution. Due to a nationwide medication shortage of physostigmine, he was administered IV benzodiazepines for sedation 12 hours after initial presentation. He was discharged home on hospital day five after psychiatric evaluation.

**Conclusion:** To our knowledge, toxic akinetic mutism due to antimuscarinic overdose has previously been described at least once [2]. Classic central antimuscarinic symptoms include hyperactivity, visual/auditory hallucinations, and pressured incoherent and mumbling speech. Physostigmine can be used as a diagnostic and therapeutic intervention and is more effective in controlling agitation and delirium than benzodiazepines [1]. Akinetic mutism is an uncommon manifestation of diphenhydramine toxicity that resolves with the administration of physostigmine.

## References

[1] Wang GS, Baker K, Ng P, et al. A randomized trial comparing physostigmine vs lorazepam for treatment of antimuscarinic (anticholinergic) toxidrome. Clin Toxicol. 2021;59:698–704.

[2] Pandey RS, Rao IV, Sreenivas KN, et al. Central anticholinergic syndrome presenting as akinetic mutism. Indian J Psychiatry. 1981;23:186–187.

## 211. Psychosis related to chronic prednisone overdose

Natanael del Ángel González[a], Yadira J. Rosales Bacilio[a], Jorge G. Pérez Tuñón[a], Sindy L. Ortega Martinez[a], Arturo G. Ponce De León[a] and Liz E. Rodríguez Hernández[b]

[a]Centro Toxicológico Hospital Ángeles Lomas, Huixquilucan, Mexico; [b]Instituto Mexicano del Seguro Social, Ecatepec, Mexico

**Objective:** Prednisone is a prodrug of prednisolone that has been associated with drug-induced psychotic disorder, characterized by delirium or hallucinations. Consequently, in order to confirm the diagnosis, other causes of psychosis should be ruled out. The mechanisms by which corticosteroids produce psychosis are probably related to tension in the hypothalamic-pituitary adrenal axis that in the presence of exogenous corticosteroids, regulates hormones such as cortisol in a negative feedback mechanism, corticosteroids can produce an induction of tyrosine hydroxylase, which increases the bioavailability of dopamine, causing psychosis. Commonly, discontinuation or reduction of steroid doses has shown improvement in 92% of patients, however, multiple treatment lines may be necessary depending on the clinical presentation [1]. We present a case of a patient with neuropsychiatric symptoms after repeated prednisone overdose.
**Case report:** A 49-year-old female with a history of perianal abscess was treated with prednisone 200 mg, cephalexin 1.5 g and metronidazole 1.5 g daily. After 7 days of treatment (accumulative dose of prednisone 1.4 g) she presented problems of family dynamics, delusional ideas, aggressiveness, unmotivated laughter and alterations of sleep pattern. She was previously evaluated in a psychiatric hospital where treatment was started with sertraline 50 mg/day orally, lorazepam 3 mg/day orally and a single dose of haloperidol 5 mg intravenously, however, prednisone continued to be administered and symptoms persisted. Fourteen days after treatment was started (accumulative dose of prednisone 2.8 g) she presented to the emergency room dysphoric and aggressive. Laboratory and imaging studies were carried out without being able to identify another possible origin of the psychosis, therefore, steroid-induced psychosis was diagnosed, initiating treatment with 10 mg of diazepam, 2.5 mg of intravenous haloperidol every 8 hours, valproic acid 400 mg orally every 8 hours and gradual suspension of steroids. She manifested improvement in the course of the first day of treatment, without new episodes of psychosis during her hospital stay, and was discharged after 7 days of hospitalization.
**Conclusion:** In the present case, an overdose of prednisone triggered neuropsychiatric symptoms and required the use of haloperidol as an antipsychotic and valproic acid as a mood stabilizer. This case report highlights the need to understand that chronic corticosteroid overdoses are not harmless and may manifest as psychosis.

### Reference

[1] Huynh G, Reinert JP. Pharmacological management of steroid-induced psychosis: a review of patient cases. J Pharm Technol. 2021;37:120–126.

## 212. Cathartic catharsis: hypermagnesemia toxicity leading to respiratory paralysis, secondary to cathartic abuse

Stephen Petrou[a,b] and Craig G. Smollina[a,b]

[a]University of California San Francisco, San Francisco, CA, USA; [b]California Poison Control System – San Francisco Division, San Francisco, CA, USA

**Objective:** Hypermagnesemia may cause symptoms of somnolence, loss of deep tendon reflexes, and respiratory paralysis [1,2]. Although rarely reported, ingestion of magnesium (Mg) containing medications especially in conjunction with acute kidney injury can result in serious clinical effects. We describe a case of a patient with a history of anorexia nervosa who presented in respiratory failure requiring intubation with hypermagnesemia secondary to both renal dysfunction and exogenous abuse of a magnesium containing cathartic.
**Case report:** A 38-year-old female with a history of anorexia nervosa presented to the emergency department (ED) with weakness, emesis, and diarrhea for two days. She appeared frail, lethargic, and was intubated due to respiratory paralysis. She was found to have multiple impressive electrolyte derangements on laboratory analysis including hyponatremia (128 mmol/L), hypokalemia (2.6 mmol/L), severe hypochloremia (65 mmol/L), metabolic alkalosis and alkalemia with bicarbonate 57 mmol/L and pH 7.74, creatinine 2.21 mg/dL, and hypermagnesemia (7.8 mg/dL). She received supportive treatment including intravenous fluids and electrolyte replacement with clinical improvement and was subsequently extubated on hospital day two. Following extubation she was fixated on having bowel movements for which she requested her home medications. It was further determined she had been misusing a magnesium citrate-containing cathartic.
**Conclusion:** The paralytic effect of magnesium has long been recognized but the mechanism incompletely understood. It is thought to suppress the release of acetylcholine and block transmission at the neuromuscular junction (NMJ). In addition, it may antagonize the effects of calcium, diminishing responsiveness at the NMJ hindering muscular contraction [2,3]. Magnesium homeostasis is tightly regulated by the kidneys and may be hampered through multiple disease processes or drugs. High doses of Mg containing medications given iatrogenically or through misuse may lead to toxicity. Treatment includes supportive care, administration of calcium and in severe cases hemodialysis. We outline a unique and interesting presentation of hypermagnesemia leading to respiratory paralysis requiring intubation, developed secondarily to kidney dysfunction along with Mg cathartic abuse in the setting of an anorexia nervosa patient.

### References

[1] Lameris AL, Monnens LA, Bindels RJ, et al. Drug-induced alterations in Mg2+ homoeostasis. Clin Sci. 2012;123:1–14.
[2] Mordes JP, Wacker WE. Excess magnesium. Pharmacol Rev. 1977; 29:273–300.
[3] Agus ZS, Wasserstein A, Goldfarb S. Disorders of calcium and magnesium homeostasis. Am J Med. 1982;72:473–488.

## 213. Acute midodrine overdose

Byung Hak So

Department of Emergency Medicine, College of Medicine, St. Vincent's Hospital, The Catholic University of Korea, Seoul, South Korea

**Objective:** Midodrine is a potent, peripherally acting alpha-1 agonist, and is used in the treatment of orthostatic hypotension, recurrent reflex syncope and dialysis-associated hypotension. In several case reports, severe hypertension and bradycardia developed from overdose [1]. We report a rare case of midodrine overdose complicated with partial chordae rupture of mitral valve and subarachnoid hemorrhage.
**Case report:** A 21-year-old woman presented with a headache and dizziness for 2 hours. She had intentionally overdosed on 125 mg of midodrine 5 hours earlier, which had been prescribed for vasovagal syncope. At the scene, the patient was alert with the following vital signs: blood pressure 150/100 mmHg; pulse 48 beats/min; and respiratory rate 20 breaths/min. In the emergency room, vital signs were blood pressure 120/70 mmHg, pulse 49/min, respiratory rate 22/min, body temperature 37.0 °C, and oxygen saturation 99%. The electrocardiogram showed sinus bradycardia with T wave inversion in lead II, III, aVF, and V1–V6. The high-sensitive troponin T level was 134 ng/L, and the CK-MB level was 3.86 ng/mL. All other electrolytes, glucose, blood urea nitrogen, creatinine, and hepatic enzymes were normal. She was admitted to the intensive care unit where a transthoracic echocardiography showed a partial chordae rupture of mitral valve with moderate mitral regurgitation and a left ventricular ejection fraction of 53.3%. On day 2, the blood pressure gradually decreased to 90/50 mmHg, while headache and dizziness were sustained. A contrast brain computer tomography (CT) scan revealed thin subarachnoid hemorrhage in the left frontal lobe with no significant steno-occlusive lesion or aneurysm. She was treated with analgesics for a headache and observed for 4 days and improved with a blood pressure of 100/60 mmHg and a heart rate of 60/min.
**Conclusion:** Midodrine overdose can potentially cause severe hypertension and reflex bradycardia. Patients with an abnormal electrocardiogram and elevated cardiac enzymes should have an echocardiogram. Brain imaging should be performed for patients who have neurological symptoms such as sustained headache.

### Reference

[1] Wong LY, Wong A, Robertson T, et al. Severe hypertension and bradycardia secondary to midodrine overdose. J Med Toxicol. 2017;13:88–90.

## 214. Assessment of acute methylphenidate toxicity

Marianne J. Petscher, Florian Eyer and Tobias Zellner

Department of Clinical Toxicology, Technical University of Munich, Munich, Germany

**Objective:** Methylphenidate is one of the most prescribed psychotropic drugs for children [1]. Despite years of use, there is little data about the relationship between toxic dose and effect. We attempted to identify appropriate dose thresholds between the different severities of poisoning according to the Poison Severity Score (PSS).
**Methods:** Retrospective cross-sectional study including all monomethylphenidate exposures registered by the Poison Control Center Munich between January 2002 and July 2018. Screening all single-exposures to methylphenidate, a data set with a total number of 433 cases was obtained. Several receiver operating characteristic (ROC) analyses in the different age groups were performed to identify the best cut-off value in relation to the severity of intoxication by PSS (none/asymptomatic, mild, moderate, severe) as a function of the ingested dose.
**Results:** Most of the analyzed intoxications were mild (52.4%) or were classified as no or asymptomatic poisoning (44.8%). Moderate intoxications occurred in eleven cases (2.5%), two in schoolchildren and nine cases in adults. In the dataset, there was only one adult with a severe intoxication (0.2%). The thresholds in the adult age-group (18–65 years) were 114 mg to differentiate between asymptomatic and mild intoxication (AUC 0.63, $p = 0.005$), 310 mg between mild and moderate intoxication (AUC 0.53, $p = 0.75$) and 590 mg between moderate and severe intoxication (AUC 0.78, $p = 0.38$). In adolescents (14–17 years) the threshold between asymptomatic and mild intoxication was 95 mg (AUC 0.64, $p = 0.007$). In schoolchildren (7–13 years) it was 53 mg to differentiate between asymptomatic and mild intoxication (AUC 0.68, $p = 0.002$) and 55 mg between mild and moderate intoxication (AUC 0.30, $p = 0.34$). In young children (2–6 years), the threshold between asymptomatic and mild intoxication was 8.75 mg (AUC 0.60, $p = 0.13$) and for babies (<=1 year) it was 25 mg (AUC 0.64, $p = 0.52$).
**Conclusion:** Our analysis resulted in useful dose thresholds for methylphenidate intoxication to differentiate between asymptomatic and mild intoxications for adults (114 mg), adolescents (95 mg) and schoolchildren (53 mg). Unfortunately, due to the small number of cases for moderate and severe intoxications, the resulting thresholds can only be considered as guidance. In addition, there are too few data to define the dose thresholds for babies and infants. In conclusion, further research will be needed for a complete dose-dependent toxicological profile of methylphenidate.

### Reference

[1] Chirdkiatgumchai V, Xiao H, Fredstrom BK, et al. National trends in psychotropic medication use in young children: 1994–2009. Pediatrics. 2013;132:615–623.

## 215. Same initial drug name and pharmacist dispensing errors: a case series

Anna A. Celentano, Marcello M. Ferruzzi, Fabrizio F. Sesana and Francesco F. Scaglione

Milan Poison Control Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

**Objective:** Methotrexate is a folate antimetabolite that reversibly inhibits dihydrofolate reductase which generates tetrahydrofolic acid, therefore the generation of the N-methylene derivative donor of monocarbon units and blocks the transition from uridine monophosphate to thymidine monophosphate. Gastrointestinal, neurologic and hematologic adverse effects may appear during treatment. The initial letters "meth" of common drug name are the same letters of other active ingredients like methylergometrine maleate. The aim of this study is to describe how the storage of medicines in pharmacies by route of administration, pharmaceutical form and alphabetical order can confuse

the pharmacist in dispensing the drug. We report three dispensing errors of methylergometrine maleate with methotrexate that required hospitalization.
**Case series:** A 27-year-old female, took a 2.5 mg methotrexate tablet for 13 days. She was admitted to the emergency department (ED) with inappetence, nausea, vomiting and myalgia. Hydration was performed and she was observed. Blood tests were normal. Symptoms resolved within a day. She was discharged after 48 hours. A 25-year-old female, took a 2.5 mg methotrexate tablet for 5 days. From the third day, she experienced abdominal pain and myalgia. The patient was admitted to the ED. Blood tests were normal. Hydration was performed and symptoms resolved within a day. She was discharged after 48 hours. A 26-year-old female, took one 2.5 mg methotrexate tablet for 15 days. Transaminases were elevated on admission: alanine aminotransferase 85 U/L, aspartate aminotransferase 80 U/L, gamma-glutamyl transferase 50 U/L. A basic metabolic panel was monitored every 12 hours and transaminases stabilized within 10 days. She was discharged after 10 days of hospitalization. Methotrexate concentrations were not measured in these cases. All cases involved lactating women. Breastfeeding was suspended in all cases and the newborns were clinically observed without complications.
**Conclusion:** The initial letters "meth" of methylergometrine maleate and methotrexate are the same but they are completely different drugs. The risk for medication error is much higher when the two drugs are in close proximity. Pharmacists must be very careful in dispensing the drugs, especially if two drugs with similar names are stored closely. In this type of error, breastfeeding must be suspended and medical attention is required for both mother and baby. A separate storage location and a marker attention of the methotrexate tablets stock can be a strategy to prevent this kind of therapeutic error.

## 216. Survival after severe bupropion toxicity treated with extracorporeal membrane oxygenation (ECMO)

Brian G. Wiener[a], Sage W. Wiener[b], Mary Ann Howland[c], Mark K. Su[d] and Emily Cohen[a]

[a]Department of Emergency Medicine, Division of Medical Toxicology, New York University Grossman School of Medicine, New York, NY, USA; [b]Department of Emergency Medicine, SUNY Downstate Medical University, New York, NY, USA; [c]College of Pharmacy and Health Sciences, St. John's University, New York, NY, USA; [d]New York City Poison Control Center, New York, NY, USA

**Objective:** Cardiotoxicity from bupropion poisoning can be life-threatening, resulting in prolonged QRS and QT intervals, dysrhythmias, and refractory cardiogenic shock. Extracorporeal membrane oxygenation (ECMO) has been successfully used to treat refractory bupropion cardiotoxicity. We describe a patient with severe bupropion poisoning and cardiotoxicity who survived after treatment with veno-arterial (VA) ECMO.
**Case report:** A 15-year-old 76 kg boy with a history of major depressive disorder presented to the emergency department (ED) 4.5 hours after intentionally ingesting 6000 mg of bupropion extended-release tablets (79 mg/kg) in a suicide attempt. Upon ED arrival he was hallucinating and initial vital signs were: BP 130/80 mmHg; pulse 157/minute; respirations 16/minute; temperature 37.2 °C orally; oxygen saturation 99% (room air). Physical examination was notable for slight confusion and dilated reactive pupils. Initial laboratory test results were within normal limits. Initial electrocardiogram (ECG) showed sinus tachycardia at 110/minute, QRS duration of 104 ms; QTc duration of 560 ms. The patient was given 50 g of activated charcoal and a nasogastric tube was placed with initiation of whole bowel irrigation. Four hours after ED presentation, the patient experienced multiple generalized tonic-clonic seizures which ceased following administration of 10 mg of intravenous midazolam. Midazolam infusion at 10 mg/h was continued for maintenance. Six hours after ED presentation, he developed status epilepticus requiring endotracheal intubation and a continuous propofol infusion to halt seizure activity. Follow-up ECG obtained 14 hours after ED presentation showed sinus tachycardia, rate 151/minute; QRS duration of 122 ms; QTc duration of 567 ms; and ST segment depression in the precordial leads. Administration of 150 mEq sodium bicarbonate did not shorten the QRS interval. The patient was cannulated on VA-ECMO 15 hours after ED presentation and remained on VA-ECMO for 72 hours. Upon decannulation, a thrombus was found in the right femoral artery. It was surgically removed with good return of blood flow. The patient was evaluated by psychiatry and ultimately discharged from the hospital without any known or perceived deficits.
**Conclusion:** Despite ingesting a potentially lethal dose of bupropion and developing significant signs of toxicity, this patient made a complete recovery following treatment with VA-ECMO. Determining which patients with bupropion toxicity should receive ECMO is not well-established and further research is required.

## 217. Vitamin-K antagonist toxicity from empagliflozin dispensing error

Zachary P. Schmitz, Mark K. Su and Robert S. Hoffman

New York City Poison Control Center, New York City, NY, USA

**Objective:** We report a patient who developed coagulopathy after incorrectly receiving Jantoven (warfarin) instead of his prescribed Jardiance (empagliflozin) to highlight the risks of pharmacy errors.
**Case report:** A 66-year-old man with hypertension, hyperlipidemia, diabetes mellitus, and coronary artery disease presented to the emergency department (ED) with three days of flank pain and hematuria. His prescribed medications included aspirin, amlodipine, empagliflozin, lisinopril, metoprolol, rosuvastatin, and sitagliptin-metformin. His vital signs and physical examination were unremarkable, however, his laboratory evaluation was notable for hemoglobin 111 g/L, glucose 10.4 mmol/L, calcium 1.65 mmol/L, magnesium 1.0 mEq/L, prothrombin time (PT) $>$ 100 seconds, International Normalized Ratio (INR) $>$ 9.31, and partial thromboplastin time (PTT) 71.5 seconds. His urinalysis showed "large blood" and $>$50 red blood cells per high power field (RBC/HPF). A computed tomography (CT) scan of the abdomen and pelvis with intravenous contrast was unremarkable. He was given vitamin K, 10 mg orally, and hospitalized for observation and evaluation of his coagulopathy. His INR the following morning decreased to 1.5 and he was discharged home without a diagnosis. Soon after discharge, the toxicology team encouraged the patient to return to the ED with his home medications. Two days after his initial ED presentation, he was reevaluated and we discovered that his Jardiance (empagliflozin) was actually generic, but similarly named Jantoven (warfarin). His repeat INR was 3.15. Factor levels from his initial admission (before vitamin K administration) were: Factor II 4%; Factor V 126%; Factor VIII 136%; Factor IX 8%; and Factor X 4%. He was readmitted to the hospital and received vitamin K, 10 mg orally. The following morning his INR was 1.16. He was discharged home with instructions to discard his remaining empagliflozin. After discharge, he had no further INR elevation and at 4-month urology follow-up had had no additional episodes of hematuria. Internal review by

the pharmacy identified that the incorrect bottle was selected by a technician, and subsequent visual verification by a pharmacist did not identify the error. Mistaking Jantoven for Jardiance is not identified on the Institute for Safe Medication Practice's list of confused drug names [1].
**Conclusion:** Pharmacy-related errors can lead to life-threatening situations. Patients with unexplained signs, symptoms, or laboratory findings should have their home medications physically examined to ensure they are accurate. Pharmacies should avoid stocking similarly-named bottles in close proximity.

## Reference

[1] Institute for Safe Medication Practices (ISMP). List of confused drug names; February 28 2019 [cited 2022 Oct 10]. Available from https://www.ismp.org/recommendations/confused-drug-names-list.

# 218. Acute toxicity profile of promazine in overdose: a consecutive case series

Evelyne L. Jina Prüss, Colette Degrandi, Katrin Faber and Alexander Jetter

National Poisons Centre, Tox Info Suisse, Associated Institute of the University of Zurich, Zurich, Switzerland

**Objective:** Promazine is a phenothiazine neuroleptic drug approved in adults and children >12 years. The daily oral dose varies between 100 and 800 mg. Doses of 1000 mg daily should not be exceeded. Promazine is widely used in psychotic disorders and to relieve nausea and vomiting in various medical conditions. However, information on the clinical features of promazine poisoning is lacking. The aim of this study is to investigate the demographics and clinical features of acute promazine overdose.
**Methods:** Retrospective review of single-substance acute oral overdoses with promazine in adults and children (<16 years), reported to our poison centre 1997–2021 by physicians and with a high causality assessment. Severity was graded according to the Poisoning Severity Score.
**Results:** Overall, 156 patients (median age 30, range 1.2-75 years) were included with 119 females (76%), 35 males (22%) and 2 unknown. There were 141 adults (90%) and 15 children (10%, median: 3.3 years, range 1.2–15.0). No symptoms developed in 14 adults (10% of adults) and 6 children (40% of children). Mild symptoms were seen in 101 adults (72%) and 7 children (47%). Moderate symptoms occurred in 22 adults (16%) and 1 child (7%), and 4 adults (3%) and 1 child (7%) had severe symptoms. There were no fatalities. Effects predominantly involved the central nervous system, with somnolence reported in 60% of patients. Further, more frequently reported central nervous system (CNS) effects were drowsiness (8%), vertigo (8%), dry mouth (7%), dysarthria (5%) and miosis (4%). Tachycardia (25%), hypotension (12%) and prolongation of QT (12%) were common cardiovascular findings. Gastrointestinal symptoms (nausea, vomiting, and epigastric pain) were also common (12%). Severe symptoms occurred in 4 adults after intentional ingestion (coma with a Glasgow Coma Score (GCS) ≤ 7 in 2, status epilepticus and severe hypotonia each in 1 patient), while one case with severe symptoms (coma) after accidental ingestion concerned a child (1.2 year; 4.2 mg/kg). The majority of adult patients (14/22) with moderate symptoms ingested ≥1000 mg (median 1875 mg, mean 2195 mg, range 300–8500 mg); 4/4 adult patients with severe symptoms ingested ≥2500 mg (median 3475 mg, range 2500–5000 mg).
**Conclusion:** Promazine displays an acute toxicity profile similar to other phenothiazine neuroleptics [1]. In adults, severe courses occurred only with doses 2.5-times above the maximum recommended dose. Accidental ingestions by toddlers may be of concern.

## Reference

[1] Parsons M, Buckley NA. Overdose of antipsychotic drugs: practical management guidelines. CNS Drugs. 1997;7:427–441.

# 219. Are methotrexate plasma quantifications important in intoxications with low-dose methotrexate?

Alexander Jetter, Seraina Kägi, Colette Degrandi, Cornelia Reichert and Katrin Faber

National Poisons Centre, Tox Info Suisse, Associated Institute of the University of Zurich, Zurich, Switzerland

**Objective:** Methotrexate is either given as an antineoplastic agent in single intravenous doses of up to 30 g and more in patients with lymphoma, sarcoma and other malignancies, or as an oral low-dose immunosuppressive therapy of between 5 and 30 mg weekly in patients with rheumatoid disorders. While for high-dose therapies, serum or plasma concentration monitoring is crucial to counteract life-threatening side effects, in low-dose therapies, concentrations are not routinely quantified. However, in intoxications and when overdoses have been administered to patients on low-dose methotrexate, concentration quantifications are often recommended. Our aim was to investigate whether concentrations are useful to predict symptom severity or outcome, or to manage calcium folinate therapy.
**Methods:** Retrospective data analysis of methotrexate associated cases reported to our National Poison Control Centre between January 1997 and December 2021. Only those cases were included where the treating physicians reported a follow-up to our centre and if causality of symptoms was reasonable. Severity was graded according to the Poisoning Severity Score.
**Results:** Methotrexate was among the causative agents in 117 cases. Eleven patients were treated with high-dose methotrexate and were therefore excluded. Of the 106 cases who did not receive a high-dose methotrexate regimen, 20 cases were without symptoms. These 106 cases could be divided in a group where the weekly low-dose regimen had erroneously been given more frequently, e.g., daily for a certain time span ($n = 73$), and a group with accidental ingestion of methotrexate, e.g., children or as a result of a medication mix-up ($n = 33$). In 52 cases, methotrexate quantifications were carried out after the intoxication had taken place. The concentrations were below the (lab-specific) quantification limit in 12 cases. In 40 cases with no ($n = 10$), mild ($n = 9$), moderate ($n = 5$) and severe ($n = 8$) toxicity symptoms as well as in the fatal cases ($n = 4$), medians of concentrations were 0.59, 0.09, 0.34, 0.17, and 0.15 μmol/L, respectively. There was no relationship between the severity of the intoxication and methotrexate concentrations. Calcium folinate was administered to 68 patients, of which 22 patients had no (reported) quantification results, and 8 had no quantifiable methotrexate concentrations.
**Conclusion:** Quantifications of methotrexate in serum or plasma of patients with intake errors of low-dose methotrexate are not useful to predict intoxication symptom severity or outcome. There was no clear link between methotrexate quantification

results and calcium folinate administration management, possibly also due to the small numbers.

## 220. Chronic doxepin toxicity from supratherapeutic dosing, drug interactions, and pharmacogenomic variability masquerading as pediatric epilepsy

James D. Whitledge[a], Christopher J. Watson[b] and Michele M. Burns[a]

[a]Harvard Medical Toxicology Fellowship, Boston Children's Hospital, Boston, MA, USA; [b]Department of Emergency Medicine, Maine Medical Center, Portland, OR, USA

**Objective:** Describe chronic doxepin toxicity initially masquerading as epilepsy in a child from supratherapeutic dosing, drug interactions, and pharmacogenomic variability.
**Case report:** A 10-year-old 68 kg boy with insomnia and epilepsy presented to an academic pediatric hospital emergency department (ED) with increasing seizure frequency and confusion. At initial epilepsy diagnosis six months prior, seizures occurred monthly, however by ED presentation were occurring 2–3 times every other day. Medications included doxepin 300 mg daily for insomnia, and clobazam 10 mg and topiramate 300 mg daily for seizures. He had normal vital signs and was confused, dysarthric, and ataxic. Serum clobazam and topiramate concentrations were normal. The patient was admitted to the neurology service for suspected epileptic encephalopathy and doxepin, topiramate, and clobazam were discontinued. He had two seizures on hospital day 2 (HD2). Brain magnetic resonance imaging (MRI) was normal. Serial electroencephalograms (EEG) showed seizures, decreased seizure threshold, and encephalopathy. On HD4, he was persistently encephalopathic and toxicology was consulted for possible doxepin withdrawal. Electrocardiogram (EKG) review by toxicology, however, was suspicious for doxepin toxicity, with rate of 110, QRS 144 ms, right axis deviation, right bundle branch block, 11 mm terminal R-wave and 1:1 R:S ratio in aVR, therefore serum doxepin concentrations were obtained. Peak doxepin-nordoxepin combined concentration, obtained HD1 29 hours after last dose, was 1419 ng/mL (therapeutic range 100-300 ng/mL). HD8 doxepin-nordoxepin concentration was 528 ng/mL. Elimination kinetics were first-order. Pharmacogenomic testing of cytochrome p450 (CYP) enzymes responsible for doxepin metabolism, 2C19 and 2D6, showed normal 2C19 but reduced 2D6 function. Prior outpatient records review revealed seizure onset after doxepin dose increase to 200 mg six months prior for insomnia, with confusion and ataxia occurring weeks before first seizure. Worsening of confusion and seizure frequency coincided with initiation of topiramate (2C19 inhibitor) and clobazam (2D6 inhibitor) for worsening epilepsy, and doxepin dose increase to 300 mg. During hospitalization the patient experienced no arrhythmias. Confusion and ataxia resolved by HD10 when he was discharged. At follow-up outpatient neurology appointment, EKG and EEG normalized. The patient has had no seizures in six months since discharge.
**Conclusion:** This patient developed chronic doxepin toxicity with confusion, ataxia, and seizures without hemodynamically significant cardiotoxicity from supratherapeutic doxepin dosing (maximum daily dose 3 mg/kg, or 204 mg), decreased baseline CYP2D6 activity, and CYP2C19 and CYP2D6 inhibition by co-prescribed antiepileptics. His six-month seizure history was, in fact, doxepin-induced and not due to epilepsy.

## 221. Delayed salicylate toxicity requiring urinary alkalinization after undetectable eight-hour serum salicylate concentration

Chris Y. Feng, James D. Whitledge, Michael Simpson, Andrew Troger and Michele M. Burns

Boston Children's Hospital, Boston, MA, USA

**Objective:** To describe a case of delayed salicylate toxicity requiring urinary alkalinization after multiple nontoxic and undetectable serum salicylate concentrations up to eight hours post-ingestion
**Case report:** A 16-year-old female liver transplant recipient presented after a single, acute ingestion of an estimated 950 mg/kg of valganciclovir and 430 mg/kg of aspirin. It was uncertain whether the aspirin tablets were enteric-coated. She initially presented to a community emergency department with nausea and emesis. Physical exam and vitals were unremarkable. The chemistry and venous blood gas were normal. Serum salicylate concentrations were $<$0.3 mg/dL at 2.9 hours, 0.4 mg/dL at 4.8 hours, and $<$0.3 mg/dL at 7.8 hours after ingestion. No activated charcoal was given. More than 12 hours post-ingestion the patient developed tinnitus. At 30 hours post-ingestion she was transferred to a tertiary-care pediatric hospital after developing mild acute kidney injury with the history of liver transplant. Upon arrival the patient had baseline mentation and was noted to have persistent nausea and tinnitus. A repeat serum salicylate concentration was obtained given the large ingestion and the concern for delayed toxicity in the setting of continued symptoms of aspirin toxicity. A 40 hour serum salicylate concentration was 30.5 mg/dL, prompting the initiation of a sodium bicarbonate infusion and a one-time 50 g dose of activated charcoal. Serial serum salicylate concentrations subsequently downtrended without recurrent peak and with complete resolution of tinnitus.
**Conclusion:** Delayed aspirin absorption in large ingestions is hypothesized to result from pylorospasm, pharmacobezoar formation, and altered toxicokinetics. Case reports illustrate several salicylate-toxic patients with initial undetectable serum salicylate concentrations up to three hours post-ingestion [1]. Undetectable concentrations were also reported up to 225 minutes in one retrospective cohort study of salicylate-toxic patients [2]. This case demonstrates several nontoxic and undetectable salicylate concentrations up to eight hours post-ingestion, nearly twice as long as previously described. Although the second salicylate concentration was minimally detectable at 0.4 mg/dL, this nontoxic concentration would have been undetectable with less sensitive testing assays used at most other hospitals. This case suggests that a prolonged laboratory monitoring approach may be necessary in some patients after large aspirin ingestions despite reassuring early undetectable serum concentrations.

### References

[1] Wortzman DJ, Grunfeld A. Delayed absorption following enteric-coated aspirin overdose. Ann Emerg Med. 1987;16:434–436.
[2] Moss MJ, Fisher JA, Kenny TA, et al. Salicylate toxicity after undetectable serum salicylate concentration: a retrospective cohort study. Clin Toxicol. 2019;57:137–140.

## 222. Late ventricular fibrillation cardiac arrest in a case of bupropion overdose with status epilepticus

Joshua Bloom[a], Nata Cisse[b], Mary Ann Howland[c], Donald Doukas[c], Sage W. Wiener[d] and Mark K. Su[e]

[a]Ronald O. Perelman Department of Emergency Medicine, NYU Grossman School of Medicine, New York, NY, USA; [b]Department of Emergency Medicine, NYCH + H/Kings County, New York, NY, USA; [c]St. John's University College of Pharmacy and Health Sciences, New York, NY, USA; [d]Department of Emergency Medicine, SUNY Downstate Health Sciences University, New York, NY, USA; [e]Department of Health and Mental Hygiene, New York City Poison Control Center, New York, NY, USA

**Objective:** Bupropion is an atypical antidepressant that can cause life-threatening neurotoxicity and cardiotoxicity when taken in overdose. Clinical effects of bupropion toxicity can be delayed, and a 24-hour observation period is commonly implemented for patients following overdose [1]. We present a case of a patient who developed status epilepticus after a bupropion overdose who initially improved after aggressive decontamination and treatment, but then developed refractory ventricular fibrillation cardiac arrest and died approximately 45 hours after the exposure.
**Case report:** A 27-year-old man with a history of major depressive disorder intentionally ingested 113 tablets of 75 mg immediate-release bupropion and presented to the emergency department (ED) approximately an hour later with agitation and confusion after a witnessed generalized tonic-clonic (GTC) seizure at home. On arrival, he had another GTC seizure and was intubated for airway protection. The ED providers performed gastric lavage and whole bowel irrigation interspersed with multiple doses of activated charcoal. He was placed on propofol and midazolam infusions under continuous electroencephalography monitoring and no further seizures occurred. Initial electrocardiography revealed a QRS duration of 110 ms (unaffected by a bolus/infusion of sodium bicarbonate) and a corrected QT interval (Rautaharju) of 575 ms. He had a kidney injury at admission that worsened with a peak serum creatinine of 224 μmol/L (normal 62–106 μmol/L). On the second hospital day he developed hypotension and a new wide-complex rhythm; minutes later, he suffered a ventricular fibrillation cardiac arrest. He could not be resuscitated with advanced cardiac life support and was pronounced dead approximately 45 hours after ingestion. Drug testing on blood drawn within an hour of ED arrival showed a bupropion concentration of >1000 ng/mL (therapeutic 10–100 ng/mL) and hydoxybupropion concentration of 1440 ng/mL (therapeutic 850–1000 ng/mL). Although no autopsy was performed, the medical examiner assigned bupropion toxicity as the cause of death.
**Conclusion:** Despite this patient's exposure to immediate release bupropion and aggressive gastrointestinal decontamination, he still experienced a malignant dysrhythmia and died almost two days after ingestion. Patients with severe bupropion toxicity should be monitored closely for adverse cardiac and neurologic events for a minimum of 24 hours. Future studies need to determine which patients require extended observation or access to extracorporeal life support.

### Reference

[1] Al-Abri SA, Orengo JP, Hayashi S, et al. Delayed bupropion cardiotoxicity associated with elevated serum concentrations of bupropion but not hydroxybupropion. Clin Toxicol. 2013;51:1230–1234.

## 223. Ifosfamide neurotoxicity treated with methylene blue complicated by serotonin toxicity

Ahmed Alsakha and Jeanna M Marraffa

Department of Emergency Medicine, SUNY Upstate Medical University, Syracuse, NY, USA

**Objective:** Ifosfamide is an alkylating chemotherapeutic used in the treatment of various malignancies. Encephalopathy ranging from self-limited to severe or even fatal, complicates ifosfamide treatment [1,2]. Methylene blue (MB) is commonly used to treat ifosfamide neurotoxicity due to its ability to inhibit monoamine oxidase, which is responsible for producing ifosfamide's neurotoxic metabolite, chloroacetaldehyde [2]. Serotonin toxicity (ST) results from excess serotonin in the central nervous system (CNS). The spectrum of toxicity varies and involves neuromuscular excitation, autonomic instability, and mental status change [3]. Methylene blue is reported to cause ST in combination with other serotonergic drugs particularly with doses greater than 5 mg/kg [4]. The use of cyproheptadine as an "antidote" is controversial, however it is widely taught to non-toxicologists [3]. We report a case of ifosfamide neurotoxicity treated with MB, complicated by ST and treated with cyproheptadine.
**Case report:** A 54-year-old female with a history of metastatic leiomyosarcoma, on bupropion and fluoxetine was started on high dose ifosfamide 1500 mg/m$^2$, mesna, and doxorubicin. Twelve hours after starting ifosfamide, she became confused, aggressive, with hallucinations, but hemodynamically stable with a nonfocal neurological exam. Ifosfamide neurotoxicity was suspected and further chemotherapy was held. She was started on methylene blue 50 mg (0.66 mg/kg) intravenously every 4 hours and thiamine 500 mg three times daily. After receiving the 4th dose of MB, she became more confused, agitated, diaphoretic, and hypertensive with ocular and lower extremity clonus, and mild rigidity. ST was suspected and she was started on cyproheptadine 12 mg. She improved with resolution of her signs and symptoms and returned to baseline.
**Conclusion:** Encephalopathy is a potentially life-threatening complication of ifosfamide that may be treated with MB. Co-administration of MB with other serotonergic drugs increases the risk of ST. In addition to discontinuation of offending agents, treatment of ST includes benzodiazepines with cyproheptadine as an option. Clinicians should be aware of the signs of ST as they may be confused as ifosfamide toxicity and go unrecognized.

Table 1. Serial coagulation studies at hour (h) relative to time (t) of argatroban overdose.

| Coagulation study (reference range) | Baseline | t + 5h | t + 11.5h | t + 17.5h | t + 30h |
|---|---|---|---|---|---|
| Prothrombin time (PT) (9.4–12.5 seconds) | 14.7 | >320.0 | 161.0 | 134.8 | 96.3 |
| International Normalized Ratio (INR) (0.85–1.13) | 1.24 | >12.80 | >12.80 | 10.88 | 7.83 |
| Activated partial thromboplastin time (aPTT) (25.1–36.5 seconds) | 28 | >400.0 | >400.0 | >400.0 | 127.5 |

## References

[1] Sweiss KI, Beri R, Shord S. Encephalopathy after high-dose Ifosfamide: a retrospective cohort study and review of the literature. Drug Saf. 2008;31:989–996.
[2] Ajithkumar T, Parkinson C, Shamshad F, et al. Ifosfamide encephalopathy. Clin Oncol. 2007;19:108–114.
[3] Isbister GK, Buckley NA, Whyte IM. Serotonin toxicity: a practical approach to diagnosis and treatment. Med J Aust. 2007;187:361–365.
[4] Ng BK, Cameron AJ. The role of methylene blue in serotonin syndrome: a systematic review. Psychosomatics. 2010;51:194–200.


# 224. Argatroban overdose without bleeding complications


Marlis Gnirke, Silas W. Smith and Robert S. Hoffman

Ronald O. Perelman Department of Emergency Medicine, Division of Medical Toxicology, NYU Grossman School of Medicine, New York City, NY, USA


**Objective:** Argatroban is a direct thrombin inhibitor used to anticoagulate patients with heparin-induced thrombocytopenia (HIT) and those with or at risk for HIT undergoing percutaneous coronary intervention. Overdoses are rare. We report a critically ill patient who received a 250 mg overdose of argatroban without bleeding complications.
**Case report:** A 61-year-old, 58 kg, woman with a history of metastatic uterine sarcoma was admitted for urosepsis and developed thrombocytopenia concerning for HIT. She was ordered for argatroban, but in a medication error, 250 mg argatroban was inadvertently administered by rapid bolus instead of 0.5 μg/kg/min. Argatroban was discontinued, and serial coagulation studies were obtained (Table 1). Although she succumbed to urosepsis two days later, she never developed bleeding.
**Conclusion:** Following this large argatroban overdose (4.3 mg/kg), coagulation studies were markedly prolonged and trended towards normalization without intervention. While the patient expired prior to complete normalization, she never developed bleeding, and her death was unrelated to the argatroban overdose. Two previously reported argatroban overdoses describe similar normalization of prolonged coagulation studies over approximately 48 hours without bleeding complications [1,2]. One patient received fresh frozen plasma with a transient numerical reduction of coagulation studies. Our case adds to the rare literature of argatroban overdose. We suggest a conservative management approach guided by serial coagulation studies with therapy indicated for clinical bleeding or the need for a procedural intervention, rather than abnormal coagulation studies.


## References

[1] Yee AJ, Kuter DJ. Successful recovery after an overdose of argatroban. Ann Pharmacother. 2006;40:336–339.
[2] Knoblauch R, Pollak ES, Russell JE. Toxicity of argatroban overdose in a 65-year-old man. Am J Hematol. 2005;79:248–249.


# 225. Accidental minoxidil overdose with hypotension effectively managed with noradrenaline, rather than dopamine


Bashir Chakar, Mark Salter and Darren M. Roberts

NSW Poisons Information Centre, Sydney, Australia


**Objective:** Minoxidil is an arterial vasodilator used to treat androgenic alopecia. Overdose manifests as distributive shock, pulmonary oedema, and myocardial ischaemia. Published cases are uncommon, and they suggest dopamine as a first line vasopressor due to concerns about arrhythmias from noradrenaline and adrenaline. We report a case of severe minoxidil poisoning responding poorly to dopamine infusion, but effectively managed with noradrenaline.
**Case report:** A 36-year-old man without a significant medical history unintentionally ingested 10–30 mL of minoxidil 5% topical liquid (500–1500 mg minoxidil). Six hours following ingestion, he developed abdominal pain and vomiting so presented to hospital. Initial assessment demonstrated blood pressure (BP) 81/60 mmHg, sinus tachycardia (120 beats/minute), hyperlactataemia (4.9 mmol/L) and acute kidney injury (creatinine 174 μmol/L). Fluid resuscitation with 3L crystalloid over 3 hours had minimal effect on haemodynamics, but lactate decreased to 1.9 mmol/L. Approximately 12 hours post-ingestion he complained of chest pain. He had systolic BP 90mmHg with no clinical features of systemic hypoperfusion, electrocardiograph (ECG) demonstrated ST elevation in aVR with widespread reciprocal ST depression; high sensitivity troponin was normal. Based on published literature, a dopamine infusion was initiated and quickly uptitrated to 20 μg/kg/min with minimal haemodynamic improvement (systolic BP 80-90 mmHg and heart rate 120 beats/minute). A further 4 L of crystalloid resulted in short-lived BP improvements but the patient developed pulmonary oedema. A transthoracic echocardiogram showed hyperdynamic contractility without regional wall motion abnormalities, ECG showed persistent global ischaemia and repeat troponin 19 ng/L (reference $<$15 ng/L). A noradrenaline infusion and 40 mg intravenous furosemide were initiated. The haemodynamic improvement was marked, the dopamine was rapidly weaned and ceased as the noradrenaline was uptitrated to 15 μg/min. He required noradrenaline for two days. Within 36 hours of overdose the patient's troponin peaked at 67 ng/L, his ECG normalised, and acute kidney injury resolved. A repeat echocardiogram on day two showed normal cardiac function. He was discharged medically well without complications.
**Conclusion:** Minoxidil overdoses are uncommon, manifesting predominantly as distributive shock requiring pressor support. In this case, there was an inadequate response to dopamine, pulmonary oedema exacerbated by excessive volume loading, and myocardial ischaemia. Two other cases document failure of dopamine infusion, followed by an excellent response to alpha1 agonists such as phenylephrine or noradrenaline in this context. Therefore, we recommend that volume loading and noradrenaline are the preferred vasopressors for shock due to minoxidil.

# 226. Acute toxicity profile of Deanxit®: a consecutive case series of overdoses over 48 years


Katrin Faber[a], Arsenije Stojkovic[b], Cornelia Reichert[a] and Alexander Jetter[a,c]

[a]National Poisons Centre, Tox Info Suisse, Associated Institute of the University of Zurich, Zurich, Switzerland; [b]Faculty of Medicine, University of Bern, Bern, Switzerland; [c]Department of Clinical Pharmacology and Toxicology, University Hospital of Zurich, Zurich, Switzerland

**Objective:** Deanxit® comprises 10 mg melitracen, a tricyclic antidepressant, and 0.5 mg flupenthixol, a phenothiazine neuroleptic drug. It is licensed for the treatment of depressive conditions and anxiety in adults only, and prescribed since the 1970s in Switzerland. It is also approved in Austria, Spain and Belgium. The maximum daily dose is 4 pills (corresponding to 40 mg/2 mg). Detailed information on Deanxit® poisoning is scarce [1]. We investigated the demographics and effects of acute Deanxit® overdoses.
**Methods:** Retrospective case series of single-drug overdoses with Deanxit® reported by physicians to our National Poisons Centre from 1973 (first case of overdose in our database) to 2021 with high causality assessment. Severity was graded according to the Poisoning Severity Score.
**Results:** Overall, 269 cases met the inclusion criteria: 72 children ≤6 years (median age 2.5 years, range 0.7–6 years; 43.1% females, 44.4% males, 12.5% unknown), 2 schoolchildren (9 and 11 years), 11 adolescents (≥12 – <16 years) and 184 adults (median age 30 years, range 16–87 years; 78.8% females, 19.0% males, unknown 2.2%). All overdoses in children >6 years were intentional and grouped in the adult cohort ($n = 197$). Symptoms predominantly involved the central nervous system. Moderate and severe cases were characterized by agitation or coma, with complications such as aspiration pneumonia and rhabdomyolysis. Convulsions were reported in only two cases and notably no severe electrocardiogram (ECG)-alterations occurred. Severity and estimated dose (number of cases with known dose; median number of pills; range) in children ≤6 years ($n = 72$) were: 72.2% asymptomatic cases (43/52: 2; 0.5–8) and 16.7% mild symptoms (11/12: 6; 1–25). Moderate symptoms occured in 11.1% (5/8: 20; 1–27). Severity and estimated dose (number of cases with known dose; median number of pills; range) in adults and children >6 years ($n = 197$) were: 18.3% asymptomatic cases (34/38; 18.8; 5–65) and 44.2% minor symptoms (85/87; 20; 4–106). All patients >6 years with moderate symptoms (29.9%) ingested ≥10 pills (56/59; 40; 10–275), whereas severe symptoms (6.1%) only occurred with ≥20 pills (9/12; 70; 20–100). There was one fatality (0.5%) with missing details.
**Conclusion:** In this cohort, there were no severe symptoms in accidental ingestions by children ≤6 years. Severe symptoms were only seen in ingestions of ≥5-fold the maximal recommended daily dose of Deanxit®.

## Reference

[1] Fuhrmann M, Hruby K, Gössinger H, et al. Clinical aspects and therapy of acute poisoning by the drug combination melitracen-flupenthixol (Deanxit). Wien Med Wochenschr. 1983;133:283–286.

# 227. Two are better (worse) than one: dapagliflozin and metformin combination drug overdose

Ophir Lavon
Carmel Medical Center, Haifa, Israel

**Objective:** To report a case of dapagliflozin and metformin combination drug overdose.
**Case report:** A 29-year-old male without chronic comorbidities was referred to the emergency department about 2 hours after an intentional overdose with 8 of his mother's tablets containing the combination of dapagliflozin propanediol 5 mg and metformin hydrochloride 1,000 mg. Upon admission he was alert, hypertensive (150/88 mmHg) and tachycardic (100/min), without noticeable respiratory distress, and complaining of a headache. Shortly after, he vomited once. He reported vomiting also 30 minutes before admission. Activated charcoal was withheld due to the repeated vomiting. Physical examination was unremarkable. Blood tests revealed mild lactic metabolic acidosis with responsive respiratory alkalosis (venous blood pH 7.34, bicarbonate 21 mmol/L, lactate 3.8 mmol/L, $pCO_2$ 38 mmHg), mildly elevated hepatic enzymes (aspartate aminotransferase (AST) 44 U/L, alanine aminotransferase (ALT) 84 U/L, gamma-glutamyl transferase (GGT) 98 U/L) and hypokalemia (3.1 mEq/L). Blood glucose and amylase were within normal ranges (93 and 71 mg/dL, respectively). Urinalysis was unremarkable, with no ketones. About one hour later, the lactic acidosis had slightly worsened (pH 7.30, bicarbonate 18 mmol/L, lactate 4.4 mmol/L, $pCO_2$ 37 mmHg), and remained at similar levels for another 5 hours before gradually improving. No ketones appeared in repeated urinalysis. He was treated with IV fluids (normal saline 0.9%, 1,000 mL). During hospital observation, the patient gradually improved. The headache subsided and vital signs returned to normal ranges. Twelve hours after admission, pH normalized (7.36), and bicarbonate and lactate were close to normal ranges (22.4 mmol/L and 2.5 mmol/L, respectively). Potassium normalized (3.7 mEq/L) and liver enzymes were partially improved (AST 40 U/L, ALT 75 U/L, GGT 83 U/L). The patient was transferred to a psychiatric facility for further dedicated treatment. No toxicological sequelae were reported.
**Conclusion:** In the presented case, ingestion of 8 g of metformin and 40 mg of dapagliflozin by a young healthy adult resulted in symptomatic poisoning with mild lactic metabolic acidosis. Synergistic effect of the drug combination cannot be excluded. As diabetic drug combinations are more frequently used, an increase in the incidence of overdoses with such medications is expected with higher risk for more serious poisonings. Overdose with sodium-glucose co-transporter-2 (SGLT2) inhibitors and metformin combinations can potentially increase the risk for clinically significant metabolic acidosis with fewer tablets ingested.

# 228. A case of large intravenous terbutaline overdose

Kyle D. Pires[a], Mark K. Su[b] and William Chiang[a]
[a]Ronald O. Perelman Department of Emergency Medicine, Division of Medical Toxicology, NYU Grossman School of Medicine, New York, NY, USA; [b]New York City Poison Control Center, New York, NY, USA

**Objective:** Terbutaline is a beta-adrenergic agonist used off-label via the intravenous route for refractory bronchospasm. We report a case of intravenous terbutaline overdose in a child with reactive airway disease (RAD).
**Case report:** A 4-year-old 22 kg female with a history of RAD presented to a pediatric emergency room with acute shortness of breath. Her vital signs on presentation were: blood pressure (BP) 122/79 mmHg; heart rate (HR) 147 beats/minute; RR 42 breaths/minute; temperature 37.6 °C; oxygen saturation 95% (room air). Her physical examination was notable for diffuse wheezing and retractions. She received nebulized albuterol and intravenous corticosteroids but eventually required non-invasive positive pressure ventilation (NIPPV). Given ongoing bronchospasm, the medical team administered terbutaline. The patient

received an intravenous dose of 220 μg (10 μg/kg), followed by an inadvertent supratherapeutic intravenous dose of 10,000 μg (454.5 μg/kg); over 45 times the off-label intravenous recommended dosing. Repeat vital signs after terbutaline administration were: BP 115/48 mmHg; HR 205 beats/minute; RR 40 breaths/minute; temperature, 37.6 °C; oxygen saturation 96% (NIPPV). Repeat examination was notable for somnolence but decreased wheezing. The patient's laboratory results obtained minutes after the medication error demonstrated: potassium 3.1 mmol/L, pH, 7.35, lactate 2.6 mmol/L, and troponin I, 0.30 ng/mL (normal <0.03 ng/mL). Her ECG demonstrated sinus tachycardia without ischemic changes. Three hours later, after 20 mL/kg of IV crystalloid, her vital signs were: BP 122/54 mmHg; HR 172 beats/minute. Over the next 48 hours, serial serum troponin values decreased.

**Conclusion:** There is a paucity of literature on intravenous terbutaline overdose. Three studies have examined troponin concentrations in pediatric patients receiving therapeutic dosing of terbutaline for asthma exacerbation with equivocal results [1–3]. To our knowledge, this is the first report of a large intravenous terbutaline overdose associated with an elevated troponin. Although our patient had no apparent sequelae following the overdose, pediatric patients who receive terbutaline in overdose may be at risk for myocardial injury.

## References


[1] Chiang VW, Burns JP, Rifai N, et al. Cardiac toxicity of intravenous terbutaline for the treatment of severe asthma in children: a prospective assessment. J Pediatr. 2000;137:73–77.

[2] Carroll CL, Coro M, Cowl A, et al. Transient occult cardiotoxicity in children receiving continuous beta-agonist therapy. World J Pediatr. 2014;10:324–329.

[3] Kalyanaraman M, Bhalala U, Leoncio M. Serial cardiac troponin concentrations as marker of cardiac toxicity in children with status asthmaticus treated with intravenous terbutaline. Pediatr Emerg Care. 2011;27:933–996.


# 229. A case series of hydroxychloroquine poisoning in Australia


Betty S. H. Chan[a], Katherine Z. Isoardi[b], Geoffrey K. Isbister[c] and Angela L. Chiew[a]

[a]Prince of Wales Hospital, Sydney, Australia; [b]Princess Alexandra Hospital, Brisbane, Australia; [c]Mater Calvary Newcastle Hospital, Newcastle, Australia


**Objective:** Hydroxychloroquine (HCQ) is used as an anti-malarial or anti-rheumatic agent and is known to be a sodium and potassium channel blocker. The toxic dose is thought to be 4 g [1]. Recent literature has opposing views regarding the use of high dose diazepam (2 mg/kg) and adrenaline for the management of hydroxychloroquine poisoning [2,3]. This study aims to determine the management of HCQ poisoning in Australia.

**Methods:** This is a retrospective review of patients with HCQ poisoning from three toxicology units and New South Wales Poisons Information Centre. Data was entered into a pre-formatted Excel spreadsheet that contain patient demographic, signs and symptoms and treatment, length of stay and outcome.

**Results:** From 2013 to 2022, there were 11 females with HCQ poisoning. The median age and ingested dose were 25 (IQR: 18–47) and 3.5 g (IQR: 2–7 g, range: 1.5–26 g). Median heart rate and blood pressure were 78 bpm (IQR: 70–82) and 71 mmHg (IQR: 47–84), respectively. Median potassium concentration was 2.7 mmol/L (IQR:2–3.5). Median QRS and QT were 110 ms (IQR: 88–113) and 550 ms (IQR: 442–600). Six patients received activated charcoal (AC), 4 of whom had multiple doses AC. Five patients required intubation, 6 had inotropes (a combination of adrenaline or noradrenaline, metaraminol). Diazepam or midazolam was used in 4 patients for sedation, 3 patients had sodium bicarbonate (NaHCO3). All but one patient who reported taking ≥4 g had significant haemodynamic instability. Two patients had recurrent ventricular tachycardia (VT). Median length of stay was 3 days (IQR: 1–12 days). One patient received VA extracorporeal membrane oxygen (ECMO) therapy for 48 hours. There was no death.

**Conclusion:** In Australia, hydroxychloroquine poisoning is managed with supportive care, use of a combination of vasopressors including adrenaline and noradrenaline to maintain haemodynamic stability, correcting hypokalaemia and electrolytes. High dose benzodiazepines are not used for the routine management of HCQ poisoning.

## References


[1] Isbister GK, Dawson A, Whyte IM. Hydroxychloroquine overdose: a prospective case series. Am J Emerg Med. 2002;20:377–378.

[2] Lebin JA, LeSaint KT. Brief review of chloroquine and hydroxychloroquine toxicity and management. West J Emerg Med. 2020; 21:760–763.

[3] Mégarbane B, Schicchi A. Management of chloroquine and hydroxychloroquine poisoning: do not miss the time of tracheal intubation and mechanical ventilation. West J Emerg Med. 2021; 22:454–455.


# 230. A case report of hydroxychloroquine poisoning


Betty S. H. Chan[a] and Nicholas A. Buckley[b]

[a]Prince of Wales Hospital, Sydney, Australia; [b]Sydney University, Sydney, Australia


**Objective:** In the past, hydroxychloroquine, a sodium and potassium channel blocker, has been managed with supportive care, primarily with managing hypokalaemia and electrolytes within the normal range. In recent years, the use of sodium bicarbonate ($NaHCO_3$) has been advocated for the management of severe hydroxychloroquine poisoning [1]. We present a severe case of hydroxychloroquine poisoning, where the electrocardiogram (ECG) changes did not respond to repeated doses of sodium bicarbonate and could have precipitated severe hypokalaemia, hypocalcaemia and multiple polymorphic ventricular tachycardia (VT).

**Case report:** A 17-year-old girl 53 kg took 4 g hydroxychloroquine and 80 mg fluoxetine 1.5 hours before presentation to hospital. She has a heart rate 83 bpm, blood pressure 70/40 mmHg. Initial ECG showed QRS 120 ms and QT 400 ms. She was intubated, given activated charcoal (50 g), adrenaline infusion and 250 mmol $NaHCO_3$ within 30 minutes. Initial potassium was 2.6 mmol/L and a potassium infusion (10–40 mmol/h) was commenced for persistent hypokalaemia (1.9 mmol/L). ECG showed initial QRS prolongation 160 ms, then evolved to QT prolongation up to 700 ms and polymorphic VT. She developed 8 series of polymorphic VT treated with 43 DC shock. She received another 600 mmol $NaHCO_3$; sodium increased from 141 to 168 mmol/L while pH increased from 7.4 to 7.7 with no obvious reduction in the QRS duration. She then developed complete heart block at 13 hours post-ingestion and was managed with isoprenaline infusion. Veno-arterial extracorporeal membrane oxygenation (VA ECMO) was commenced at 2.5–2.6 L/min during which she

continued to have runs of VT. ECMO was ceased at 48 hours. The serum hydroxychloroquine concentration was 6.8 mg/L (therapeutic 0.5–2 mg/L) at 1.5 hours post-ingestion with a half-life of 25 hours. Her recovery was complicated by blood loss requiring multiple blood transfusions, right femoral artery occlusion requiring thrombectomy, gastroparesis, ventilator-acquired pneumonia and staphylococcus bacteraemia. The patient was discharged on day 14 with no neurological deficit.
**Conclusion:** We report hydroxychloroquine in a teenager who developed severe toxicity with both sodium and potassium channel blocking effect, complete heart block and over 40 VT arrests. She was given large doses of sodium bicarbonate (850 mmol) which exacerbated the hypokalaemia and hypocalcaemia that may have had a deleterious effect. Sodium bicarbonate treatment did not have any apparent effect on the QRS duration in this patient. She was managed successfully with ECMO and supportive care.

### Reference

[1] Bruccoleri RE, Burns MM. A literature review of the use of sodium bicarbonate for the treatment of QRS widening. J Med Toxicol. 2016;12:121–129.

## 231. A case of severe serotonin syndrome

Ildikó Urbán[a] and Ágnes Szombath[b]

[a]Clinical Toxicology Department, Péterfy Sándor Hospital, Budapest, Hungary; [b]Intensive Care Unit, Péterfy Sándor Hospital, Budapest, Hungary

**Objective:** Serotonin syndrome is a potentially life-threatening syndrome due to the use of serotonergic drugs that cause overstimulation of peripheral and central postsynaptic 5HT-1A and 5HT-2A receptors. The syndrome is characterized by changes in mental status, neuromuscular and autonomic hyperactivity. The appearance of the syndrome can be very different, from mild symptoms to severe, complicated cases [1]. We report a patient successfully treated following severe toxicosis with complications requiring intensive care unit (ICU) treatment.
**Case report:** A 26-year-old women with a history of depression was admitted to hospital after she was found at home confused and agitated with vomit and urine around her. She took 84 tablets of escitalopram, 10 tablets of zolpidem, 60 tablets of moclobemide and 30 tablets of sertraline. On admission she was alert and agitated. She had flushed, sweaty skin, high temperature (38.9 °C), hypotension (107/81 mmHg), tachycardia (145/min.), and her oxygen saturation was 94.6%. Neurological examination revealed tremor, hyperreflexia, rigidity, trismus, and two-sided Babinski tendency. Shortly after her body temperature rose to 41 °C, oxygen saturation dropped to 86%. Based on history and symptoms severe serotonin syndrome was assumed. She was sent to our ICU, intubated and placed on mechanical ventilation. Along with analgosedation, neuromuscular blockade and aggressive cooling had to be introduced. Massive fluid replacement was performed due to hypovolemia, and vasopressor support provided. She was later given nitroprusside for hypertension. Neuromuscular blockade had to be maintained for 6 days, because when it was stopped, rigidity and tremor returned, and her temperature rose sharply. She received cyproheptadine as an antidote for 16 days. Rhabdomyolysis, urinary tract and respiratory infections, hyponatremia, polyuria, anemia, and subileus developed as complications. She received supportive care, forced diuresis, alkalization, targeted, combined intravenous antibiotics, total parenteral nutrition, and transfusions. She required desmopressin 11 times due to polyuria. Her poisoning and severe serotonin syndrome were prolonged; she received mechanical ventilation for 16 days and remained in ICU for 19 days. Finally, her condition and laboratory parameters settled and she was transferred to the psychiatric ward on the 23rd hospital day.
**Conclusion:** Severe serotonin syndrome is rare; it most often develops in connection with an overdose or an interaction between two serotonergic agents. Life-threatening cases require complex care.

### Reference

[1] Volpi-Abadie J, Kaye AM, et al. Serotonin syndrome. Ochsner J. 2013;13:533–540.

## 232. Usefulness of intravenous lipid emulsion for the management of cardiac toxicity in acute flecainide overdose

Gaspar Tuero[a], Jesús González[a], Nértor González[a], Isabel Gomila[b,c], Laura Sahuquillo[d], Miguel A. Elorza[c,e] and Bernardino Barceló Martín[c,e]

[a]Intensive Care Unit, Hospital Can Misses, Ibiza, Spain; [b]Clinical Analysis Department, Hospital Universitari Son Llàtzer, Palma de Mallorca, Spain; [c]Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain; [d]Clinical Analysis Department, Hospital Can Misses, Ibiza, Spain; [e]Clinical Analysis Department, Clinical Toxicology Unit, Hospital Universitari Son Espases

**Objective:** Intravenous lipid emulsion (ILE) has been shown to be effective in reversing severe cardiotoxicity which is refractory to other more conventional measures in cases of intoxication by fat-soluble agents [1]. The following case report illustrates the contribution of ILE in the treatment of a flecainide intoxication.
**Case report:** A 54-year-old woman treated with flecainide was transferred to the Emergency Department after ingesting an unknown number of flecainide and diazepam tablets, with suicide intention 3 hours before admission. She presented probable cardiogenic shock, altered mental status, bradycardia, and extreme hypotension. The electrocardiogram (ECG) showed an atrial fibrillation (AF) with ventricular response of 60 bpm, prolongation of the QRS complex (180 ms), with a Brugada pattern in V1–V2 and a QTc of 520 ms. Nasogastric placement of a gastric lavage tube was done and a dose of activated charcoal was then administered. Boluses of epinephrine (E) were administered and perfusion of bicarbonate and norepinephrine (NE) was started. The patient was admitted to the intensive care unit (ICU), undergoing orotracheal intubation and placement of a transvenous pacemaker. With the pacemaker, 1 M bicarbonate perfusion and high doses of NE and E, the heart rate and the mean blood pressure improved, but without resolution of any signs of hypoperfusion. The ECG revealed a similar pattern as the one performed on admission. For this reason, 12 hours after admission ILE 20% was administrated (1.5 mL/Kg bolus in 3 min and 0.25 mL/Kg/min infusion in 60 minutes). After ILE perfusion, it was possible to decrease vasoactive support and pacemaker stimulation thresholds. In the following hours, recovery of normal sinus rhythm and normalization of diuresis and lactate were observed. The patient could be extubated and vasoactive support withdrawn 36 hours after the infusion and discharged 48 hours later with normal echocardiography. Urine drug screening was positive for benzodiazepines and ethylglucuronide. Flecainide was identified in urine and quantified in four serum samples. At ICU admission,

serum concentration was 2.97 μg/mL (therapeutic range 0.2–1 μg/mL). Half-life elimination pre-ILE and post-ILE were calculated; both being 12.6 hours and 13.2 hours, respectively.
**Conclusion:** Despite the fact that there are currently no randomized controlled trials proving the efficacy of ILE, patients intoxicated by flecainide, who are refractory to conventional treatments, should be given the opportunity of ILE rescue.

## Reference

[1] Gosselin S, Høgberg LCG, Hoffman RS, et al. Evidence-based recommendations on the use of intravenous lipid emulsion therapy in poisoning. Clin Toxicol. 2016;54:899–923.

# 233. Nothing is as it seems: hypoglycaemia, serotonin syndrome and arrhythmic storm in a non-diabetic patient

Lorenzo Socias[a], María Ortega[a], María Sala[a], Isabel Gomila[b], Miguel Servera[b], Miguel A. Elorza[c,d] and Bernardino Barceló Martin[c,d]

[a]Intensive Care Unit, Hospital Universitari Son Llàtzer, Palma de Mallorca, Spain; [b]Clinical Analysis Department, Hospital Universitari Son Llàtzer; Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain; [c]Clinical Analysis Department, Clinical Toxicology Unit, Hospital Universitari Son Espases, Palma de Mallorca, Spain; [d]Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain

**Objective:** Venlafaxine (VLX) is an antidepressant that inhibits neuronal reuptake of serotonin and norepinephrine. It can cause serotonin syndrome (SS). Arrhythmias are possible after high doses. An analytically confirmed fatal clinical case, which was initially oriented as an insulin overdose, is described.
**Case report:** A 33-year-old woman with previous suicide attempts presented. Her usual treatment was topiramate, lurasidone and VLX. On the day of admission, she had an unstable gait associated with abnormal eye movement. She reported ingestion of 600 mg of diazepam. In the Emergency Department (ED), she was conscious, responding to simple orders, with multidirectional nystagmus, dysarthric speech, spontaneous movement of the limbs, and negative bilateral plantar cutaneous reflex. Vital signs: BP 150/60, HR 125, RR 24, temperature 37.5 °C and oxygen saturation 96% (room air). Electrocardiogram (ECG): sinus tachycardia (125 bpm), narrow QRS complex and normal QTc. Hypoglycaemia (50 mg/dL), despite treatment with 50% glucose. Normal chest X-ray. The stroke code was activated but computed tomography angiography was normal. A few hours later, she presented a decreased level of consciousness, tonic-clonic seizures associated with hypoglycaemia (30 mg/dL), with normal lactate (0.9 mmol/L) and high insulinemia (384.9 μIU/mL). The clinical picture was oriented as a suicide with insulin and diazepam. Subsequently, an elevated c-peptide (21.7 ng/mL) was obtained. The patient was admitted to ICU where she was connected to mechanical ventilation. After administration of flumazenil, she presented tonic-clonic seizures that subsided with midazolam without recovery of the level of consciousness. Toxicology serum concentrations at admission were: VLX + desmethyl-VLX: 21,510 ng/mL, diazepam + nordiazepam: 8,061 ng/mL topiramate: 4.8 μg/mL. Metformin and lurasidone were undetectable. Serum concentrations 11 hours later were: VLX + desmethyl-VLX and diazepam + nordiazepam: 76,845 ng/mL and 1,638 ng/mL, respectively. The subsequent evolution was towards cardiogenic shock. She presented an arrhythmic storm with ventricular tachycardia refractory to defibrillation 12 hours after admission. Advanced cardiopulmonary resuscitation manoeuvres were performed. The patient died.
**Conclusion:** Hypoglycaemia in a patient with no prior history of diabetes may reveal an initial finding of high doses of VLX acute overdose, which may also have a delayed onset. Serotonin increases insulin secretion and glucose utilization in muscle [1]. To prevent progression of SS and severe cardiotoxicity, and given that haemodialysis is ineffective, other therapeutic options would be possible in refractory patients.

## Reference

[1] Ling Y, Khara L, Alvarez G, et al. Persistent hypoglycemia in venlafaxine overdose. Arch Clin Med Case Reports. 2019;3:94–99.

# 234. Serotonin toxicity in a confirmed overdose of fluoxetine and lamotrigine

Brian G. Wiener[a], Silas W. Smith[a], Mary Ann Howland[b], Rana Biary[a] and Mark K. Su[c]

[a]Ronald O. Perelman Department of Emergency Medicine, Division of Medical Toxicology, New York University Grossman School of Medicine, New York, NY, USA; [b]College of Pharmacy and Health Sciences, St. John's University, New York, NY, USA; [c]New York City Poison Control Center, New York, NY, USA

**Objective:** Serotonin toxicity is a potentially life-threatening constellation of signs and symptoms caused by excess serotonergic activity. We report a case of serotonin toxicity in a patient due to a confirmed overdose of the novel combination of fluoxetine and lamotrigine, with supratherapeutic drug concentrations of both agents.
**Case report:** A 19-year-old woman, 52 kg, with a history of anxiety and depression intentionally ingested a 3-week supply of approximately 500 mg of fluoxetine, 3,750 mg of lamotrigine, and 7.5 mg of clonazepam in a suicide attempt. Her vital signs 5 hours post ingestion were: blood pressure 128/87 mmHg; heart rate 121 beats/minute; respiratory rate 25 breaths/minute; temperature 37.0 °C orally; oxygen saturation 97% (room air). Her initial electrocardiogram demonstrated sinus tachycardia at 105/minute, QRS duration of 82 ms, and QT duration corrected by Rautaharju's method of 473 ms. Her physical examination was notable for agitation, nystagmus, diffusely increased muscle tone, and marked hyperreflexia, which was more pronounced in the lower compared to the upper extremities. Bicep and triceps reflexes were 3+/4, while patellar and Achilles tendon reflexes were 4/4 bilaterally. Bilateral ankle clonus was present (8–10 beats), and Babinski's sign was positive bilaterally. Her serotonin toxicity resolved within 4 days after treatment with rigorous supportive medical care, intravenous hydration, sedation with benzodiazepines, and cyproheptadine. She had a hospital course that was complicated by mediastinitis, pneumonia, seizures, and rhabdomyolysis (peak creatine kinase 13,876 U/L). Her serum lamotrigine concentration on hospital day 3 was 27.1 μg/mL (therapeutic range, 3–15 μg/mL). Her serum fluoxetine and norfluoxetine concentrations were greater than 1000 ng/mL (therapeutic range, 91–302 ng/mL) and 210 ng/mL (reporting limit, <10 ng/mL), respectively, on hospital day 4.
**Conclusion:** Although lamotrigine is not traditionally conceptualized as a medication which causes serotonin toxicity, in overdose it can act both as a monoamine oxidase inhibitor and as a serotonin reuptake inhibitor and contribute towards serotonin

toxicity. It is possible that the serotonergic effects of clonazepam also contributed to this patient's toxicity. Clinicians should be aware that fluoxetine and lamotrigine in combination or overdose can potentially lead to serotonin toxicity; a finding that is poorly reported in the literature.

## 235. Fluoxetine toxicity in a neonate due to maternal exposure with apparent improvement on cessation of breastfeeding

Nathaniel I. Keymer[a], Akshay Phakey[b], Sally M. Bradberry[c], Euan A. Sandilands[d], Ruben H. K. Thanacoody[e] and Laurence A. Gray[a]

[a]National Poisons Information Service, Cardiff, United Kingdom; [b]Royal Free London NHS Foundation Trust, London, United Kingdom; [c]National Poisons Information Service, Birmingham, United Kingdom; [d]National Poisons Information Service, Edinburgh, United Kingdom; [e]National Poisons Information Service, Newcastle, United Kingdom

**Objective:** Selective serotonin re-uptake inhibitors (SSRIs) are commonly prescribed in pregnancy. We report a case of fluoxetine toxicity in a neonate following maternal exposure.
**Case report:** A male neonate weighing 3645 g was delivered using forceps following induction of labour at 39 weeks for suspected foetal macrosomia and polyhydramnios. The mother had a history of depression and took fluoxetine 40 mg daily. There was no other significant medical history. Epidural analgesia was given. Apgar Scores were 1 at 1 minute, 9 at 5 minutes and 9 at 10 minutes. A venous cord gas taken at delivery showed a pH of 7.38. At 45 minutes postpartum, the baby developed respiratory distress syndrome with mixed respiratory and metabolic acidosis, becoming cyanosed and floppy requiring admission to the neonatal unit. Glucose was 3.4 mmol/L on admission. Abnormal movements, tremor, and extensor posturing were present initially but resolved within hours, although irritability and poor sleep were noted subsequently. Magnetic resonance imaging (MRI) and electroencephalogram (EEG) were normal, and microbiological testing was negative. Gestational diabetes was excluded. Neonatal fluoxetine and norfluoxetine concentrations at age 7 days were measured at 17.2 and 108 ng/mL respectively (adult reference range 120–500 ng/mL). The mother elected to cease breastfeeding temporarily until she could become established on an alternative SSRI, and the patient switched to formula milk. Symptoms improved and the patient was discharged at age 16 days. He remained well at follow-up but was referred for routine echocardiography for a heart murmur detected on admission.
**Conclusion:** Maternal exposure to fluoxetine was deemed to have caused serotonin toxicity on the basis of clinical presentation, measured drug concentrations, reduction in the severity of symptoms following cessation of breastfeeding, and exclusion of other potential causes. Fluoxetine is primarily metabolised by CYP 2D6, which is known to have relatively lower activity in early life, and has been shown to be transferred to infants in breast milk. Similar cases have been reported [1]. Fluoxetine toxicity in this neonate was managed supportively and through cessation of breastfeeding. Neonates may be particularly susceptible to toxicity due to their immature nervous system and drug metabolism pathways. Maternal transmission of fluoxetine is potentially easily missed as a cause of fever and irritability. Utilisation of advice specialist services such as the UK Teratology Information Service and the UK Drugs in Lactation Advisory Service can also aid management.

### Reference

[1] Morris R, Matthes J. Serotonin syndrome in a breast-fed neonate. BMJ Case Rep. 2015;2015:bcr2015209418.

## 236. Relative toxicity of calcium channel blockers

Geoffrey K. Isbister, Shane Jenkins and Michael A. Downes

Clinical Toxicology Research Group, University of Newcastle, Newcastle, Australia

**Objective:** Calcium channel blocker (CCB) overdose remains an important cause of severe poisoning, with increasing availability of dihydropyridines. We aimed to compare the severity of different CCBs in overdose.
**Methods:** We reviewed all cases of CCB overdose (>16 years) presenting to the Hunter Area Toxicology Service from 2014 to 2022. We extracted prospectively collected data from a clinical database, including demographics, defined daily dose (DDD), co-ingestants, clinical effects, complications, treatments and outcomes, and compared the relative toxicity of five different CCBs.
**Results:** There were 103 CCB overdoses and the median age was 57 years (interquartile range [IQR]: 44–73 years); 58 were females. The commonest agent was amlodipine (53), then lercanidipine (17) and diltiazem (17), verapamil (11) and felodipine (5). The median DDD ingested was higher for dihydropyridines, and cardiac co-ingestants were common except for verapamil (Table 1). The median length of hospital stay was 18 hours ([IQR]:10–40 hours), which was similar for different CCBs. Twenty patients were admitted to ICU, three times more often for diltiazem and verapamil. Hypotension occurred in 34 patients, most

Table 1. Comparison of dose, clinical effects, complications and treatments for five different calcium channel blockers in overdose.

| | Amlodipine | Alone | Lercanidipine | Alone | Felodipine | Diltiazem | Alone | Verapamil | Alone |
|---|---|---|---|---|---|---|---|---|---|
| Number of patients | 53 | 7 | 17 | 4 | 5 | 17 | 6 | 11 | 8 |
| Dose (DDD) | 8.8 | 14.5 | 9.0 | 15.0 | 10.0 | 5.3 | 4.5 | 2.8 | 3.3 |
| Cardiac co-ingestant | 87% | | 76% | | 80% | 65% | | 27% | |
| LOS (median; h) | 18 | 11 | 15 | 12.5 | 20 | 21 | 20.5 | 17 | 18.5 |
| ICU admission | 13% | 14% | 12% | 0% | 0% | 41% | 11% | 36% | 27% |
| Arrhythmia | 4% | 0% | 6% | 0% | 0% | 53% | 22% | 9% | 0% |
| Hypotension | 30% | 0% | 24% | 25% | 40% | 53% | 17% | 27% | 18% |
| Acute kidney injury | 4% | 0% | 6% | 0% | 0% | 53% | 22% | 9% | 0% |
| Calcium | 6% | 0% | 6% | 0% | 0% | 35% | 17% | 18% | 9% |
| Inotropes | 17% | 14% | 18% | 0% | 20% | 47% | 11% | 27% | 18% |
| High dose insulin | 4% | 0% | 6% | 0% | 0% | 29% | 6% | 18% | 9% |

DDD: defined daily dose; ICU: intensive care; LOS: length of stay.

commonly with diltiazem. Twenty four patients were administered inotropes and ten high-dose insulin therapy, again more commonly with diltiazem. Arrhythmias occurred in 13 admissions: diltiazem (9, 53%), verapamil (2, 9%) and amlodipine (2, 4%). Calcium was administered in 12 patients, most commonly for diltiazem and verapamil. Two patients died in hospital, both after amlodipine.
**Conclusion:** Dihydropyridines were more common CCBs in overdose, amlodipine making up half. More severe toxicity occurred with diltiazem then verapamil, despite almost twice the DDD being taken for dihydropyridines ingestions.

## 237. Accidental tetrahydrocannabinol ingestion in a child resulting in refractory hypotension requiring vasopressor medication

Abigail Kerns and Christopher Holstege
University of Virginia, Charlottesville, VA, USA

**Objective:** Decriminalization and legalization of cannabis can result in unintended adverse societal consequences. The objective of this report is to highlight the case of a child and her grandmother who inadvertently purchased candy containing tetrahydrocannabinol (THC). Both were hospitalized after ingestion, with the child transferred to a regional pediatric critical care unit due to altered mental status, hypothermia, and refractory hypotension requiring vasopressor medication.
**Case report:** A 64-year-old female purchased a candy product from a convenience store. She believed the product to be a Nerds Rope© and split it with her 5-year-old granddaughter. After consuming the product, it was later discovered to contain delta-9 THC 500 mg. Both presented to the emergency department (ED). The grandmother became hypertensive and anxious, but recovered without sequelae and was discharged from the ED. The 5-year-old granddaughter presented somnolent, but maintained her airway with appropriate oxygen saturation. Presenting vital signs were: temperature 37.3 °C, pulse 151 beats/minute, respiratory rate 14 breaths/minute, and blood pressure 101/69 mmHg. Electrocardiogram demonstrated a sinus tachycardia with normal intervals. Laboratory studies were remarkable for a potassium 2.7 mEq/L, bicarbonate 21 mEq/L, and anion gap 13 mmol/L. The child received an intravenous normal saline bolus (20 mL/kg) and potassium repletion. She remained markedly sedated and required transfer to a regional pediatric intensive care unit. Her temperature decreased to 33 °C and she required external warming. Despite three boluses of normal saline 20 mL/kg and maintenance fluids, she remained hypotensive. She was started on an epinephrine infusion. At 24 hours from ingestion, the child became more alert, but was agitated and delirious. Symptoms ultimately resolved, the blood pressure improved, and the epinephrine infusion was weaned off. The child was discharged 40 hours after presentation.
**Conclusion:** Cannabis is becoming decriminalized and legalized across the world. Depending on the associated laws, edible THC-containing products subsequently emerge. Products may be marketed as candies and desserts in packaging that appears similar to popular non-THC containing candies. Accidental ingestions by the public unaware of the contents can occur. This case illustrates a severe outcome from an accidental pediatric ingestion that resulted in altered mental status, hypothermia, and fluid-refractory hypotension requiring vasopressor medications.

## 238. Accidental child exposure to a fentanyl patch: what is the lesson?

Gabija Valauskaite[a], Dovydas Burkojus[b], Robertas Badaras[c], Andrius Macas[d] and Rimantas Kevalas[e]
[a]Department of Intensive Care Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [b]Department of Neurology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [c]Faculty of Medicine, Centre of Toxicology, Clinic of Anaesthesiology and Intensive Care, Vilnius University, Vilnius, Lithuania; [d]Department of Anesthesiology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [e]Department of Paediatrics, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Objective:** Medicines are the leading cause of poisoning in children. Fentanyl is a synthetic opioid with a strong analgesic effect and has dangerous adverse effects: respiratory depression, hypotension, and somnolence. Accidental exposure to fentanyl patches in children has a case-fatality rate of 48% [1]. We present a case of accidental child exposure to a fentanyl patch.
**Case report:** A 9-year-old male presented to the emergency department (ED) unconscious and with respiratory insufficiency. His parents reported that the day before he had fallen and abraded his left knee, and his mother has placed a skin plaster on his knee. After placement of the plaster, the boy started to feel nauseous and vomited several times. Later, he fell asleep and was found unresponsive in the morning. Upon admission to ED the Glasgow Coma Score was 7–8, he had pinpoint pupils and shallow breathing, oxygen saturation was 95% (on 6 L/min of oxygen by nasal canulae), and arterial blood pressure was 93/60 mmHg with tachycardia 120/min. The patient's knee was covered by a 100 μg/h fentanyl patch which was removed immediately. Biochemistry results showed amylase 2121 U/L, alkaline phosphatase (ALP) 262 U/L, alanine aminotransferase (ALT) 32.6 u/L, and aspartate aminotransferase (AST) 166.6 U/L. A brain computerised tomography (CT) scan showed no specific pathological findings. An magnetic resonance imaging (MRI) scan revealed bilateral, symmetric lesions consistent with hypoxic and toxic encephalopathy. Patient treatment included intravenous naloxone 0.1 mg, mechanical ventilation, and continuous infusion of dopamine 10 mcg/kg/min. The patient was discharged from the Children's Intensive Care unit 4 days after admission in a hemodynamically stable condition. The boy was fully conscious but had profound anxiety. The patient became blind and had tetraparesis with only minimal movements of proximal limbs. At the time of writing this case report, he is continuing his treatment in a rehabilitation center.
**Conclusion:** in this case, accidental intoxication happened to a child because his mother mistook the fentanyl patch for a sticker plaster, which she had kept after the death of her relative who had been using the patches. Even though in Lithuania there are laws regulating the utilization of drugs, this case proves that regulation is not effective and information for patients is scarce.

### Reference

[1] Stoecker WV, Madsen DE, Cole JG, et al. Boys at risk: fatal accidental fentanyl ingestions in children: analysis of cases reported to the FDA 2004–2013. Mo Med. 2016;113:476–479.

## 239. First series of massive paracetamol overdose cases: risk factors for hepatotoxicity

Isabel Gomila[a,b], Jordi Puiguriguer Ferrando[b,c], Yolanda Ibáñez Borau[d], Guillermo Frontera[e], Catalina Homar Amengual[b,c], Miguel Elorza[b,f] and Bernardino Barceló Martin[b,f]

[a]Clinical Analysis Department, Hospital Universitari Son Llàtzer, Palma de Mallorca, Spain; [b]Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain; [c]Emergengy Department, Clinical Toxicology Unit, Hospital Universitari Son Espases, Palma de Mallorca, Spain; [d]Emergengy Department, Hospital Universitari Son Llàtzer, Palma de Mallorca, Spain;; [e]Methodological Support Department of the Research Institute, Hospital Universitari Son Espases, Palma de Mallorca, Spain; [f]Clinical Analysis Department, Clinical Toxicology Unit, Hospital Universitari Son Espases, Palma de Mallorca, Spain

**Objective:** Massive paracetamol overdose can pose a healthcare problem if cases are treated according to established protocols based on a "one size fits all" approach [1]. The aim of this study is to define the clinical characteristics of these patients and identify variables of cases which developed symptoms of hepatotoxicity in order to make early detection a possibility.
**Methods:** Observational retrospective study of patients who met massive paracetamol overdose criteria at two tertiary hospitals over a 7-year period (2015–2021). (1) Paracetamol concentration extrapolated at 4 hours post-intake (C4) greater than 250 μg/mL from the formula $C4 = Ct/2e^{-(0.693/4)t}$ (method 1). (2) Reported intake greater than 30 g. Additionally, C4 was calculated from representing graphically per patient the Ln of the concentrations available from 4 h post-intake as a function of the post-intake time in hours (method 2). Half-life elimination (t1/2) was calculated graphically when at least two concentrations were available in the post-intake period ≥4 hours. Variables relating to the development of hepatotoxicity (AST or ALT >1000 IU/L) were analysed.
**Results:** Thirty patients fulfilled the inclusion criteria representing 7.1% of the total cases of paracetamol overdose; 80% were women, age (mean ± standard deviation) 35.5 (± 20.4) years. The interval between intake and assistance was 7.3 ± 5.3 hours. The ingested dose was 27.5 ± 11.9 g. In all cases, it was a single intake. Paracetamol serum concentration at admission was 245.1 ± 92.27 μg/mL. The C4 values obtained by method 1 and 2 were 889.7 ± 1771.3 μg/mL and 533.1 ± 422.1, respectively. All patients received N-acetylcysteine and 8 (26.6%) required intensive care unit (ICU) admission. No deaths occurred. Six patients developed hepatotoxicity; t1/2 was higher ($p < 0.05$) in the hepatotoxicity group (5.3 ± 1.1 versus 3.8 ± 1.3 hours). The variables compared at admission, that were statistically significant ($p < 0.05$) between hepatotoxicity group versus no hepatotoxicity group, were: care interval from intake (14.0 ± 5.9 versus 5.2 ± 3.0 hours), alanine aminotransferase (ALT) (160.2 ± 153.0 versus 20.9 ± 19.2 U/L), ALT*procalcitonin (PCT) (34919 ± 46310 versus 5809 ± 7385), INR (1.29 ± 0.12 versus 1.11 ± 0.11). Additionally, C4 value obtained by methods 1 (2264.9 ± 3334.6 versus 431.5 ± 291.2 μg/mL) and 2 (894.1 ± 651.3 versus 388.6 ± 157.6) were higher in the hepatotoxicity group ($p < 0.05$).
**Conclusion:** These results may serve to improve detection of massive paracetamol overdose and recognize variables that may be associated with a greater risk of developing hepatotoxicity. The ultimate goal is to individualize patient treatment.

## Reference

[1] Bateman DN, Dear JW. Should we treat very large paracetamol overdose differently? Br J Clin Pharmacol. 2017;83:1163–1165.

Table 1. Salicylate concentrations following overdose in an adult.

| Admission day | Time | Salicylate level (mg/L) |
|---|---|---|
| 1 | 0932 | 950 |
| | 1230 | 927 |
| 2 | 0051 | 390 |
| | 0135 | 797 |
| | 0224 | 910 |
| | 0530 | 1004 |
| | 0800 | 1090 |
| | 1000 | 1350 |
| | 1200 | 1570 |
| | 1400 | 1436 |
| | 1820 | 705 |
| | 2230 | 625 |
| 3 | 0030 | 528 |
| | 0240 | 478 |
| | 0747 | 307 |
| | 1000 | 279 |
| | 1600 | 149 |
| | 1955 | 170 |
| | 2355 | 117 |
| 4 | 0400 | 71 |
| | 0830 | <50 |

# 240. Management of severe salicylate toxicity compromised by staff shortages

Ryan J. Cole, Will R. Goodrich, Aaron S. Frey, Nathan P. Charlton and Christopher P. Holstege

Department of Emergency Medicine, Division of Medical Toxicology, University of Virginia Health, Charlottesville, VA, USA

**Objective:** To highlight how treatment delays caused by personnel shortages attributed to the pandemic impacted a case of severe salicylate toxicity.
**Case report:** A 62-year-old female ingested 480 tablets of 325 mg "coated" aspirin 2 hours prior to arrival to the emergency department (ED) in a suicide attempt. She reported tinnitus on arrival with initial vital signs: blood pressure 154/99 mmHg, heart rate 105 beats/min, respiratory rate 22 breaths/min, temperature 36.4 °C, and pulse oximetry 100% (room air). Multidose activated charcoal was initiated. Initial electrocardiogram (EKG) showed sinus tachycardia (QRS 90 ms, QTc 468 ms). Initial salicylate concentration was 950 mg/L. Sodium bicarbonate infusion with potassium was initiated and nephrology contacted for emergent hemodialysis (HD). HD was ordered 7 hours after ingestion. Following completion, the salicylate concentration improved (390 mg/L) but rose again (Table 1) to dialyzable levels. Staffing shortage delayed repeat HD by 7 hours. When HD was reinitiated 26 hours after ingestion, salicylate concentration had risen to 1570 mg/L. The patient became hypotensive requiring norepinephrine (50 μg/min) and vasopressin (0.03 units/min). She seized and repeat EKG showed QRS widening (174 ms) with intermittent ventricular tachycardia. HD was switched to continuous renal replacement therapy (CRRT) due to sustained hypotension despite vasopressors. HD was reattempted 41.5 hours after ingestion and aborted due to worsening hypotension requiring phenylephrine (50 μg/min). CRRT was resumed, resulting in declining salicylate concentration with improvements in hemodynamics and mentation. Salicylate concentration became undetectable 73.5 hours after ingestion with the patient surviving to discharge.
**Conclusion:** Personnel shortage during the pandemic lead to treatment delays in a patient with severe salicylate toxicity who survived despite having the highest recorded salicylate concentration in a non-fatal case [1].

## Reference

[1] Baselt RC. Disposition of toxic drugs and chemicals in man. 12th edition. Seal Beach, California: Biomedical Publications; 2020. p. 27–29.


## 241. Self-induced pregabalin coma successfully resolved using continuous renal replacement therapy


Lotte C. G. Høgberg[a,b], Visti T. Nielsen[b] and Søren Bøgevig[a,c]

[a]Danish Poisons Information Centre, Copenhagen, Denmark; [b]Department of Anaesthesia and Intensive Care, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [c]Department of Clinical Pharmacology, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark


**Objective:** Pregabalin and the structurally related gabapentinoid gabapentin, affect the excitability of the neuron by blocking the voltage-dependent calcium channels but have no activity at GABA-A or GABA-B receptors. Massive overdose ingestions may cause severe toxic effects, and management has been symptomatic, a few reports describe the use of additional intermittent hemodialysis (IHD) with no clear benefit [1]. We describe the first case with pregabalin self-induced coma, successfully resolved with continued renal replacement therapy (CRRT) during supportive intensive care.
**Case report:** A 66-year-old female was admitted to hospital with impaired consciousness, Glasgow Coma Score 3, and hypotension. Circumstances indicated that the patient had ingested around 30 tablets zopiclone (225 mg), and possibly other medications. Arterial blood gas showed respiratory and metabolic acidosis. Hyperkalemia (6.9 μmol/L; normal 3.5–4.4 μmol/L) was treated with intravenous glucose-insulin infusion. Electrocardiogram (ECG) showed sinus tachycardia without conductive disturbances or signs of ischemia. Flumazenil was without effect. Following intubation, the patient was admitted to the intensive care unit for mechanical ventilation. Blood samples revealed rhabdomyolysis and decreasing kidney function. Sedative medication was retained, but the patient remained comatose during the following 24 hours with no signs of consciousness. On Day 2, repeated computerised tomography (CT)-angiography, electroencephalogram, and lumbar puncture were normal. Poisoning was then suspected based on the clinical signs including continued deep areflexia, universal hypotonia, no ocular-cephalic-reflexes, but eyes with pupils equal and reacting to light. Plasma drug analyses was reconsidered and showed a plasma-pregabalin concentration of 722 mmol/L (therapeutic reference 10–35 mmol/L). CRRT was initiated (blood flow rate 120 mL/min, dialysate flow 2,000mL/hour). After 6 hours the patient regained consciousness. After 8 hours, plasma-pregabalin was 255 mmol/L. CRRT was continued, and concentration decreased to 133 and 31 mmol/L after 17 hours and 24 hours, respectively. Calculated pregabalin elimination half-life during CRRT was approximately 8 hours (elimination half-life, therapeutic dose 6.6–10.2 hours). Twenty-four hours after CRRT initiation, the GCS was 14 and circulation stabilized. Due to rhabdomyolysis and kidney impairment CRRT was continued for a total of 2.5 days. She was discharged from the ICU on Day 5 to the medical neurology ward and continued psychiatric follow-up.
**Conclusion:** The use of CRRT in this case led to reversal of neurotoxicity and improved level of consciousness in compliance with accelerated pregabalin elimination from highly elevated plasma concentrations.


## Reference

[1] Bouchard J, Yates C, Calello DP, et al. Extracorporeal treatment for gabapentin and pregabalin poisoning: systematic review and recommendations from the EXTRIP Workgroup. Am J Kidney Dis. 2022;79:88–104.


## 242. Clinical characteristics of acute lacosamide poisoning: a case series


Lucia Bernasconi[a], Azzurra Schicchi[b], Valeria M. Petrolini[c], Benedetta Brolli[a], Monica Carnovale[a], Alberto Malovini[d], Francesca Crema[e] and Carlo A. Locatelli[c]

[a]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Postgraduate School of Pharmacology and Clinical Toxicology, Istituti Clinici Scientifici Maugeri IRCCS, University of Pavia, Pavia, Italy; [b]Experimental Medicine PhD Program, Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, University of Pavia, Pavia, Italy; [c]Toxicology Unit, Pavia Poison Control Centre – National Toxicology Information Centre – Clinical and Experimental Lab, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [d]Laboratory of Informatics and Systems Engineering for Clinical Research, Istituti Clinici Scientifici Maugeri IRCCS, Pavia Institute, Pavia, Italy; [e]Department of Internal Medicine and Therapeutics, Section of Pharmacology, University of Pavia, Pavia, Italy


**Objective:** Lacosamide is a third-generation anticonvulsant selectively enhancing slow inactivation of voltage-gated-sodium-channels. Since its approval in 2008, few cases of lacosamide overdose have been described in literature. We conducted a retrospective study evaluating clinical characteristics of lacosamide overdose.
**Methods:** All patients with acute lacosamide intentional overdose referred to our Poison Control Center from February 2012 to December 2020 were enrolled. For each patient age, sex, ingested dose, intake modality, co-ingestants, clinical manifestations, treatment and outcome were collected.
**Results:** A total of 46 patients (69.6% females; median age 41.0 years) were included. In 34.8% (16/46) lacosamide was the sole ingested substance, while in 65.2% (30/46) co-ingestants were also present. The average lacosamide ingested dose was 1701 mg. The reported co-ingestants varied from 1 to 7, with the more common being clonazepam, valproic acid, topiramate, lamotrigine, levetiracetam, alcohol, quetiapine, and lorazepam. Most (89.1%, 41/46) patients were symptomatic with vomiting (26%), drowsiness (23.9%), coma (21.7%), seizures (19.5%), agitation (15.2%), tachycardia (13%), bradycardia/bradyarrhythmias (6.5%), hypertension (6.5%), and headache (4.3%). When analyzing coma and convulsions, they were found in 12.5% ($n = 2$) and 25% ($n = 4$) of patients with pure lacosamide intoxication and in 26.6% ($n = 8$) and 16.6% ($n = 5$) of patients with mixed intoxication, respectively. Considering cardiac manifestations: one patient with pure lacosamide intoxication presented with tachycardia, and electrocardiogram (ECG) alteration was found in one case (QRS prolongation with left bundle branch block), compared to patients with co-ingestants that presented with tachycardia in 20% of cases (6/46) and bradycardia in 6.6% (2/46). Considering treatments, 95.6% (44/46) of patients underwent gastrointestinal decontamination, 21.7% (10/46) required orotracheal intubation and 2.1% (1/46) sodium-bicarbonate administration for cardiotoxicity. No lethal cases were recorded, and all patients recovered fully.
**Conclusion:** Our data on acute lacosamide poisoning are in accordance with literature reports in which reported symptoms

Table 1. Measurements of the valproate concentration (VAC) in the patient's serum and the simulated gastric acid.

| Time (hours) | Simulated gastric acidVAC (μg/mL) | Patient's serumVAC (μg/mL) |
|---|---|---|
| 0.5 | 381.5 | |
| 1 | 767.6 | |
| 2 | 976.1 | |
| 4 | 1138.4 | 154 |
| 8 | 1131.4 | |
| 10 | | 81 |
| 12 | 1259 | |
| 16 | | 309 |
| 22 | | 656 |
| 24 | 1559.8 | |
| 27 | | 616 |
| 35 | | 392 |
| 39 | | 286 |
| 45 | | 171 |
| 55 | | 107 |
| 62 | | 81 |

were convulsions and ECG alterations. Importantly, it seems that co-ingestants, particularly neurodepressants, may alter neurologic manifestations of pure lacosamide toxicity. In fact, coma was more common in patients with mixed intoxication; in contrast convulsions that were found with higher prevalence in patients with pure lacosamide intoxication. The main limitation of this study was the unavailability of lacosamide plasma measurements; this could be addressed in a future prospective study aiming to correlate lacosamide plasma value with clinical manifestations.

## 243. Severe valproate intoxication with delayed toxicity because of pharmacobezoar formation with *in vitro* verification

Miriam Mayor- Echave-Sustaeta[a], Thais Lizondo[b], Emilio Salgado García[c], Silvia González[b], Carmen López[b] and Carlos García[a]

[a]Hospital Clinic of Barcelona – Internal Medicine, Barcelona, Spain; [b]Hospital Clinic of Barcelona – Hospital Pharmacy, Barcelona, Spain; [c]Hospital Clinic de Barcelona – Toxicology Department, Barcelona, Spain

**Objective:** To test pharmacobezoar formation as a cause of delayed intoxication after a severe valproate overdose by an *in vitro* assay.
**Case report:** A 16-year-old woman with a history of major depression was admitted to the emergency room after ingestion of 23.7 g valproate (427.7 mg/kg) 3 hours prior. At arrival she was conscious, oriented, hemodynamically stable, eupneic, with no notable physical findings. She received oral activated charcoal (25 g), intravenous rehydration and L-carnitine (1 g/6 h) [1]. Serum valproic concentration at 10 hours was 81 μg/mL (therapeutic range 50–100). At 16 hours she presented agitation, nausea, vomiting, choreic movements and diminished consciousness so intubation and mechanical ventilation were required. Cranial tomography showed no findings. Progressive hyperammonemia peaked at 107 μmol/L. Incipient signs of cranial hypertension were detected through transcranial ultrasound and an electroencephalogram showed diffuse cerebral dysfunction. Clinical status improved, and she was extubated within 48 hours without sequelae. Pharmacobezoar hypothesis was investigated through an *in vitro* model [2]. The ingested dose (47 extended-release valproate 500 mg tablets) was placed in a polyester mesh bag, immersed in 1 L of simulated gastric fluid (SGF) and placed under magnetic stirring at 30 revolutions per minute and 37 °C. After 2 hours a drug conglomerate of 5 × 6 cm was observed. The valproate concentrations in the SGF and patient serum showed concordance with a peak around 24 hours (Table 1).
**Conclusion:** Pharmacobezoar formation was confirmed in a large overdose and should be suspected if there is discrepancy between severe extended-release valproate overdose (>400 mg/kg) and mild symptomatology.

### References

[1] Patel AR, Nagalli S. Valproate toxicity. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.
[1] Høgberg LCG, Refsgaard F, Pedersen SH, et al. Potential pharmacobezoar formation of large size extended-release tablets and their dissolution – an *in vitro* study. Clin Toxicol. 2019;57:271–281.

## 244. Outcome of acetaminophen-poisoned patients admitted to a non-liver intensive care unit with liver failure: an observational cohort study

Alice Vottero[a] and Bruno Mégarbane[b]

[a]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris Cité University, Paris, France; [b]Department of Medical and Toxicological Critical Care, INSERM UMRS-1144, Paris Cité University, Paris, France

**Objective:** Acetaminophen overdose may be responsible for severe acute liver injury, liver failure and fatality despite the use of N-acetylcysteine, an antidote proven effective and safe for almost forty years. Our objective was to investigate the outcome of acetaminophen-poisoned patients admitted to a non-liver intensive care unit (ICU) with acute liver failure.
**Methods:** We conducted an observational retrospective cohort study including all acetaminophen-poisoned patients admitted over a 10-year period to our ICU with acute liver injury (defined by serum alanine aminotransferases (ALT) > 6N) and signs of acute liver failure (encephalopathy, prothrombin time ratio <20%, and/or elevated blood lactate concentration) present on admission or during the first 24 hours of hospitalization. Univariate comparisons were performed between subgroups according to the outcome.
**Results:** Over a 10-year period, 46 patients (14M/32F; median age, 38 years [24–57]) were included in the study. Features on admission included nausea/vomiting (41%), abdominal pain (33%), headaches (22%), sleepiness (7%), and confusion (4%). Serum ALT was 3,091 IU/L [1,271–6,699], serum procalcitonin 18.2 ng/mL [6.6–38.5], and blood lactate 2.65 mmol/L [1.30–5.70]. Time from ingestion to hospital referral was prolonged (>24 hours in most patients) with a relatively low serum acetaminophen concentration of 61.6 mg/L [20.4–151.1] on admission. N-acetylcysteine (300 mg/kg/day) was started immediately on admission. Six patients received fomepizole (15 mg/kg/12h) in combination. Supportive care included norepinephrine infusion (33%), mechanical ventilation (15%), and hemodialysis (9%). Despite organ support and antidotes, six patients died (13%). Only two patients were successfully liver-transplanted. Based on univariate comparisons, non-survivors presented higher body mass index ($p = 0.05$), lower arterial pH ($p = 0.0004$), lower serum bicarbonate ($p = 0.001$), higher blood lactate ($p = 0.0005$) and higher serum procalcitonin ($p = 0.03$) on admission. They more frequently required norepinephrine infusion ($p < 0.0001$) and hemodialysis ($p = 0.005$) during the first 24 hours of hospitalization. Of note, only 1 patient among the six who were treated with fomepizole died.

**Conclusion:** Acetaminophen poisoning managed with delay may result in severe liver injury, organ failure and death. Severity of lactic acidosis and vasodilatation during the first 24 hours are prognosticators. Improving effectiveness of antidotal treatment is mandatory and possible benefit from fomepizole/N-acetylcysteine combination worthy of investigation.

## 245. The association between paracetamol dose/plasma concentration and the severity of methemoglobinemia: a case-control study

Tonny S. Petersen[a], Alaa Daoud[a], Søren Bøgevig[a] and Lotte C. G. Høgberg[b]

[a]Department of Clinical Pharmacology, Copenhagen University Hospital - Bispebjerg and Frederiksberg, Copenhagen, Denmark; [b]Department of Anaesthesia and Intensive Care, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** Paracetamol is the most common pharmaceutical taken in overdose and has been associated with development of methemoglobinemia [1]. However, there are currently no studies or reports characterizing paracetamol-induced methemoglobinemia in detail including a more detailed analysis of the association between dose/plasma concentrations of paracetamol and the severity of methemoglobinemia. Hence, our aim was to describe this specific association.
**Methods:** A retrospective case-control study of patients with suspected paracetamol poisoning with a methemoglobin measurement in the Capital Region of Denmark in the period 2010–2017. Cases were defined as having a methemoglobin fraction above 0.02. Controls were chosen at random from the remaining patients. Data were extracted from the electronic health record from each case and control patients.
**Results:** We identified 27 cases and selected 97 controls at random from a pool of 953 patients with suspected paracetamol poisoning with a methemoglobin measurement. Among the cases 5 patients had a methemoglobin fraction >0.05. The median time from paracetamol ingestion to peak methemoglobin was 19 hours (IQR 8–20). Only a single case was treated with methylene blue. Case patients were significantly older than control patients, median 53 (IQR 43–67) years versus 41 (24–54) years. The median paracetamol dose was higher in cases, 53 g (IQR 37.5–100) versus 15 g (9.5–25) in controls. Only a single case (3.7%) did not have a plasma paracetamol concentration above the lower concentration of quantification versus 34 (35%) of the control patients. The median maximum plasma paracetamol concentration among patients with detectable concentrations were 3.3 mmol/L (IQR 2.2–4.5) among cases and 0.73 mmol/L (IQR 0.33–1.3) among controls. Cases were more likely to be comatose compared to controls, 52% versus 9.3%, odds-ratio 10.2 (95%CI 3.4–33.1). A significant higher proportion of cases died 14.8% versus 1.0% of the control patients, odds-ratio 16.2 (95%CI 1.5–826).
**Conclusion:** Methemoglobinemia is a rare event and is positively associated with dose and a worse outcome.

### Reference

[1] Sahu KK, George SV, Siddiqui AD. Systematic review of methemoglobinemia in acetaminophen poisoning. QJM. 2022;115:575–581.

## 246. Brugada phenocopy after successful bicarbonate resuscitation in a patient with severe amitriptyline overdose

Carlos García-Gutiérrez, Julia Calvo-Jiménez, Blanca Coll-Vinent Puig, Míriam Mayor Echave-Sustaeta and Emilio Salgado García

Hospital Clínic i Provincial de Barcelona, Barcelona, Spain

**Objective:** To present an uncommon finding in tricyclic antidepressant poisoning.
**Case report:** A 35-year-old homeless male with a history of borderline personality disorder, drug abuse, and multiple suicide attempts was admitted in the emergency department (ER) after being found unconscious in the street with multiple opened medication packages on and around him. Drug doses were estimated from the missing tablets in the recovered packages: amitriptyline (up to 1375 mg), tramadol (up to 2000 mg) and lorazepam (up to 13 mg). Upon arrival at the ER the patient was unconscious (Glasgow Coma Score (GCS) 3), tachycardic and hypotensive; he suffered a generalized tonic-clonic seizure. The initial electrocardiogram showed wide QRS (160 ms) regular tachycardia with right-bundle block morphology. Venous blood gas analysis showed pH 7.04, $pCO_2$ 63.6 mmHg, bicarbonate 16.7 mmHg, base excess (BE) − 15.2 mmol/L, and lactate 117.1 mg/dL. He was intubated for airway protection and digestive decontamination was performed by gastric lavage, which did not retrieve any tablets, followed by administration of activated charcoal through a nasogastric tube. Fluid resuscitation was started with a bolus of 250 mL of 1 mol/L sodium bicarbonate followed by pH-directed sodium bicarbonate infusion [1]. After 35 minutes the pH was 7.49 and the electrocardiogram (EKG) reversed to narrow-QRS (120 ms) sinus tachycardia with a Type-1 Brugada morphology on V1–V2 leads, which was not present in the previous EKG available in his medical history. He was admitted to the intensive care unit (ICU) and had a favourable outcome, being discharged after 9 days with outpatient psychiatry follow-up. In order to establish if the patient had a Brugada syndrome unveiled by the amitriptyline poisoning or rather a Brugada phenocopy [2,3], a flecainide challenge test was performed, which was negative.
**Conclusion:** Despite a decrease in the use of tricyclic antidepressants in favor of safer alternatives, tricyclic antidepressant poisoning remains a common and potentially lethal emergency. Electrocardiographic abnormalities, arrhythmia, decreased consciousness and seizures are the most common findings in severe tricyclic antidepressant overdose [4].

### References

[1] Bruccoleri RE, Burns MM. A literature review of the use of sodium bicarbonate for the treatment of QRS widening. J Med Toxicol. 2016;12:121–129.
[2] Otero D, Petrovic M, Liao SL. Brugada phenocopy: a case of incessant ventricular tachycardia in a patient with tricyclic antidepressant overdose. Methodist Debakey Cardiovasc J. 2020;16:245–248
[3] Yap YG, Behr ER, Camm AJ. Drug-induced Brugada syndrome. Europace. 2009;11:989–994.
[4] Eyer F, Stenzel J, Schuster T, et al. Risk assessment of severe tricyclic antidepressant overdose. Hum Exp Toxicol. 2009;28:511–519.

## 247. The SNAP protocol: further benefits, further afield

Ruadhan O. Laoi[a], Cormac Kennedy[a], Emer Kidney[b] and Arthur Hennessy[c]

[a]Department of Pharmacology and Therapeutics, St James' Hospital, Dublin, Republic of Ireland; [b]Tallaght University Hospital, Dublin, Republic of Ireland; [c]Emergency Department, St James' Hospital, Dublin, Republic of Ireland

**Objective:** In Ireland, the complex 3-bag 21-hour protocol for administration of N-acetylcysteine (NAC) has remained largely unchanged for 40 years. The "SNAP" regimen is a novel way of delivering NAC that is used in the United Kingdom. It administers the same total dose of NAC in just 2 bags over 12 hours, whilst also avoiding a massive loading dose. This boasts reduced rates of adverse drug reactions (ADRs) and a shorter infusion duration, without sacrificing efficacy [1]. Whilst these benefits are well researched, the impact of the SNAP protocol on overall length of stay is less well documented, and its effect on interruptions to antidotal therapy has not yet been published.
**Methods:** A retrospective audit of all Emergency Department presentations in 2019 to St James' Hospital Dublin was conducted to identify patients with paracetamol poisoning requiring admission for NAC therapy. Using our electronic patient records, further details including delays in changing NAC infusions and overall length of stay were documented. We met with local stakeholders, drafted hospital protocols, and implemented the SNAP regimen as the primary method for delivering NAC in our hospital in January 2022. A re-audit was conducted 6 months post-implementation.
**Results:** In 2019, 54 presentations requiring NAC were analysed. The median total delay from changing over infusions was 2 hours and 17 minutes. The median length of stay was 47 hours. By 6 months post-implementation, 41 presentations requiring NAC were analysed. The median delay from changing infusions was 55 minutes and the median length of stay was 39 hours.
**Conclusion:** In January 2022, we became the first Irish hospital to implement the 2-bag 12-hour SNAP regimen for delivering N-acetylcysteine. Amongst other benefits, use of this simple SNAP regimen has reduced treatment interruptions and overall length of stay for patients presenting to our hospital with a paracetamol overdose.

### 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.

## 248. Paediatric overdoses of melatonin: data from a national poison center

Karl Sebastian Johansson[a], Lotte C. G. Høgberg[b] and Søren Bøgevig[a]

[a]Department of Clinical Pharmacology, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark; [b]Department of Anaesthesia and Intensive Care, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark

**Objective:** A recent report shows that paediatric melatonin overdoses in the USA have increased, including those requiring hospitalisation. We investigated the evolution of paediatric melatonin overdoses in Denmark.
**Methods:** We gathered data from the Danish Poison Information Center (DPIC) and Danish Prescription Registry from 2007 to 2021. Only individuals <18 years (groups 0–5, 6–11, 12–17 years) of age were included. Age was categorised into 0–10 and 11–17 years of age. Individual records were manually evaluated to identify hospitalisation due to melatonin overdose alone. Incidence rates were evaluated using Poisson regression. Data was analysed using R version 4.3.
**Results:** A total of 725 melatonin overdoses were reported in the study period. The annual number of overdoses increased annually with an average of 19%, from 9 in 2007 to 115 in 2021 (IRR 1.19, 95%CI 1.17–1.22, $p < 0.0001$). The older age group, increased from 6 to 87 annual inquiries (1,450% increase), while the younger group increased from 3 to 28 annual inquiries (933% increase). Similarly, the amount of sold melatonin, measured as the defined daily dose (DDD), increased 20% annually, from 3,000 to 6,723,000 (IRR 1.20, 95%CI 1.198–1.205, $p < 0.0001$)). Therefore, there was no change between the number of overdoses per 1,000 DDDs sold in 2007 compared to 2021 (IRR 0.99, 95%CI 0.97–1.01, $p = 0.4$). Admission to hospital for cases reported to the DPIC regarding melatonin overdose alone is generally never advised, unless other concerns are raised. Co-ingestion was more common in the older age group (Table 1). The most common co-ingestions for the older age group were antipsychotics ($n = 112$), antidepressants ($n = 96$), paracetamol ($n = 86$), and centrally acting sympathomimetics (n = 50), compared to unknown substances ($n = 42$) for the younger age group.
**Conclusion:** The number of reported paediatric melatonin overdoses in Denmark has steadily increased proportional to the amount of melatonin sold. The majority of the overdoses were in individuals aged 10-17 years. Intake of melatonin alone did not lead to any hospitalisations.

Table 1. Characteristics of paediatric patients with melatonin ingestion.

| | | Age group | | | |
|---|---|---|---|---|---|
| Characteristic (where known) | Overall, $N = 718$ | 0–5, $N = 127$ | 6–12, $N = 94$ | 13–17, $N = 497$ | $p$-Value |
| Age, median (IQR) | 15 (10, 16) | 2 (1, 3) | 9 (7, 12) | 16 (14, 17) | <0.001 |
| Sex, $n$ (%) | | | | | <0.001 |
| Female | 506 (71%) | 64 (50%) | 35 (38%) | 407 (83%) | |
| Male | 205 (29%) | 63 (50%) | 58 (62%) | 84 (17%) | |
| Reason for ingestion, $n$ (%) | | | | | <0.001 |
| Accident | 68 (9.5%) | 25 (20%) | 23 (24%) | 20 (4.0%) | |
| Play | 103 (14%) | 83 (65%) | 16 (17%) | 4 (0.8%) | |
| Suicidal | 400 (56%) | 0 (0%) | 14 (15%) | 386 (78%) | |
| Unknown | 147 (20%) | 19 (15%) | 41 (44%) | 87 (18%) | |
| Co-ingestions, $n$ (%) | | | | | <0.001 |
| Multiple substances | 332 (46%) | 34 (27%) | 34 (36%) | 264 (53%) | |
| Only melatonin | 386 (54%) | 93 (73%) | 60 (64%) | 233 (47%) | |
| Inquirer, $n$ (%) | | | | | <0.001 |
| Civilian | 258 (36%) | 87 (69%) | 60 (64%) | 111 (22%) | |
| Healthcare professional | 460 (64%) | 40 (31%) | 34 (36%) | 386 (78%) | |

## 249. Acetaminophen/opioid combination in overdose: can opioid-related toxicity be observed without acetaminophen poisoning?

William Tayebaly and Bruno Mégarbane

Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris Cité University, Paris, France

**Objective:** Whether acetaminophen/opioid combination overdoses may cause more severe effects such as respiratory depression than lone paracetamol overdose is a debated issue in the literature [1,2]. We aimed to investigate this important clinical question using more specific outcome measures and temporal data than in previous works.
**Methods:** We performed an observational cohort study. All poisoned patients admitted to our intensive care unit during a 10-year period with a documented exposure to a marketed formulation of acetaminophen/opioid combination (including either codeine, tramadol or opium) were included. Data were extracted from patients' records. Patients not treated with N-acetylcysteine (based on the decision of the treating physicians) were considered as not acetaminophen-poisoned. In these patients, clinical effects (Glasgow Coma Score $<9$, respiratory rate $<12$/min, miosis and $PaCO_2$ $<45$ mmHg) and specific treatments (naloxone injection and mechanical ventilation) possibly explained or administered to counteract opioid toxicity were analysed on a case-by-case basis. The possible contribution of co-ingestants was checked using the list of presumed ingested drugs and the available routine plasma and urine toxicological screening.
**Results:** Overall, 78 patients (50 M/28 F, age 35 years [31–41]) who ingested acetaminophen + tramadol ($n=36$, 44%), codeine ($n=33$, 40%) or opium ($n=13$, 16%) were identified. On admission, patients were asymptomatic ($n=49$, 63%) or presented nausea/vomiting ($n=21$, 27%) and abdominal pain ($n=9$, 12%). N-acetylcysteine ($n=61$, 78%) and activated charcoal ($n=16$, 21%) were administered on admission. Seventeen non-acetaminophen-poisoned patients who co-ingested opioids (i.e., tramadol ($n=9$), codeine ($n=4$), and opium ($n=4$)) were identified. Among these patients, four presented Glasgow Coma Score $<9$ and required mechanical ventilation, in relation to documented co-ingested sedative drugs. Two patients (1 with codeine and 1 with tramadol ingestion) developed bradypnea and two other patients (1 with codeine and 1 with tramadol ingestion) presented $PaCO_2$ $>45$ mmHg, in relation to the co-ingested opioid and in the absence of any other co-ingested drug. These four patients did not require naloxone and were not intubated.
**Conclusion:** Opioid-related toxicity can be observed without acetaminophen poisoning in patients overdosed with acetaminophen/opioid combinations. In these cases, however, opioid-related toxicity is expected to be mild.

### References

[1] Heppell SPE, Isbister GK. Lack of respiratory depression in paracetamol-codeine combination overdoses. Br J Clin Pharmacol. 2017;83:1273–1278.
[2] Floyd CN, Dargan PI. The toxicity of paracetamol-codeine combination in overdose is an unresolved issue. Br J Clin Pharmacol. 2018;84:806–807.

## 250. Indigestion: endoscopic removal and whole bowel irrigation in a patient with a pharmacobezoar

Elia Morando[a], Camilla Vecli[b], Giorgio Ricci[a], Giovanni Mantelli[a], Matilde Bacchion[a] and Ilaria Costantini[a]

[a]Poison Centre of Verona, Verona, Italy; [b]Emergency Department of Santa Maria del Carmine Hospital, Rovereto, Italy

**Objective:** We describe gastrointestinal decontamination in a patient with a pharmacobezoar.
**Case report:** We present the case of a 40-year-old female intubated after being found at home with a Glasgow Coma Score (GCS) 3, surrounded by numerous empty blister packs comprising 23 packets of quetiapine, 56 of citalopram, and 2 of pregabalin. She had a history of major depression, borderline personality disorder and multiple psychiatric hospitalisations. The patient remained hemodynamically stable without support throughout. The family last heard from her 4 hours before calling 118. On arrival to the Emergency Room (ER), after monitoring and primary evaluation, the doctors consulted with our PCC. A gastric lavage was performed, returning only a small amount of gastric material. We then suggested she undergo an abdomen computerised tomography (CT) scan, which showed a voluminous bezoar in the gastric area and other conglomerates in the ileal loops and in the ascending colon. After multiple unsuccessful attempts, the conglomerate was fragmented and partially removed by endoscopy. At the end of the procedure, activated charcoal was administered every 4 hours, followed by bowel cleansing with PEG 4000. The patient was admitted to the intensive care unit (ICU) still intubated, with a GCS of 3 without any sedation and hemodynamically stable. Six hours after ingestion, we suggested continuing administration of activated charcoal in multiple doses (for a total of 4 administrations) due to the persistence of alteration of consciousness. An electroencephalogram (EEG) and renal function were unremarkable. There was an increase of creatine kinase (CK) from 71 to 440 U/L, which was treated effectively only with fluid administration. The patient was extubated after two days. The following day she was transferred to the Psychiatric Unit with a GCS of 15 and without any electrocardiographic or laboratory alterations.
**Conclusion:** This clinical case stresses the importance of a global vision in the management of complex intoxications. The use of an advanced imaging technique led to the decision to use an invasive decontamination method, since classic procedures were ineffective and time-consuming as a first approach in this context.

## 251. Low volume therapeutic plasma exchange with low dose steroid therapy as treatment of toxin-induced acute liver failure: a case series

Varada Aravindan[a], Indira Madhavan[b], Rohith Sasidharan[a] and Ajmal Nm[a]

[a]Government Medical College, Thrissur, India; [b]Department of General Medicine, Government Medical College, Thrissur, India

**Objective:** High volume therapeutic plasma exchange (TPE HV) is considered as category I indication, grade IA recommendation in acute liver failure (ALF) [1]. There are reports that low volume

Table 1. Characteristics of 4 patients treated with toxin induced acute liver failure treated with low volume therapeutic plasma exchange (TPE).

| | Patient 1 | | Patient 2 | | Patient 3 | | Patient 4 | |
|---|---|---|---|---|---|---|---|---|
| Age | 16 | | 21 | | 22 | | 20 | |
| Gender | Male | | Female | | Male | | Male | |
| Toxin | Zinc phosphide (3%, 15 g) | | Zinc phosphide (3%, 7 g) | | Paracetamol 12.5 g | | Zinc phosphide (3%, 15 g) | |
| Time post-ingestion NAC started | 24 hours | | 48 hours | | 16 hours | | 120 hours | |
| Number of cycles of TPE | 3Started at 25 hours | | 3Started at 48 hours | | 2Started at 86 hours | | 3Started at 130 hours | |
| Outcome | Survived | | Survived | | Survived | | Survived | |
| Complications | Coagulopathy | | Coagulopathy, encephalopathy, hypotension | | Coagulopathy | | Coagulopathy | |
| Days before and after TPE | D2* | D6 | D3 | D14 | D1 | D7 | D7 | D14 |
| AST/ALT in U/L | 63/33 | 49/57 | 93/40 | 61/97 | 68/86 | 126/520 | 100/137 | 71/101 |
| Serum bilirubin (mg/dL) | 0.4 | 0.9 | 1.2 | 2.9 | 2.5 | 0.8 | 0.9 | 0.8 |
| Serum creatinine (mg/dL) | 1.4 | 0.8 | 0.7 | 0.5 | 0.7 | 0.9 | 0.9 | 0.7 |
| INR | 2.2 | 1.2 | 2.53 | 1.3 | 1.75 | 1.28 | 2.3 | 1.9 |
| MELD score | 23 | 8 | 23 | 13 | 22 | 9 | 22 | 9 |

*Days after ingestion; ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; MELD: model for end-stage liver disease; NAC: N-acetylcysteine.

TPE (TPE LV) is also effective in ALF [2]. Zinc phosphide rodenticide poisoning and paracetamol poisoning are two common causes of fatal toxin-induced ALF in south India and are treated with TPE LV and low dose steroid. Removal of inflammatory cytokines and von Willebrand factor by TPE are the proposed mechanism by which multiorgan dysfunction is prevented in ALF.

**Case series:** We present 4 cases of toxin induced ALF treated with TPE LV and low dose steroid therapy (Table 1). All were given N-acetylcysteine as a bolus dose followed by 100 mg/kg/day infusion until clinical improvement. All satisfied criteria for referring to a liver transplantation centre as per the Model for End-stage Liver Disease (MELD) score. As they denied referral due to affordability, we started TPE LV and prednisolone 20 mg daily until the MELD score improved. In each cycle of TPE, 1–1.5 L of plasma was removed by membrane filtration over 4 hours and replaced with 6 units of fresh frozen plasma (FFP) and 100 mL of 20% human albumin. All patients survived.

**Conclusion:** TPE LV with low dose steroid therapy can improve transplant free survival in toxin-induced ALF patients in resource poor setting. Larger studies are needed to generate good quality evidence.

## References

[1] Padmanabhan A, Connelly-Smith L, Aqui N, et al. Guidelines on the use of therapeutic apheresis in clinical practice – evidence-based approach from the Writing Committee of the American Society for Apheresis: the eighth special issue. J Clin Apher. 2019; 34:171–354.

[2] Zachariah U, Kumar SE, Alexander V, et al. Low-volume plasma exchange and low-dose steroid to treat severe liver injury. Gastroenterol Hepatol Endosc Pract. 2021;1:47–54.

# 252. Cocaine-associated chest pain risk factors: a single centre experience

Mark Jovanović[a] and Miran Brvar[b]

[a]Department of Cardiology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [b]Faculty of Medicine, Centre of Clinical Toxicology and Pharmacology, University Medical Centre Ljubljana and Centre for Clinical Physiology, University of Ljubljana, Ljubljana, Slovenia

**Objective:** Cocaine abuse presents an important, but often underrecognized risk factor for evolution of cardiovascular disease. The third most frequent complaint after anxiety and agitation or aggressive behavior in cocaine abuse is cocaine-associated chest pain (CACP) with symptoms similar to those of acute coronary syndrome, including constrictive or oppressive retrosternal pain. The proportion of patients with a history of cocaine abuse and CACP or myocardial infarction (cocaine-induced myocardial infarction, CIMI) is estimated at 40 and 6%, respectively [1]. Nevertheless, the risk factors of CACP remain incompletely understood. The aim was to evaluate risk factors associated with CACP in patients admitted due to acute cocaine intoxication.

**Methods:** We retrospectively reviewed medical records of 178 patients with acute cocaine intoxication admitted to the Medical Emergency Department in Ljubljana in the last decade. All patients had a positive urine cocaine test. The primary endpoint was presence of CACP in this patient cohort.

**Results:** The mean patient age was 31.7 ± 7.3 years, and the majority of patients were male (76%). Overall, 76 (43.7%) and 8 (4.5%) patients presented with CACP and CIMI, respectively. However, 5 out of 8 CIMI patients presented without CACP. The most frequent co-ingested psychotropic drugs were benzodiazepines (36.0%) and synthetic opioids (34.8%), followed by methamphetamines (11.8%) and ethanol (6.7%). In multivariate analysis, factors associated with higher risk of CACP were age (OR 1.09, CI 95% 1.03–1.16) and co-ingestion of methamphetamines (OR 7.06, CI 95% 2.27–21.99). Nevertheless, co-ingestion of benzodiazepines (OR 0.42, CI 95% 0.22–0.81) and synthetic opioids (OR 0.12, CI 95% 0.05–0.24) was associated with lower risk of CACP.

**Conclusion:** Cocaine-associated chest pain depends on multiple factors. Co-ingestion of benzodiazepines and synthetic opioids were associated with lower risk of cocaine-associated chest pain in this patient cohort. This finding might indicate underdiagnosis of cocaine-induced myocardial infarction in patients with co-ingestion of benzodiazepines and synthetic opioids due to the absence of chest pain. Prospective studies are needed to confirm our preliminary findings.

## Reference

[1] Agrawal PR, Scarabelli TM, Saravolatz L, et al. Current strategies in the evaluation and management of cocaine-induced chest pain. Cardiol Rev. 2015;23:303–311.

# EAPCCT abstracts author index 2023, by abstract number

# EAPCCT keyword index 2023, by abstract number