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1. An illicit drug early warning system utilising comprehensive toxicological analysis of emergency department presentations in Victoria, Australia

Shaun Greene[a], Jennifer Schumann[b], Bek Syrjanen[b], Dimitri Gerostamoulos[b], Sarah Hodgson[a], Rachelle Abouchedid[a] and John Fitzgerald[c]

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

Objective: In response to the evolving threat of illicit drug use, combined with anticipated SARS-CoV-2 (COVID-19) pandemic-related market volatility, we created a multi-institution network supplying high-quality data on illicit drug presentations to Victorian emergency departments (EDs). Primary objective: timely data provision to a state Early Warning System (EWS) utilising multiple intelligence sources (including syringe residue and wastewater analysis) to inform public health interventions.
Methods: The Emerging Drugs Network of Australia VIC (EDNAV) project is a multi-site prospective observational study collating de-identified clinical and analytical information within an electronic clinical registry (Research Electronic Data Capture secure web-based software platform). Case inclusion criteria: individuals $\geq$16 years of age presenting with suspected illicit drug toxicity requiring venepuncture as part of standard care. Hospital ethics committee approved waiver of patient consent for inclusion of deidentified data. Nine metropolitan and one regional ED contributed blood samples for weekly toxicological analysis at the Victorian Institute of Forensic Medicine. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) screened for 327 pharmaceuticals and illicit substances, as well as 268 novel psychoactive substances. EDNAV data was reviewed weekly as a component of the state EWS. High-risk signals were disseminated to government and external stakeholders.
Results: During September 2020 – March 2021, 320 cases were analysed (70% male, mean age 30 years, 72% ambulance arrival). Sedation (Glasgow Coma Score (GCS) $<$ 9, 35%) and agitation (33%) were the commonest reasons for presentation; 33% of patients required parenteral sedation, and 18% were administered naloxone. In addition, 8% were intubated and 11% required critical care admission; 85% had a Poisoning Severity Score of $\geq$2. There were two deaths. There were 815 separate detections (345 illicit substances, 470 pharmaceuticals). At least one illicit drug was detected in 87% of cases ($>$ 1 illicit drug in 43%). Common illicit drugs included methylamphetamine (52% of cases), gamma-hydroxybutyrate (GHB), 3,4-methylenedioxymethamphetamine (MDMA), cocaine and opioids. Eight novel benzodiazepines, 7 cathinones, 5 hallucinogens, 3 synthetic cannabinoid receptor agonists (SCRAs) and one novel opioid (Beta-U10) were detected. In 90% of cases, reported exposure differed from analytical findings. During COVID-19 related lockdowns, there was evidence of substance substitution including benzodiazepines in products sold as heroin. Three public health warnings were released in association with EDNAV findings (N-ethylpentylone in cocaine, 25B-NBOH sold as lysergic acid diethylamide (LSD), paramethoxymethamphetamine (PMMA) sold as MDMA).
Conclusion: For the first time in Victoria, a network of healthcare institutions working together enabled timely detection of illicit drug related harm, facilitating early public health warnings and notification of peer-based harm reduction services.

2. 4-Fluoroamphetamine (4-FA) intoxication results in exaggerated blood pressure effects compared to 3,4-methylenedioxymethamphetamine (MDMA) and amphetamine: a retrospective analysis

F.M.J. Gresnigt[a], Anouk Snik[b], Eric J.F. Franssen[b], Joost W Vanhommerig[b], Dylan W. de Lange[c] and Robert K. Riezebos[b]

[a]OLVG, Utrecht, Netherlands; [b]OLVG, Amsterdam, Netherlands; [c]UMC Utrecht, Utrecht, Netherlands

Objective: 4-Fluoroamphetamine (4-FA) is an amphetamine-type stimulant, with effects comparable to amphetamine and 3,4-methylenedioxymethamphetamine (MDMA) [1]. Severe 4-FA cardiac and neurological complications and fatalities have been described [2,3]. We explore the cardiovascular effects in 4-FA compared with MDMA and amphetamine intoxicated patients.
Methods: Between November 2015 and March 2020, all self-reported and/or toxicology analysis confirmed 4-FA, MDMA and amphetamine intoxicated adult patients presenting at the emergency department (ED) of OLVG Hospital, Amsterdam, were retrospectively analyzed for vital parameters, cardiovascular symptoms and complications. To determine normality of distribution of continuous data, Shapiro-Wilk's tests, Skewness and Kurtosis values, and visual histogram inspection, normal Q-Q plots and boxplots were used. Independent samples T-tests were

used to compare normally distributed data, Mann-Whitney U tests for non-normally distributed data, and chi-square tests and Fisher's Exact tests for categorical data. Statistical significance was defined as a p-value <0.05.
Results: Of 582 patients, 31 (5.3%) had 4-FA (10 mono-intoxications, 32.3%), 406 (69.8%) MDMA (59 mono-intoxications, 14.5%), 100 (17.2%) amphetamine (10 mono-intoxications, 10.0%), and 45 (7.7%) a mix of these drugs. Toxicological confirmation was performed for 21.7% of MDMA and 16% of amphetamine users (urine toxicology screening) and for one 4-FA patient (Toxtyper® analysis). 4-FA mono-intoxicated patients experienced more headache (n = 8; 80.0%) compared to MDMA (n = 2; 3.3%; $p < 0.001$) and amphetamine mono-intoxicated patients (n = 0; 0.0%; $p < 0.001$) and higher systolic blood pressure (164 ± 31 mmHg versus 139 ± 19 mmHg; $p = 0.031$ versus 135 ± 22 mmHg; $p = 0.033$, respectively). 4-FA-related cardiovascular complications included Takotsubo cardiomyopathy (n = 1; 3.2%), subarachnoid hemorrhage (n = 1; 3.2%), and hypertensive urgency (n = 2; 6.5%). Cardiovascular complications for MDMA were out-of-hospital cardiac arrest (OHCA) (n = 2; 0.5%, one death), intracranial hemorrhage (n = 1; 0.25%), and dilated cardiomyopathy (n = 1; 0.25%), and amphetamine, hypertensive urgency (n = 2; 2%), and atrial fibrillation (n = 1; 1%).
Conclusion: 4-FA intoxicated ED patients had a significantly lower heart rate, higher systolic blood pressure, and more frequent headache, compared to MDMA and amphetamine. Severe 4-FA and MDMA-related cardiovascular complications, included hypertensive crisis, Takotsubo cardiomyopathy, intracranial hemorrhage and OHCA.

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3. Single nucleotide polymorphisms of mu opioid receptor gene OPRM1 in emergency department patients with acute opioid overdose

Alex F. Manini, Lynne D. Richardson, Carmen Vargas-Torres, Kavey Vidal and Yasmin L. Hurd

Icahn School of Medicine at Mount Sinai, New York, United States

Objective: Genetic variations in the mu-opioid receptor (MOR) gene (OPRM1) mediate individual differences in response to pain and opioid addiction. Several common MOR single nucleotide polymorphisms (SNP) have been previously associated with opioid addiction in humans. For example, the rs2075572 SNP is responsible for alternative splicing of the MOR to form a single trans-membrane version, while the rs1799971 SNP results in a missense amino acid change that affects the stability of the MOR. We studied whether three common MOR SNPs (rs3778150, rs1799971, rs2075572) were associated with overdose severity in patients presenting to the emergency department (ED) with acute opioid overdose.
Methods: This observational cohort study at two urban teaching hospitals evaluated consecutive adult ED patients presenting with suspected acute opioid overdose over 5 years (June 2015-February 2020). Patients were excluded if waste clinical samples were unavailable. Specimens were linked with clinical variables (demographics, urine toxicology screens, clinical outcomes) then de-identified prior to genetic SNP analysis. The study outcome, overdose severity, was defined as the following composite outcome: in-hospital occurrence of either (A) respiratory arrest (mechanical ventilation or repeat naloxone administration), or (B) cardiac arrest (loss of pulse). Blinded Taqman genotyping (Applied Biosystems) of the SNPs were performed after standard DNA purification (Qiagen) and whole genome amplification (Qiagen REPLI-g). STATA/SE 16.1 was used to analyze individual SNPs using multivariable logistic regression.
Results: We evaluated 331 patients (37.5% female, mean age 45.7 (SD 16.6) years) of whom 64 (19.3%) suffered severe outcomes. Urine toxicology was positive in 59.4%, of which there were positives for 14 benzodiazepines, 15 cocaine, 22 opiates, 19 methadone, and 6 barbiturates. All genotypes examined conformed to Hardy-Weinberg equilibrium. When controlling for demographics, clustering by year, and number/type of drug exposures, the rs2075572 variant allele was significantly associated with over 4-fold increased odds of overdose severity (aOR 4.49, CI 1.2-17.3), while the rs1799971 variant allele was associated with 43% decreased odds (aOR 0.57, CI 0.50-0.64). Finally, the rs3778150 (p = 0.96) had no significant association with the study outcome.
Conclusion: These data demonstrate that in ED patients with acute opioid overdose, two OPRM1 SNPs were independent predictors of opioid overdose severity - the rs2075572 variant allele (higher severity) and the rs1799971 variant allele (lower severity). This adds to the growing body of evidence linking OPRM1 SNPs with clinical outcomes and confirm that OPRM1 SNP testing is a potential target for personalized medical prescribing practices with regard to overdose vulnerability.

4. Ketamine in acute recreational poisonings in the Balearic Islands

Juan Ortega Pérez[a], Jordi Puiguriguer Ferrando[a], Bernardino Barceló Martín[b], Isabel Gomila Muñiz[b] and Miguel Ángel Elorza Guerrero[c]

[a]Unidad de Toxicología, Servicio de Urgencias, Hospital Universitario Son Espases, Grupo de Trabajo en Toxicología Clínica del Área de Neurociencias del Institut d'Investigació Sanitària de Baleares (IdiSBA), Palma de Mallorca, Spain; [b]Servicio de Análisis Clínicos, Hospital Universitari Son Llàtzer, Palma de Mallorca; Instituto de Investigación Sanitaria de las Islas Baleares (IdISBa), Palma de Mallorca, Spain; [c]Instituto de Investigación Sanitaria de las Islas Baleares (IdISBa), Palma de Mallorca; Servicio de Análisis Clínicos, Unidad de Toxicología Clínica, Hospital Universitari Son Espases, Palma de Mallorca, Spain

Objective: Ketamine is a dissociative anesthetic, synthesized in the 1960s. Its non-medical use began in the 1990s as an adulterant of ecstasy for recreational purposes in electronic rave music venues. A relatively high dose of ketamine during recreational use can lead to a number of health problems. Repetitive ketamine use is also associated with cognitive decline, increased impulsivity, depression, ulcerative cystitis and accidental deaths. The objective of this study was to characterize the epidemiological, clinical and toxicological profile of these patients, based on the verification of the increase in positive confirmations of

ketamine in samples received from Emergency Departments (ED) of the Balearic Islands since 2018.
Methods: Retrospective observational study of patients treated for acute recreational drug intoxication with analytically confirmed ketamine exposure in the Balearic Islands between January 2018 and December 2020. Demographic and clinical characteristics of the cases were recorded using structured data collection. Toxicological analysis in urine samples was performed using screening for drugs of abuse by immunoassay and general drug screening and confirmation of positive immunoassays by gas chromatography coupled to mass spectrometry.
Results: During the study period, 81 patients with a positive result of ketamine and/or its metabolites in urine were included. The consumption of ketamine was declared or suspected in 34 (42%) cases and 4 (4.9%) patients declared consumption of 2C-B (as tucibi, tussi, or nexus). The mean age of patients was 26.6 ± 6.9 years. The majority were men. Most patients (n = 59; 72.8%) were not residents of the Balearic Islands. The clinical profile of patients was recreational intoxication. The most frequent clinical signs were tachycardia (n = 35; 43.2%), hypertension (n = 24; 29.6%), decreased consciousness (n = 23; 28.4%), mydriasis (n = 21; 25.9%), agitation/aggressiveness (n = 21; 25.9%), hypothermia (n = 17; 21.0%) and anxiety (n = 12; 14.8%). Complementary tests revealed rhabdomyolysis (n = 38; 46.9%), elevated lactate (n = 21; 25.9%) and acidosis (n = 19; 23.5%). The electrocardiogram was unaltered in 29 (35.8%) patients; the most frequent abnormality was sinus tachycardia (n = 18; 22.2%). The destination after treatment in the ED was medical discharge in 65 (80.2%) cases. The drugs most frequently detected with ketamine were cocaine (n = 75; 92.6%), 3,4-methylenedioxymethamphetamine (MDMA) (n = 58; 71.6%), ethanol (n = 32; 39.5%), cannabis (n = 28; 34.6%) and amphetamine (n = 9; 11.1%).
Conclusion: We confirmed the presence of ketamine in recreational drug intoxications in individuals with a characteristic profile in our geographical area (young male, non-resident, events of electronic music, with toxic polydrug use), with a high percentage of ignorance of this consumption. These analytical/clinical studies allow complementing epidemiological studies based on drug use surveys.

5. The neuro-respiratory effects of pregabalin and the potential deleterious effects of its combination with diazepam or morphine – a rat investigation

Laurène Dufayet, Lucie Chevillard, Patricia Risède, Nadia Benturquia, Dominique Vodovar and Bruno Mégarbane

Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris University, Paris, France

Objective: Pregabalin is increasingly used as a recreational drug leading to abuse, mainly in opioid users. The potential respiratory depression of pregabalin in overdose is still debated. However, life-threatening poisoning with severe neuro-respiratory depression and fatalities have been attributed to pregabalin with a benzodiazepine or an opioid. We investigated the neuro-respiratory toxicity of pregabalin alone and in combination in a rat model.
Methods: Sprague-Dawley rats were randomized and pregabalin administered by gavage. Sedation and ataxia (using a four stage-clinical scale), body temperature, plethysmography and arterial blood gases were measured before and during 240 min post-treatment administration. We first studied the dose/effect relationships of pregabalin at increasing doses (saline control; 41 mg/kg, pregabalin, 91 mg/kg, 200 mg/kg, 439 mg/kg and 965 mg/kg; N = 5 rats/dose). We studied the effects of pregabalin (965 mg/kg; administered by gavage) + diazepam (20 mg/kg, dose lacking significant respiratory effects; administered subcutaneously 45 minutes after the gavage) combination in comparison to pregabalin alone, diazepam alone and saline control (N = 5 rats/group). Finally, we studied the effects of pregabalin (965 mg/kg; administered by gavage) + morphine (10 mg/kg, dose lacking significant respiratory effects; administered subcutaneously 45 minutes after the gavage) combination comparison to pregabalin alone, morphine alone and saline control (N = 5 rats/group). We determined the area under the curve for each parameter versus time and comparisons between the groups were performed using ANOVA with Dunnett's post-tests.
Results: Pregabalin was responsible for a non-dose-dependent rapid-onset short-duration (60 min) decrease in sedation ($p < 0.01$) and increase in inspiratory time ($p < 0.01$) leading to a significant decrease in minute volume at the highest dose (138,116 ml/min [125,332-157,406] versus 201,815 mL/min [194,273-235,940] (median [interquartile interval], $p < 0.05$) when comparing the highest pregabalin dose versus saline. No significant respiratory effects were observed with the pregabalin/diazepam combination in comparison to pregabalin alone. By contrast, combination of pregabalin + morphine deepened sedation ($p < 0.01$) and induced a rapid-onset short-duration (140 min) decrease in minute volume compared to pregabalin alone (67,100 mL/min [52,869-131,426] versus 135,807 mL/min [125,531-165,389], $p < 0.05$). Similarly, arterial gas analyses confirmed the onset of significant but mild hypoxemia (75 mmHg [69-79] versus 98 mmHg [95-101], $p < 0.005$) and marked hypercapnia (52 mmHg [50-53] versus 35 mmHg [31-39], $p < 0.05$) and respiratory acidosis (pH, 7.37 [7.35-7.39] versus 7.47 [7.45-7.49], $p < 0.05$) in the rats treated with the pregabalin/morphine but not with pregabalin/diazepam combination in comparison to pregabalin alone.
Conclusion: In our rat model, respiratory depression results from the administration of an extremely high dose of pregabalin. Combination of a toxic dose of pregabalin with a pharmacological dose of morphine but not diazepam markedly enhances pregabalin-related neuro-respiratory effects. Physicians should be cautious when prescribing pregabalin to opioid users due to potential synergic central nervous system depressive effects if pregabalin is abused.

6. High-dose insulin therapy delays gastric emptying: a human randomized controlled trial

Søren Bøgevig[a], Tonny S. Petersen[a], Lotte C.G. Hoegberg[b], Troels Riis[a], Mathies M. Jepsen[a], Kim P. Dalhoff[a] and Mikkel B. Christensen[a]

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

Objective: High dose insulin/glucose therapy (HIT) has gained considerable attention as a treatment option in severe beta-adrenergic antagonist and/or calcium channel blocker overdose refractory to conventional therapies. Knowledge concerning the therapeutic effectiveness of HIT is generated from animal studies and human case reports, whereas randomized human trials investigating the effectiveness and adverse effects of HIT are lacking. Gastric emptying is of importance in the poisoned patient as it may play a role in further absorption of toxic

substances, but also affect the transit time of activated charcoal. We performed a randomized controlled trial investigating HIT, and as a secondary endpoint investigated the effect of high dose insulin therapy on gastric emptying evaluated by paracetamol absorption.
Methods: In a clinical, randomized, crossover study, ten healthy male participants were intravenously administered a beta-adrenergic antagonist (esmolol infusion 0.25 mg/kg/min) or placebo combined with an intervention with high dose insulin (10 IE/kg/h as infusion) or placebo on four separate days. Prior to the intervention all participants ingested a single dose of immediate release paracetamol (1500 mg) with 100 mL of tap water. Plasma paracetamol concentrations were monitored at intervals over the following 4 hours.
Results: Maximal concentration (C_{max}) of paracetamol was (mean ± SEM) 19.6 ± 3.3 mg/L on placebo days versus 7.8 ± 1.2 mg/L on intervention days with HIT. Time to maximum concentration (T_{max}) was 57 ± 7.5 minutes on placebo days versus 248 ± 54 minutes on HIT days. Differences in both C_{max} and T_{max}, were significant ($P = 0.02$) between days with and without insulin. Esmolol did not have a significant individual or HIT-modifying effect on C_{max} or T_{max} of paracetamol.
Conclusion: HIT significantly delays gastric emptying evaluated by the paracetamol absorption method. A delay may affect the effectiveness of gastrointestinal decontamination and treatment with activated charcoal, since transit time and distribution to the small intestine may be further delayed, if HIT is initiated.

7. Cobaltism from metal-on-metal (MoM) hip implants: how to manage and treat with acetylcysteine

Monica Carnovale, Davide Lonati, Azzurra Schicchi, Valeria M. Petrolini, Valentina Negrini, Lucia Bernasconi, Benedetta Brolli, Cristina Grazioli, Anna Ronchi and Carlo A. Locatelli

Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy

Objective: Chronic cobalt toxicity due to the release from metal-on-metal (MoM) hip implants has been associated with both severe local and systemic toxicity. Our primary aim was to identify the appropriate toxicological management and therapeutic approach including N-acetylcysteine (NAC) as an effective and safe chelator.
Methods: All cases referred to our Poison Centre (PC) with metal hip implants (total hip arthroplasty (THA) and/or hip resurfacing arthroplasty (HRA) devices) were retrospectively evaluated (last 12-years, 2010-August 2021). Data regarding sex, age, HRA/THA data, clinical course, cobalt concentration (blood/urine), clinical response to NAC and outcome were evaluated. Patients were divided into two sub-groups: Group A (implant *in situ*) and Group B (implant removed). Statistical tests were applied.
Results: Overall 83 patients (ranging 18-91 years, male 50.6%) were included. Twenty-six (31%) had bilateral implants and 60% THA. Devices were implanted mostly between 2005 and 2011 (mean time from MoM-implant to toxicological evaluation, 8.4 years). Twenty-four (29%) received a recall from the manufacturer. At first evaluation, 56 patients (67%) had symptoms: systemic (20%), systemic and local (23%), local (57%: metallosis (12%), pseudotumor (7%), hip pain (31%)). Seventy-nine (95%) had elevated blood cobalt concentrations (mean value 15.7 μg/L). The urinary cobalt mean concentration was higher in symptomatic patients versus asymptomatic (51.1 versus 10.8 μg/L, p 0.0211). In group A (n = 22) and group B (n = 61) cobalt mean concentration was 7.9 and 15.9 μg/L, respectively. There were 82% symptomatic patients in group A and 62% in group B. Considering clinical and toxicological data, 19 patients (23%) were treated with NAC [13 oral (3600 mg/day), 2 IV (300 mg/kg/day), 4 oral/IV]: no adverse reactions were registered. Despite NAC-treatment, 6 patients underwent surgical revision. Only 1 patient received NAC after surgery due to very high cobalt blood concentrations. Statistical analysis shows intra-individual reduction of median cobalt blood concentration after treatment (-5.5 μg/L). No lethal cases were registered.
Conclusion: Cobalt toxicity due to release from MoM hip implants is an underestimated phenomenon. Many patients are asymptomatic despite high concentrations of metal. They require an expert multidisciplinary (orthopedic and toxicologic) evaluation and follow-up. Our experience permitted proposal of a decisional flow-chart in which a cut-off of 10 μg/L is considered a decision-making threshold for treatment with NAC. Although surgery remains the definitive therapy, we suggest NAC as an effective and safe chelating agent useful in post-revision, as bridge-to-surgery and, when surgery cannot be performed, as oral treatment in outpatients for long-term management.

8. Analytically-confirmed polydrug use is more common in drug misuse patients attending emergency departments in Scotland compared with those in England and Wales

Simon H.L. Thomas[a], Simon Hudson[b], Alberto Oteo[c], Jamie Cooper[d], Elia Stelios[e], Mark Haden[f], Rebecca Macfarlane[g], Andy Ketchin[h], Gareth Hardy[i], George Bailey[j], Simon L. Hill[k], Liza Keating[l] and Michael Eddleston[m]

[a]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom; [b]LGC Ltd, Fordham, United Kingdom; [c]Health Improvement & Disparities, Department of Health and Social Care, London, United Kingdom; [d]Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [e]Barts and the London NHS Foundation Trust, London, United Kingdom; [f]St George's University Hospitals NHS Foundation Trust, London, United Kingdom; [g]Epsom and St Helier NHS Trust, Epsom, United Kingdom; [h]Royal Devon and Exeter NHS Foundation Trust, Exeter, United Kingdom; [i]Blackpool Teaching Hospitals NHS Foundation Trust, Blackpool, United Kingdom; [j]Imperial College Healthcare NHS Trust, St Mary's Hospital, London, United Kingdom; [k]Newcastle Hospitals NHS Foundation Trust, Newcastle, United Kingdom; [l]Royal Berkshire NHS Foundation Trust, Reading, United Kingdom; [m]Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Objective: Deaths (per million population) associated with drug misuse are substantially more common in Scotland than England and Wales (E&W), with drivers including local high prevalence of problematic opioid and polydrug use. To better understand this, we compared Scottish and E&W patient-reported and analytically confirmed drug exposures for people attending emergency departments participating in the Identification Of Novel psychoActive substances (IONA) study.
Methods: Consenting adults (≥16 years) presenting to participating hospitals (2 [Edinburgh, Aberdeen] in Scotland, 25 E&W) between January 2020 and October 2021 with toxicity after suspected drug misuse of any type and severity were included. Clinical details were recorded and blood and/or urine samples analysed in a single laboratory using high-resolution accurate mass liquid chromatography–mass spectrometry.

Table 1. Frequency of reporting and detection of common drugs of misuse between Scotland and England and Wales.

	Scotland (n = 78)	England and Wales (n = 274)	Chi^2 P=
Suspected use (reported by patient or clinician)			
Benzodiazepines/related	38 (48.7%)	49 (17.9%)	<0.0001
Stimulants	28 (35.9%)	149 (54.4%)	0.004
Opioids	20 (25.6%)	70 (25.5%)	N.S.
Cannabinoids	8 (10.3%)	68 (24.8%)	0.0061
Gabapentinoids	6 (7.7%)	12 (4.4%)	N.S.
Ketamine	4 (5.1%)	17 (6.2%)	N.S.
Cathinones	4 (5.1%)	1 (0.4%)	0.0022
Gamma hydroxybutyrate/related	3 (3.8%)	26 (9.5%)	N.S.
Confirmed exposure (detected in at least one sample)			
Benzodiazepines/related	69 (88.5%)	189 (69.0%)	0.0006
Stimulants	53 (67.9%)	190 (69.3%)	N.S.
Opioids	58 (74.4%)	171 (62.4%)	N.S.
Cannabinoids	55 (70.5%)	111 (40.5%)	<0.0001
Gabapentinoids	28 (35.9%)	64 (23.4%)	0.0269
Ketamine	15 (19.2%)	57 (20.8%)	N.S.
Cathinones	6 (7.7%)	6 (2.2%)	0.0185
Gamma hydroxybutyrate/related	0 (-)	6 (2.2%)	N.S.
Drug combinations			
Opioid with benzodiazepine	47 (60.3%)	129 (47.1%)	0.04
Opioid with gabapentinoid	27 (34.6%)	56 (20.4%)	0.0092
Opioid with benzodiazepine and gabapentinoids	24 (30.8%)	51 (18.6%)	0.0204

Results: Comparing Scotland with E&W there were no significant differences in median age (33 versus 31 years, respectively) or sex (males 67.9% versus 77.4%). Higher proportions of Scottish patients reported use of benzodiazepines, but lower proportions reported use of cannabinoids or stimulants. Sample analysis revealed larger numbers of separate substances in Scottish than E&W patients (median 6 versus 4, $P < 0.001$), with the following found significantly more often: benzodiazepines (including diazepam, etizolam and alprazolam), cannabinoids, gabapentinoids (gabapentin and pregabalin) and cathinones (mephedrone and eutylone). Opioid detections were not significantly different, but combinations of opioids with benzodiazepines, gabapentinoids or both were significantly more common in Scotland (Table 1). Scottish patients had longer median hospital stays but there were no significant differences in frequency of intubation/ventilation or fatality.

Conclusion: Patients attending participating emergency departments in Scotland after drug misuse are exposed to more substances than those in E&W. Although this study is too small to detect significant differences in case fatality, the higher incidence of opioid combinations with benzodiazepines and gabapentinoids may contribute to the higher rate of drug-related death in Scotland.

9. It is not always COVID-19: a case of respiratory failure from lung damage associated with electronic cigarettes (EVALI)

Marco Marano, Laura Menchini, Morida Khalil Ramla, Salvatore Perdichizzi, Alberto Villani, Giorgio Zampini, Charlie Joseph Charles Beetham, Francesca Stoppa and Mara Pisani

Bambino Gesù Children Hospital, Roma, Italy

Objective: In the period of the SARS-COV-2 pandemic, the differential diagnosis between several causes of respiratory failure can represent a challenge for clinicians. We present the case of an adolescent with e-cigarette associated lung injury mimicking COVID-19 presentation.

Case report: A previously healthy 14-year-old male was transferred to our Pediatric Intensive Care Unit for respiratory distress and history of contact with a SARS-COV-2 positive schoolmate. At admission he was febrile, tachycardic, tachypneic, and hypoxic. The laboratory findings showed increased inflammatory markers. Chest computed tomography (CT) showed ground glass opacities (GGO) predominantly in the lower lobes with sparing of the subpleural region, parenchymal consolidation with areas of lobular sparing ("atoll sign"), centrilobular nodules of GGO and nodular consolidation were visible. He was suitably isolated and treated with non-invasive ventilation. The infectious workup, including respiratory viruses, SARS-CoV-2, as well as blood and bronchial cultures, was negative. After further questions, the boy admitted that he had been vaping nicotine for more than 90 days. According to the definitions of the Centers for Disease Control and Prevention, lung damage associated with the use of vaping products (EVALI) was diagnosed [1] and methylprednisolone was started at 2 mg/kg/day. Following gradual improvement, he was transferred to the pediatric ward on the fourth day.

Conclusion: The incidence of vaping has more than doubled from 2017 to 2019. COVID-19 and EVALI share clinical symptoms and radiological findings, however the negativity of microbiological investigations and the history of vaping may help in the differential diagnosis. Additionally, as in our case, EVALI CT may present subpleural sparing, slight lower lobe predominance, centrilobular nodules and the atoll sign [2]. Finally, correct identification and early therapy of EVALI can improve the outcome and minimize the length of hospital stay. In patients presenting with unexplained respiratory failure, excluding COVID-19, the possibility of EVALI should be carefully evaluated as the treatment of EVALI differs from COVID-19.

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10. Accidental chlorine gas intoxication in children at a swimming pool: a case series

Coriolan Ulmeanu, Ana Mocanu, Ioana Alexandra Ilisei, Mihaela Constantinescu and Viorela Nitescu
Pediatric Poisoning Centre, Bucharest, Romania

Objective: Chlorine gas can be used as a disinfecting agent at swimming pools and is classified as a pulmonary irritant depending on the dose and duration of exposure [1]. We present 12 children hospitalized for acute symptoms and modified chest X-ray post-exposure to chlorine gas at a swimming pool.
Case series: Twelve children were hospitalized in the Intensive Care and Toxicology Department after accidental exposure to chlorine gas at the swimming pool. There were 11 male patients and one female, aged between 4 and 12 years. The earliest arrival at the emergency room was 10 hours after the exposure and the latest was 55 hours after the exposure (mean arrival 28 hours). Amongst all symptoms reported by patients, there was immediate coughing in all patients, followed by dyspnea and respiratory difficulties in 10 patients, vomiting in 4, wheezing and odynophagia each in 2 children. Acute respiratory failure (SpO_2 <92%) was noted in 8 patients. Related to allergies, four patients had a history of allergies and two patients manifested allergic reactions to medication during hospitalization. The value of total immunoglobulin E was raised in all six patients. Radiological changes, consisting of diffuse interstitial thickening, bilateral diffusely decreased pulmonary transparency, bilateral enlargement of hilar regions were noted in 11 patients. All these patients received intravenous corticotherapy with methylprednisolone, antibiotics (ampicillin or ceftriaxone), antihistamines, and oxygen therapy in cases with acute respiratory failure. Theophylline completed the treatment in 3 patients with very severe acute respiratory failure. All patients were discharged without clinical symptoms after a mean hospitalization period of 3.8 days (SD ±0.9).
Conclusion: Respiratory symptoms are the main effects from chlorine gas exposure, cough being noted in all cases, and acute respiratory failure in the majority of the patients. Specific radiological changes: diffuse interstitial thickening, bilateral diffusely decreased pulmonary transparency were noted in the majority of cases (in 11 of the 12 children) regardless of clinical form. The outcome under correct treatment (oxygen therapy and corticotherapy) is favorable in acute chlorine gas exposure in children.

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11. The main features of acute chemical pneumonitis in poisoned children: a five-year study

Viorela Nitescu[a], Ioana Nicolau[a], Cristina Raduta[a], Alexandru Ulmeanu[b] and Coriolan Ulmeanu[a]
[a]Pediatric Poisoning Centre, Bucharest, Romania; [b]Pneumology Department, Emergency Clinic for Children, Grigore Alexandrescu, Bucharest, Romania

Objective: To describe the clinical and radiological features of acute chemical pneumonitis in poisoned children.
Methods: We performed a five-year retrospective study of cases with acute chemical pneumonitis in a pediatric department of intensive care and toxicology. We analyzed all the medical records identified with ICD-10-Diagnosis CM CODE J68.0 taking into consideration: age, gender, environment, implicated agent, route of exposure, symptoms, radiological features, treatment, and outcome.
Results: A total of 26 poisoned children with acute chemical pneumonitis were identified between 2016-2021, involving 7 girls and 19 boys, the majority being from urban areas (n = 21, 81%). Of the 26 patients, 50% (n = 13) were aged 6-12 years. Regarding the etiology, there were three implicated agents: chlorine gas in 13 cases, smoke from house fire in 8 cases and, hydrocarbons in 5 cases, the main route of exposure was inhalation in 21 cases. The majority of cases (n = 18, 69%) had acute respiratory failure (SpO_2 <92%) of which 13 presented severe bronchospasm. Of 8 children without acute respiratory failure, 6 had a spastic cough as a unique symptom. The main radiological features were diffuse interstitial thickening [1], bilateral diffusely decreased pulmonary transparency, bilateral enlargement of hilar regions, and was noted in 23 patients (88%). Bilateral peribronchovasculary infiltrates were noted in 2 cases and lobar opacity in 1 child. All the patients received intravenous treatment with: antibiotics (ampicillin/amoxicillin + clavulanate in 10 cases, ceftriaxone in 14 cases and meropenem in 2 cases), intravenous corticosteroids (methylprednisolone) in 19 cases (76%) and corticosteroids and theophylline in 5 cases. Out of the 24 children that received intravenous corticosteroids, 15 patients also received inhaled corticosteroids. The average length of hospitalization was 3 days, the longest being 5 days in 2 cases with hydrocarbon poisoning. All the patients recovered without sequelae.
Conclusion: The main etiology of acute chemical pneumonitis in poisoned patients is chlorine gas and inhalation was the main route of exposure. The majority of poisoned children with acute chemical pneumonitis presented with acute respiratory failure which rapidly responded to corticosteroids ± theophylline.

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12. Poisoning from tobacco-free nicotine pouches often occurs in adolescents

Antoinette J.H.P. van Riel[a], Iris C. van Sommeren-de Potter[a] and Dylan W. de Lange[b]
[a]Dutch Poisons Information Center/University Medical Center Utrecht, Utrecht, Netherlands; [b]Dutch Poisons Information Center, Utrecht, Netherlands

Objective: Tobacco-free nicotine pouches (TFNP) are small permeable bags that contain mainly nicotine salt in various concentrations, flavourings, sweeteners and alkaline agents (to increase nicotine bioavailability). Users place the pouch between gums and lip, enabling effective absorption of nicotine via the mucous membranes, thus by-passing the first-pass effect [1]. The pouch is discarded after use. TFNP are relatively new on the consumer market and their market share has increased worldwide in the

last few years. In our country, TFNP are regulated under the Commodities Act and not under the Tobacco Law, like tobacco-containing pouches. TFNP are marketed as a healthier and nuisance-free alternative to smoking. TFNP are sold in colourful packages and in various fruit and candy flavours and may be appealing to young non-smokers, possibly inducing nicotine dependence. We examined cases of TFNP exposure reported to our PIC.
Methods: Analysis of cases reported to our PIC. The data collected included the number, user characteristics and symptoms of poisonings.
Results: From April 2019 to August 2021 29 cases of TFNP poisoning were reported, 4 in 2019, 10 in 2020 and 15 up to August 2021. The median age was 15 years (IQR 25%-75%: 15-20), with 18 users (62%) aged 13-17 years. Seventeen (59%) were male, 12 (41%) female. Five patients (17%) reported no symptoms and one patient reported paresthesia probably unrelated to TFNP use. Twenty-three patients (79%) reported symptoms consistent with nicotine poisoning: nausea (52%), vomiting (48%), dizziness (45%), pale/sweaty skin (24%) and fainting (17%) (% relative to the total of 29 patients). Two patients were hospitalized and both recovered with supportive care. The first hospitalized patient was a 14-year-old female with transient nausea and hypertension after using a TFNP at school during a "challenge". The second was an adult male non-smoker, who developed confusion, muscle weakness, diaphoresis, hypothermia (34.3 °C), first-degree AV-block and bradycardia (40 bpm) after using a TFNP.
Conclusion: The number of TFNP poisonings is increasing since market introduction. Serious nicotine intoxication can occur with intended, buccal use. Symptomatic nicotine poisoning from TFNP often involves adolescents. This indicates that TFNP are commonly used by adolescents. TFNP are aimed at smoking cessation, but also carry the risk of introducing young non-smokers to nicotine use and addiction. More strict legislation for TFNP is currently being considered in our country.

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13. A 19-year review of enquiries regarding intoxication with poppers to the Austrian Poisons Information Centre (PIC) with two case reports

Kinga Bartecka-Mino, Susanna Dorner-Schulmeister and Tara Arif

Poisons Information Centre, Vienna, Austria

Objective: Poppers is the slang name for a drug containing various nitrites. It is used as an aphrodisiac in the party scene. We reviewed cases from our poison centre.
Methods: A retrospective evaluation of enquiries to the Poisons Information Centre (PIC) in Austria regarding mono-intoxications of poppers from 2002 to 2021. The extracted data included age, gender, history, and symptoms at the time of PIC consultation. We describe two cases in detail.
Results: Overall, 52 cases of mono-intoxications with poppers were extracted from the database. Except for 3 adolescents aged 16 to 17 years, patients were adults (n = 49) aged 19-75 years. Males were involved in 41 cases. Exposure to poppers was abusive in most cases (n = 29) and most poisonings involved ingestion (n = 25). No symptoms occurred in 8 cases. In 27 cases the symptoms were mild: mucosal irritation, nausea, vomiting, headache, skin irritation, sinus tachycardia, dizziness, drowsiness, somnolence. Moderate symptoms occurred in 13 patients: vomiting, dyspnoea, cyanosis, methaemoglobinaemia, coma with response to pain. Severe poisoning occurred in 4 patients: coma with no response to pain, methaemoglobinaemia, cyanosis, acidosis, hypotension, bradycardia. No fatalities were reported. We report on 2 cases of poppers intoxication, where other substances were also consumed. Case 1. A 57-year-old man was admitted to an emergency room after resuscitation which was necessary after ingestion of 24 mL of poppers. He also consumed cocaine, gamma-hydroxybutyric acid, lysergic acid diethylamide (LSD), tetrahydrocannabinol (THC) and alcohol. On admission he was comatose and cyanotic. Methaemoglobin was 70%. The PIC recommended an antidote (toluidine- or methylene blue). The patient received toluidine blue several hours later (it was not stored on site). The methaemoglobin level fell significantly, but a cranial computed tomography and an electroencephalography showed hypoxic brain damage. He died after 6 days. Case 2. A 25-year-old, alcoholized man ingested 25 mL of poppers and vomited immediately. He became comatose and cyanotic. The methaemoglobin was 60% and administration of an antidote was recommended by the PIC. Methylene blue was administered with delay because it had to be ordered from another hospital. The intubated patient was transferred to the intensive care unit but did not improve significantly, therefore we suggested a second dose of methylene blue. The methaemoglobinaemia declined rapidly and the patient was extubated the following day.
Conclusion: Taken orally, poppers can cause a life-threatening methaemoglobinaemia. Prompt administration of the antidote saves lives and should be readily available.

14. Designer benzodiazepine as self-medication for anxiety: central nervous system depression in a 17-year-old patient after liquid clonazolam use

Andrea Giampreti[a], Antonella Valli[b], Mariapina Gallo[a], Georgios Eleftheriou[a], Lorella Faraoni[a], Marco Cirronis[a], Lorenzo Plebani[a], Maria Gioia Contessa[a], Ilaria Giardini[b], Pietro Papa[b], Raffaella Butera[a] and Giuseppe Bacis[a]

[a]Bergamo Poison Control Center, ASST Papa Giovanni XXIII Hospital, Bergamo, Italy; [b]Toxicology Laboratory, Policlinico San Matteo IRCCS Foundation, Pavia, Italy

Objective: Clonazolam, a triazolo-analog of clonazepam, is reported to be highly potent (about 10 times more than diazepam), with higher risk than other designer benzodiazepines (BDZ). We report a case of toxicity following self-medication for anxiety.
Case report: A 17-year-old patient with a past history of dextromethorphan and alprazolam misuse for self-medication of anxiety, referred to our emergency department (ED) after oral use of clonazolam. He claimed that a few hours earlier, he had taken 6 drops (4 in the morning, 2 in the afternoon) of a self-made solution of clonazolam powder 250 mg (bought on the Darknet) and propylene glycol 250 mL (bought on Amazon). He found on the Internet that dilution with propylene glycol could better dilute clonazolam powder and increase oral bioavailability. At admission he was sedated with Glasgow Coma Score (GCS) 12 (E3,V4,M5), O_2 saturation 98% (room-air) and heart rate 78/min. He received only IV fluids. No flumazenil was needed and he was discharged

with normal GCS after 24 hours. Toxicological tests performed on ED arrival confirmed BDZ in urine (419 ng/mL); other substances in urine (cocaine/amphetamine/cannabinoids/opiates/methadone), blood ethanol and drugs (barbiturates/tricyclic-antidepressant/BDZ) were negative. Second level analysis confirmed blood clonazolam (liquid chromatography-mass spectrometry (LC-MS) with multiple reaction monitoring (MRM); quantitative measurement with high-pressure liquid chromatography with UV detector (HPLC-UV)) was 79 ng/mL. At ambulatory follow-up 3 days after discharge, he was in good clinical condition with normal vital parameters. He reported visual hallucinations and tunnel vision sensation on the first day after discharge, which spontaneously resolved the day after.

Conclusion: The safety-toxic profile of clonazolam, a newly identified psychoactive substance, is not well established. It has been regulated in Italy since August 2021 and our Poison Control Center provides alerts to the Italian National Early Warning System and European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) network. Clonazolam may produce sedation and amnesia at as little as 0.5 mg [1]. Our patient took an estimated dose of 0.6 mg and reached a blood concentration higher than a recently reported case [2]. Clonazolam and designer benzodiazepines should be suspected and closely monitored when young people, present with clinical signs of BDZ toxicity, and improperly self-medicate themselves for anxiety or sleep disorders [1,2].

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15. Novel psychoactive substance-related presentations to the emergency departments of the European Drug Emergencies Network Plus (Euro-DEN Plus) over the six-year period 2014–2019

Benjamin Crulli[a], Alison M. Dines[a], Georgina Blanco[a], Isabelle Giraudon[b], Florian Eyer[c], Matthias E. Liechti[d], Oscar Miro[e], Knut E. Hovda[f], Fridtjof Heyerdahl[g], Christopher Yates[h], David M. Wood[i] and Paul I. Dargan[i]

[a]Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners, London, United Kingdom; [b]European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal; [c]Klinikum rechts der Isar, School of Medicine of the Technical University Munich, Munich, Germany; [d]Division of Clinical Pharmacology and Toxicology, University Hospital Basel and University of Basel, Basel, Switzerland; [e]Emergency Department, Hospital Clínic, IDIBAPS; University of Barcelona, Barcelona, Spain; [f]The National CBRNe Centre of Medicine, Department of Acute Medicine, Medical Division, Oslo University Hospital, Oslo, Norway; [g]Department of Prehospital Medicine, Oslo University Hospital, Oslo, Norway; [h]Emergency Department, Hospital Son Espases, Palma de Mallorca, Spain; [i]Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners; Clinical Toxicology, Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom

Objective: Novel psychoactive substances (NPS) have been increasingly reported in the last 15-20 years [1]. We aimed to describe presentations to the emergency department (ED) with acute recreational drug toxicity involving NPS.

Methods: Data were extracted from the Euro-DEN Plus database [2] for all presentations (36 EDs in 24 European countries) with acute recreational drug toxicity between 2014 and 2019, inclusive. Patient demographics, agents involved, and clinical outcomes were described and the subgroup of presentations involving NPS were compared with the rest of the cohort. Categorical variables were summarized as frequency (percentage) and continuous variables as median (interquartile range).

Results: Out of 43,633 Euro-DEN Plus presentations, 3304 (7.6%) involved at least one NPS. The proportion of NPS presentations varied by centre, reaching up to 48.8% (in Gdansk). Four centres (Lugano, Monza, Pärnu, Sofia) reported no presentations involving NPS over the study period. For the 14 centres where data were available for all 6 years, NPS-related presentations peaked in 2015 (11.9%) and thereafter fell to a consistent 5.7–6.2% in 2017–2019. Amongst the same subset of centres: in 2014, 78.4% of NPS agents were cathinones while 3.4% were synthetic cannabinoids; in 2019, the proportions were 11.6% and 72.2%, respectively. Other agents (excluding ethanol) were co-used in 40.0% of presentations involving an NPS. NPS-related presentations involved younger patients (30 (23–37) versus 32 (25–40) years, $p < 0.001$) and more males (84.8% versus 75.8%, $p < 0.001$). Patients presenting to ED after using NPS were more likely to self-discharge (22.8% versus 15.1%), less likely to be admitted to critical care (3.63% versus 6.07%) and had a longer length of hospital stay (5.1 (2.7–18.7) hours) than those not involving an NPS (4.7 (2.5–9.2) hours, $p < 0.001$). There were 15 deaths in the presentations involving NPS (0.5% of all NPS presentations), 11 of these presented to ED in cardiac arrest.

Conclusion: This large multicentre series of NPS presentations to European EDs showed geographical variation and changes over time in the proportion of presentations to ED involving NPS, as well as the proportion of NPS subgroups. Triangulation with data from complementary sources will enable a greater understanding of the public health implications of NPS use in Europe.

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16. Unspecified opioids among opioid overdoses in Oslo, Norway

Zahra Zeineb Iqbal, Thanh Mai Thi Nguyen, Mette Brekke and Odd Martin Vallersnes

University of Oslo, Oslo, Norway

Objective: In Oslo, Norway, from 2017, an increasing number of opioid overdoses have been categorized as involving unspecified opioids [1], as noted in the patient records by the doctor treating the patient. In this study, we will compare the characteristics of the overdoses involving unspecified opioids to overdoses involving heroin and long-acting opioids.

Methods: Data on patients presenting with opioid overdose was retrospectively collected from 1 October 2013 to 31 December 2019 at the Oslo Accident and Emergency Outpatient Clinic, using the Euro-DEN Plus data registration tool. We included all cases of overdose related to the recreational use of opioids. Overdoses involving other drugs or ethanol were excluded. The remaining cases were categorized as involving unspecified opioids only, heroin only, and any long-acting opioid (buprenorphine and/or methadone, including combinations with other opioids except unspecified opioids). Any opioids or combinations thereof not categorizable into these groups were excluded. The three groups were compared on observation time, Glasgow Coma Scale (GCS), vital signs, naloxone administration, and transfer to hospital.
Results: There were 5236 cases of opioid overdose. We excluded the 2808 cases involving other drugs or ethanol, yielding 2428 cases involving only opioids. Another 47 cases were excluded as non-categorizable. Of the remaining 2381 cases, 459 (19.3%) involved unspecified opioids, 1788 (75.1%) heroin, and 134 (5.6%) long-acting opioids. Cases involving unspecified opioids had longer observation time, median 5:29 hours versus 4:54 hours (long-acting opioids) and 4:49 hours (heroin) ($p < 0.001$), and lower GCS, median 10 versus 13 in both other groups ($p < 0.001$). In overdoses involving unspecified opioids 23.3% received naloxone compared to 12.7% of cases with long-acting opioids and 30.2% of cases with heroin ($p < 0.001$). Cases involving unspecified opioids were similar to long-acting opioids, but different from heroin, concerning proportions with bradypnea, 17.4% and 19.4% versus 28.2% ($p < 0.001$), and transfer to hospital, 16.3% and 18.7% versus 10.1% ($p < 0.001$), respectively.
Conclusion: Cases involving unspecified opioids differed from cases involving heroin and cases involving long-acting opioids, though there were more similarities with long-acting opioids than heroin. Unspecified opioids are probably a heterogeneous group, but it seems likely that heroin is not a major constituent. Hence, the increasing proportion of unspecified opioid overdoses probably represent a shift from heroin to other opioids among opioid users in Oslo.

Reference

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17. Poisonings with new psychoactive substances reported to the Dutch Poisons Information Center from 2017-2021

Laura Hondebrink, Johanna J. Nugteren-van Lonkhuyzen, Irma S. van den Hengel-Koot, Dylan W. de Lange and Antoinette J.H.P. van Riel

Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands

Objective: The number of new psychoactive substances (NPS) reported for the first time to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has stabilized at roughly 100 annual notifications. These first reports often concern NPS seizures by law enforcement agencies, but data on NPS poisoning are scarce. Therefore, we studied the number, rate, and classes of NPS poisonings reported to our National Poisons Information Center (NPIC).
Methods: We performed a retrospective observational study on NPS poisonings for which the NPIC was consulted between 2017 and July 2021 (4.5 years). The NPS poisoning rate was calculated relative to all recreational drug poisonings reported to the NPIC. The proportion of specific classes of NPS and specific NPS were also studied.
Results: Overall 475 NPS poisonings was reported. The number increased from 128 to 205 poisonings between 2017 and 2020. In the first half of 2021, 212 poisonings were reported. The NPS poisoning rate increased from 0.11 in 2017 to 0.26 in 2021. The three most prevalent classes of NPS in 2017 were phenethylamines (58%), cathinones (19%), and designer benzodiazepines (13%). In 2021, the most prevalent classes were cathinones (44%), designer benzodiazepines (33%) and phenethylamines (15%). Poisonings with NPS from the following classes were around or below 5% in all years: tryptamines, arylcyclohexylamines, cannabinoids and opioids. Poisonings with 4-fluoroamphetamine (4-FA) peaked in 2017, comprising around half of all phenethylamine poisonings. Following severe poisonings with extensive media coverage, 4-FA became illegal in 2017 and poisonings declined. Poisonings with 4-bromo-2,5-dimethoxyphenethylamine (2C-B) were present throughout 2017-2021, although an increase was observed in 2020 and 2021 (approximately half of the phenethylamine poisonings). Within cathinone poisonings, 4-methylmethcathinone (4-MMC) was most prevalent earlier, but from 2019-2021 around 60-80% of the cathinone poisonings were due to 3-methylmethcathinone (3-MMC). Within the group of poisonings with designer benzodiazepines, most were due to etizolam (33%), clonazolam (23%) and flunitrazolam (13%). Poisonings with other designer benzodiazepines were diverse and reported only occasionally.
Conclusion: The number and rate of NPS poisonings reported to the NPIC, has strongly increased over time. The predominant classes of NPS vary over time, as do predominant specific NPS within the classes. The strongest increase in poisoning rate was observed in the last three years.

18. Intoxication after the consumption of MDMB-4en-PINACA: results from a prospective study

Michaela Sommer[a], Volker Auwärter[a], Florian Eyer[b] and Maren Hermanns-Clausen[c]

[a]Forensic Toxicology, Institute of Forensic Medicine, Medical Center - University of Freiburg, Freiburg, Germany; [b]Department of Clinical Toxicology, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; [c]Poisons Information Center, Department of General Pediatrics, Adolescent Medicine and Neonatology, Center for Pediatrics, Medical Center - University of Freiburg, Freiburg, Germany

Objective: The synthetic cannabinoid receptor agonist (SCRA) methyl-3,3-dimethyl-2-(1-(pent-4-en-1-yl)-1H-indazole-3-carboxamido)butanoate (MDMB-4en-PINACA) was notified as a new psychoactive substance (NPS) by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in August 2018. It belongs to the most recent generation of a new class of SCRAs and carries an unsaturated side-chain, and is similar in structure to JWH-022. Major severe and lethal poisonings have been reported after consumption of MDMB-4en-PINACA [1].
Methods: Prospective observational study of patients treated in hospitals after intake of NPS. Clinical and analytical data were combined and reported to a Poison Centre. Serum and/or urine samples were collected from enrolled patients and

comprehensive drug analyses were performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Only patients with analytically confirmed intake of MDMB-4en-PINACA were included.
Results: MDMB-4en-PINACA was identified in serum samples of five male patients (17-33 years). All patients were included in the second half of 2020. In 2 cases, more than one SCRA was present in the serum sample (4F-MDMB-BICA (n = 2), 5F-MDMB-PICA (n = 1)). Other psychoactive substances (amphetamines and tetrahydrocannabinol (THC)) were identified in one patient in a urine sample. Based on the Poison Severity Score, severity of poisoning was moderate (n = 4) or severe (n = 1). Reported neuropsychiatric symptoms were classified as moderate (CNS depression (n = 3), disorientation (n = 2), generalized seizures (n = 1), combativeness (n = 2), agitation (n = 2)) or major (extreme agitation (n = 1)). One patient vomited extensively, and was intubated. Another patient reported generalized muscle pain and displayed rhabdomyolysis (peak creatine kinase 7,811 U/L).
Conclusion: In this case series, the consumption of MDMB-4en-PINACA was associated with moderate to major poisoning, similar to reports from the EMCDDA [1]. This is in concordance with experimental findings on the potency of this new SCRA which showed extraordinarily high efficacies in three different CB1 activation assays when compared to structurally similar compounds [2]. Against this background, a recently published report about adulteration of cannabis with MDMB-4en-PINACA [3] raises concerns.

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19. Tapentadol: the new opioid overtaking oxycodone usage in hospital

Jennifer Mirabella[a], Deepa Ravi[b], Angela L. Chiew[b] and Betty S. Chan[b]

[a]University of New South Wales, Kensington, Australia; [b]Prince of Wales Hospital, Randwick, Australia

Objective: In Australia, tapentadol sustained-release (SR) is authorised for moderate to severe chronic pain relief. Tapentadol immediate-release (IR) is recommended for moderate to severe pain relief. Data on hospital prescription of tapentadol is rare. We investigate annual hospital prescribing trends of tapentadol, oxycodone and tramadol, and the pattern and indications of tapentadol prescription in Sydney, Australia.
Methods: This was a retrospective observational study that investigated 5-year (August 2016 to July 2021) prescribing trends of tapentadol, oxycodone and tramadol from 4 hospitals in the South Eastern Sydney Local Health District (SESLHD) of New South Wales, Australia. Drug doses were expressed as oral morphine equivalents (OME). The pattern of prescription in the specialty units at Prince of Wales Hospital (POWH) was reviewed. There was also a chart review of patients prescribed tapentadol in 3 specialty wards at POWH.
Results: Over 5 years in the SESLHD, **t**here was a 19% reduction in the total prescription of tapentadol, oxycodone and tramadol from 1,219,190 in 2016-17 to 986,478 OME milligrams in 2020-21. During this time, tapentadol IR and SR had a 223% and 18% increase in hospital prescription, respectively. In contrast, there was a decrease in oxycodone (38% IR, 65% SR) and tramadol (75% IR, 70% SR) prescription. By 2020-21, tapentadol overtook oxycodone to become the most prescribed opioid in the SESLHD at 51% (oxycodone 42% and tramadol 7%). Over 5 years at POWH, the surgical unit was responsible for 55% and 41% of tapentadol IR and SR prescriptions, respectively. The neurology ward accounted for 13% and 12% of tapentadol IR and SR prescription, respectively, while spinal rehabilitation was responsible for 5% and 11% of tapentadol IR and SR prescription. During this time, there was a 3-fold and 2-fold increase in tapentadol IR and SR prescription respectively at POWH's surgical unit.
Conclusion: In a local health district in Sydney Australia, hospital prescription of tapentadol increased significantly to overtake oxycodone as the most prescribed opioid. There was also an increasing use of tapentadol IR and SR for acute post-operative pain.

20. Tapentadol exposures and poisonings in Australia

Jennifer Mirabella[a], Katherine Allen[b], Geoffrey K. Isbister[c], Ingrid Berling[c], Katherine Z. Isoardi[b], Angela L. Chiew[d] and Betty S. Chan[d]

[a]University of New South Wales, Sydney, Australia; [b]Princess Alexandra Hospital, Brisbane, Australia; [c]Calvary Mater Hospital, Newcastle, Australia; [d]Prince of Wales Hospital, Sydney, Australia

Objective: Tapentadol, an atypical opioid with mu-receptor affinity and noradrenaline reuptake inhibition was approved for use in Australia in 2011. Due to its pharmacokinetic properties, it has a more predictable analgesic effect than oxycodone and has less gastrointestinal side effects. Data on tapentadol poisoning, however, is scarce. We investigate tapentadol poisoning exposures and related deaths reported to a Poisons Information Centre, three local toxicology units and the National Coronial Information System (NCIS) in Australia.
Methods: We performed a retrospective review of tapentadol exposure calls to New South Wales Poisons Information Centre (NSWPIC). In addition, we performed a retrospective review of tapentadol exposures and poisoning to Princess Alexandra Hospital, Calvary Mater and Prince of Wales Hospital in Australia. We searched the NCIS database to determine the number of tapentadol related deaths.
Results: Between 2016-2020, there were 220 tapentadol calls made to NSWPIC. There was a 4.5-fold increase in tapentadol exposure calls during this time, from 17 in 2016 to 76 calls in 2020. Of these, 154 (78%) were related to deliberate self-poisoning. From January 2016-October 2021, there were 104 patients who presented to the 3 toxicology units with tapentadol poisoning. The median age was 46 years (IQR: 32-58) with 56% female. Of these, 78 (75%) ingested tapentadol with deliberate self-harm, 9 accidentally (9%) and 7 for recreational use (7%). The median dose ingested was 700 mg (IQR 300-1550 mg) with 52% taking sustained-release formulations. Polypharmacy ingestions (n = 87, 84%) were the predominant clinical picture with 34% co-ingesting additional opioids and 40% benzodiazepines concurrently. Ten patients (10%) required intubation, 40 (38%) required naloxone bolus doses and 8 (8%) a naloxone infusion. The median

length of stay was 20h (IQR: 10-42h). There were no deaths in this cohort. From January 2015 to October 2021, there was an increasing trend with 35 deaths related to tapentadol. The median age was 51 years (IQR: 42-61) and 54% were female. Of these, 6 were classified as intentional with primarily tapentadol poisoning, 19 unintentional deaths, and the remaining cases had indeterminate intention. Most cases, however, had mixed drug exposures including opioids and benzodiazepines. During this time, there were 330 related oxycodone deaths.
Conclusion: There are increasing tapentadol exposures and deaths reported to the NSWPIC and NCIS in Australia. Most tapentadol poisonings were mixed with other opioids and/or benzodiazepines.

21. Hiding from the drug screen: a case of extensive nitrous oxide misuse

Avery Michienzi, Lauren Smaltz and Christopher Holstege

Department of Emergency Medicine, University of Virginia, Charlottesville, United States

Objective: To describe a case of extensive nitrous oxide (NO) misuse in a commercial airline pilot to specifically avoid detection on employer urine drug screens (UDS).
Case report: A 48-year-old male commercial airline pilot was evaluated in a Medical Toxicology clinic for history of NO misuse. He started using NO and cannabis as a teenager. When he became an airline pilot, he stopped his cannabis use to ensure he passed frequent employer drug screens. He researched that NO was not detected on UDS and continued its use. During the COVID-19 pandemic, the patient's use grew to 1,200 eight gram NO canisters daily in an attempt to alleviate his stress. He described inhaling the gas until he passed-out. Upon waking, he, would use more until he again passed-out, repetitively cycling throughout the night. His developed paresthesias, progressive weakness in legs, and difficulty walking to the point where he had to crawl to the front door to receive his shipments of NO canisters. His cognition declined and he was brought to the hospital for help after being found in his home garage. Magnetic resonance imaging (MRI) imaging of the brain showed atrophy from chronic toxic metabolic encephalopathy. MRI of the spine did not show abnormalities. Upon referral to the Medical Toxicology clinic, he had not used NO for 3 months and had been taking vitamin B172. Symptoms had improved, but he still had extremity paresthesias, memory difficulties, and required a cane to walk. The patient's NO misuse had been reported to the Federal Aviation Administration (FAA) during his hospitalization and he was no longer allowed to pilot commercial airlines.
Conclusion: Random drug testing of airline pilots is required by the FAA and the UDS test for Δ-9-tetrahydrocannabinol-9-carboxylic acid, benzoylecgonine, codeine, morphine, hydrocodone, hydromorphone, oxycodone, oxymorphone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, methylenedioxymethamphetamine and methylenedioxyamphetamine [1]. Negative drug screens may give an employer a false sense of security that a pilot is not using/misusing substances but the UDS does not pick up numerous abused substances, including inhalants. This case illustrates the dangers in relying solely on the UDS to ensure pilots are clear from illicit substances. This patient was misusing nitrous oxide for decades which lead to permanent cognitive decline that negatively impacted his ability to safely fly.

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22. Severe methemoglobinemia after popper abuse in a child

Patrizia Argiolas[a], Andrea Giampreti[b], Georgios Eleftheriou[b], Mariapina Gallo[b], Marco Cirronis[b], Lorella Faraoni[b], Maria Gioia Contessa[b], Raffaella Butera[b], Giuseppe Bacis[b] and Roberto Cosentini[a]

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

Objective: Poppers are volatile nitrites that are inhaled for recreational purposes in relation to their vasodilatory, muscle-relaxant, and euphoria-inducing properties. Direct hemoglobin-oxidizing effects may induce extreme life-threatening methemoglobinemia up to 90% [1,2]. However severe methemoglobinemia due to poppers inhalation among pediatric patients is rarely reported.
Case report: A 13-year-old male, 50 Kg, arrived to the Emergency Department with headache, labial and peripheral cyanosis. Past medical history was irrelevant except for mild pollen allergy. He denied taking nitrite-based-foods, drugs or medications. He was alert, oriented and anxious, with blood pressure 110/60 mmHg, and heart rate 70 bpm. He had mild tachypnea (20/min) without signs of respiratory distress. His oxygen saturation was 83% on room-air, with no changes in the values despite delivering oxygen therapy with low-flow (nasal-cannulae 6 L/min) and high-flow systems (Venturi-Mask 40%). The color of the blood drawn from the radial artery was chocolate-brown. The arterial blood gases showed: pH 7.57, pO_2 106.9 mmHg, pCO_2 26.6 mmHg, bicarbonate 24.2 mmol/L, hemoglobin 13.3 g/dL, oxygen saturation 96.5%, lactate 2.57 mmol/L, and methemoglobin 48.5%. Urgent toxicological consult was requested and diluted methylene blue at 1 mg/kg intravenously over 10 minutes was administered. Approximately 30 minutes later, methemoglobin dropped to 29.8%; and after 50 minutes was 16.3%. Oxygen saturation values gradually increased and the cyanosis slowly disappeared. Blood tests showed a mild increase in amylase and lipase; urine drugs tests were negative. Glucose-6-phosphate dehydrogenase (G6PD) and methemoglobin-reductase were measured and no deficit were found. The electrocardiogram and chest X-ray were normal. The patient was transferred in the Pediatric Ward for monitoring. In the following days, he admitted that the evening before coming to the Emergency Ward he had inhaled poppers (amyl nitrite/isobutyl-nitrite). The patient's friends had also taken poppers and he reported that they developed mild symptoms such as bronchospasm and periorbital edema.
Conclusion: Methemoglobinemia in pediatric patients may be difficult to diagnose due to different etiological patterns (congenital, dietary, drug-related, abuse). In our case a methemoglobinemia up to 48% resolved promptly after methylene blue. The multidisciplinary approach with specific evaluation of the patient history resulted in the correct diagnosis and treatment.

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23. The Fentanyl Ratio

Erik Lindeman and Aza Kader

Swedish Poisons Information Centre, Stockholm, Sweden

Objective: During 2014-2017 fentanyl and various fentanyl analogues were sold as "legal highs" over the Internet in Sweden. This small market, with an estimated number of customers of 2000-3000 people led to the death of 299, making fentanyls overtake heroin as the leading cause of drug-related deaths in Sweden [1]. The epidemic led to a major law enforcement effort, culminating in 2018 with the imprisonment of major suppliers on charges of manslaughter, ending further sales. The NPS-fentanyls were almost exclusively sold in the form of nasal sprays, and street drugs cut with fentanyls have not been seized in Sweden [1]. Here we compare the number of Poison Centre (PC) fentanyl calls during and after the epidemic to the (non-overlapping) cohort of forensically confirmed fentanyl deaths.
Methods: Hospital calls registered as suspected fentanyl-class drug poisoning during 2014-2020 were retrieved from the PC-data base. Case details were reviewed to determine whether NPS-fentanyl (mainly nasal sprays) or medicinal fentanyl (mainly patches) abuse was involved. The data on forensically confirmed fentanyl deaths was available from public records [1,2].
Results: See Table 1.
Conclusion: The devastatingly deadly effect of the fentanyl epidemic after the emergence of the nasal spray markets in 2014, followed by the virtual cessation of deaths after 2017 demonstrate the large impact that successful supply side interventions can have for the fentanyl drug class. Our results show that PC-cases closely paralleled forensic cases during and after the epidemic, with a PC/forensic case-ratio close to 1. An uptick in suspected PC fentanyl cases could thus constitute an important early warning of a deadly drug trend in society.

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24. Inhalational hydrocarbon poisoning in Australia 2010-2020

Ingrid Berling, Jared Brown and Angela L. Chiew

NSW Poisons Information Centre, Sydney Children's Hospitals Network, Sydney, Australia

Objective: Inhalational abuse of volatile substances has been a significant public health concern due to the risk of sudden death and associated chronic complications such as encephalopathy. Survey data of Australians aged 14 years and older shows the use of inhalants within the last twelve months has been slowing increasing from 0.4% in 2001 to 1.4% in 2019 [1]. Concerningly, use often begins in children around 12-13 years of age or younger. Data from a 2014 Australian secondary schools drug survey reported 16% of all students have deliberately sniffed inhalants at least once, and 6% reported use within the previous month [2]. We investigate hydrocarbon inhalational exposures or poisonings and related unintentional deaths reported to New South Wales Poisons Information Centre (NSWPIC) and the National Coronial Information System (NCIS) in Australia.
Methods: We performed a retrospective review of all hydrocarbon inhalational exposure calls to the NSWPIC between 1 January 2010 and 31 December 2020 (11 years). A search was made of the NCIS database in all states and territories over the same period using the activity code for chroming, petrol or solvent sniffing to determine the number of unintentional inhalational hydrocarbon related deaths in Australia.
Results: Between January 2010 and December 2020 there were 752 primary calls made to the NSWPIC regarding hydrocarbon use or exposure. Age, or age bracket, were recorded in 748 cases, with 508 (67%) calls involving children or adolescents. The number of calls per year was relatively consistent until 2019, when an increasing trend is noted. Over the same period, there were 45 unintentional deaths involving the use of inhalational hydrocarbons, averaging 4 deaths a year. The median age at death was 23 years (IQR: 14-30 years) and 69% (31 cases) were male. Cause of death was predominately due to acute suffocation/asphyxia, encephalopathy related to chronic use, cardiac arrest likely from sudden sniffing syndrome or thermal injuries secondary to unintentional fires sparked by the volatile agents.
Conclusion: Recreational abuse of inhalational hydrocarbons remains a problem, particularly within the adolescent population. Fortunately, death remains an uncommon outcome, although importantly a preventable death in an adolescent or young adult.

Table 1. Forensic data: Analytically confirmed fentanyl or analogues (novel psychoactive substance (NPS)-fentanyls) deemed to have significantly contributed to the cause of death. Heroin deaths are included as a reference point. The identity of fentanyl analogues varied over the years, with fentanyl (2014), acetylfentanyl (2015), acrylfentanyl (2016) and cyclopropulfentanyl (2017-18) consecutively dominant [1,2].

	2014	2015	2016	2017	2018	2019	2020
Forensic data							
NPS-fentanyls	30	64	104	101	11	2	0
Medicinal fentanyl (abuse)	32	28	33	29	28	26	16
Heroin	97	93	88	107	90	102	95
Poison centre data							
NPS-fentanyls	6	36	86	75	7	6	6
Medicinal fentanyl (abuse)	28	27	28	30	20	23	20
The Fentanyl Ratio: forensic data/PC data							
NPS-fentanyls	5	1.8	1.2	1.4	1.6	0.33	–
Medicinal fentanyl (abuse)	1.1	1	1.2	0.9	1.4	1.1	0.8

References

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25. A case of flubromazolam overdose

Betty S. Chan and Angela L. Chiew

Prince of Wales Hospital, Sydney, Australia

Objective: Flubromazolam is a long-acting designer benzodiazepine that has been available on the Internet since 2012. It has a long half-life of approximately 10-20 hours and its metabolites can be found in urine for up to 8 days post-ingestion [1]. We present a case of a patient who had alternating drowsiness and agitation following the ingestion of flubromazolam purchased from the Internet.

Case report: A 46-year-old male arrived by ambulance with an altered level of consciousness and a history of a fall with head injury 3.5 hours earlier. His wife volunteered that he had taken an unknown amount of flubromazolam. He had a history of chronic lower back pain and was known to abuse benzodiazepines. His initial Glasgow Coma Score (GCS) was 7 (E1V2M4), heart rate 118 bpm, blood pressure 130/70 mmHg, respiratory rate 24/min, temperature 37.5 °C with small sluggish pupils (2 mm). An initial brain computerised tomography (CT) scan was normal. He became agitated with periods of somnolence and intermittent airway obstruction. Venous access was difficult and so an intraosseous infusion was established. He was intubated for airway protection and required metaraminol infusion in the Intensive Care Unit (ICU). He was treated for aspiration pneumonia and mild acute kidney injury. He was extubated 7 hours later, however continued to have alternating period of somnolence and agitation. By day 3 post-admission, he was transferred to the ward and required 1:1 nursing due to agitation. Oral medications could not be administered due to a poor gag reflex. He was managed with a total of 35 mg sublingual olanzapine over 24 hours. On day 5 he developed severe acute behaviour disturbance and was given diazepam 10 mg per rectum (for suspected benzodiazepine withdrawal), intramuscular droperidol 10 mg and midazolam 10 mg. He was then transferred to ICU for observation. No further sedation was given for 6 hours. However, his GCS dropped to 6 and he was re-intubated 116 hours post admission to hospital. He was managed with a dexmedetomidine infusion and regular diazepam per rectum and was extubated the next day. He was discharged on day 7 with a reducing dose of diazepam. The flubromazolam concentration 1 hour after admission was 880 μg/L.

Conclusion: This case highlights that flubromazolam can cause prolonged coma alternating with agitation. This patient potentially also developed delayed withdrawal symptoms.

Reference

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26. Age- and sex-related differences in clinical presentations due to acute cannabis toxicity at European Emergency Departments

Yasmin Schmid[a], Miguel Galicia[b], Severin B. Vogt[a], Matthias E. Liechti[a], Guillermo Burillo-Putze[c], Paul I. Dargan[d], Alison M. Dines[e], Isabelle Giraudon[f], Fridtjof Heyerdahl[g], Knut Erik Hovda[h], David M. Wood[d], Christopher Yates[i] and Òscar Miró[b]

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

Objective: Cannabis is one of the most commonly used psychoactive substances and frequently involved in emergency department (ED) presentations due to acute drug toxicity in Europe [1]. Patterns in cannabis use vary according to age and sex [2], but it is not known whether age and sex also affect clinical presentations associated with the use of cannabis. Hence, we aimed to evaluate age- and sex-related differences of presentations at European EDs due to acute cannabis toxicity.

Methods: A retrospective analysis of patients presenting to EuroDEN Plus centres with acute cannabis toxicity from January 2014 to December 2019 was undertaken. Presentations related to cannabis use combined with other substances (except for alcohol) were excluded. Twelve pre-specified clinical features were analyzed according to age groups (<20, 20-29, 30-39, 40-49, and ≥50 years) and sex (female and male) using logistic and linear regression models including adjustments for alcohol co-ingestion.

Results: Overall, 43,633 ED presentations due to acute drug toxicity were recorded. Of the 9,044 (21%) involving the use of cannabis, 4,268 patients (10%) fulfilled the inclusion criteria (median age 26 years, 70% male, 52% co-ingested alcohol). The most common clinical features due to acute cannabis toxicity included anxiety (28%), vomiting (24%), and agitation (23%). Compared to other age groups, patients aged <20 years more often presented with reduced consciousness (OR =2.3, 95%CI =1.89-2.88), vomiting (OR =1.8, 95%CI =1.50-2.09), and headache (OR =2.0, 95%CI =1.53-2.64). Psychotic symptoms were more likely in patients aged 20-29 years (OR =1.4, 95%CI =1.23-1.78). With increasing age, reduced consciousness, vomiting, headache, palpitations, and anxiety were significantly less often observed (- 2.5%, -4.4%, -1.2%, -1.0%, and -2.0% of change for each additional ten years, respectively). Males more often presented with hypertension (OR =2.3, 95%CI =1.40-3.82), psychosis (OR =2.0, 95%CI =1.43-2.65), chest pain (OR =1.8, 95%CI =1.39-2.43), and seizures (OR =1.8, 95%=1.07-3. 06), but less frequently with vomiting (OR =0.8, 95%CI =0.68-0.93) and anxiety (OR =0.7, 95%CI =0.56-0.77) than females.

Conclusion: Acute cannabis toxicity is common but mostly of minor severity, yet clinical presentations differ with regard to age and sex. This could be relevant for the development of tailored prevention campaigns and treatment in specific sex and/or age groups.

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27. A "madd"-ening confounding: fruit seeds mimicking enteral drug concealment by computed tomography

Brian G. Wiener[a], Rebecca L. Burton[b], Silas W. Smith[a], Mark Su[a], Rana Biary[a] and Ee Tein Tay[b]

[a]Division of Medical Toxicology, Ronald O. Perelman Department of Emergency Medicine, NYU Grossman School of Medicine, New York, United States; [b]Division of Pediatric Emergency Medicine, Ronald O. Perelman Department of Emergency Medicine, NYU Grossman School of Medicine, New York, United States

Objective: To highlight the similarity between madd fruit seeds and enteral drug concealment ("body packing") on computed tomography (CT) when evaluated by Hounsfield Units (HU).
Case report: A 13-year-old girl without significant past medical history recently arrived in the US from Senegal and presented to the Emergency Department (ED) complaining of severe abdominal pain for 24 hours, one episode of non-bloody and nonbilious emesis, anorexia, and no bowel movements for 2 days. Vital signs were: blood pressure 122/70 mmHg; heart rate 72/minute; respiratory rate 18/minute; temperature 36.3°**C**; oxygen saturation 100% (room air). The abdominal examination was significant for right lower quadrant and suprapubic tenderness with rebound. An oral and intravenous-contrast enhanced CT scan of the abdomen and pelvis revealed smooth, well-circumscribed, multiple intraluminal foreign bodies measuring up to 2 cm with HU measuring up to 200. An urgent radiologist call to the ED reported that these were suspicious for "body packer packets" of either opioids or cocaine, based on their appearance and 200 HU characteristics [1,2]. Medical toxicology was consulted. Initial recommendations based on clinical findings and the initial radiological impression included whole bowel irrigation, surgical consultation, 1:1 observation, and child protective services referral. These recommendations were precluded by a detailed dietary history, which revealed ingestion of madd fruit (*Saba senegalensis*) and seeds against parental recommendations. This fruit is native to West Africa and ingestion of the seeds has been reported to cause abdominal pain [3]. Adherent seeds can progress to bezoar formation and intestinal obstruction [3]. The patient was admitted and had an uneventful hospital course. Two days later, a bowel movement produced the undigested madd fruit seeds.
Conclusion: madd fruit seeds may appear similar to body packer packets on CT and have similar HU characteristics. History and clinical context are paramount to avoid misdiagnosis and bias.

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28. An unusual presentation of amphetamine-induced posterior reversible encephalopathy syndrome (PRES)

Balveena K. Dhaliwal and Satish Mitter

Western Sydney Toxicology Services, Sydney, Australia

Objective: Amphetamine-induced posterior reversible encephalopathy syndrome (PRES) is rarely described. Early recognition and treatment are essential to prevent permanent neurological sequelae [1]. We report a case in a young adult.
Case report: A 23-year-old male with no-comorbidities was brought into the emergency department from a correctional facility after a first episode of witnessed, self-terminating generalized tonic/clonic seizure. He had intravenously injected an unknown quantity of methamphetamine and buprenorphine 2 hours prior. On initial assessment, he was hypertensive with a blood pressure 157/67 mmHg, heart rate 60 bpm, respiratory rate 20/minute, oxygen saturation 99% (room air). He had a severe occipital headache, nausea and intermittent bilateral visual loss. Neurological examination of the cranial nerves, upper and lower limbs, visual and cerebellar examination did not reveal any abnormality. He was persistently hypertensive with a blood pressure of up to 180/96 mmHg. He did not have a history of previous seizures or hypertension. A brain computerised tomography (CT) scan with angiogram was suggestive of reversible cerebral vasoconstriction syndrome (RCVS). A nimodipine infusion was commenced with resolution of headaches and hypertension within 36 hours. Brain magnetic resonance imaging (MRI) performed 48 hours later was consistent with PRES, with edema of bilateral parietal and occipital lobes. The patient was discharged clinically well 4 days later. It was strongly advised that he avoid all sympathomimetic agents due to risk of recurrence of PRES.
Conclusion: Poisoned patients may have a lower threshold for developing PRES due to the drug effect on endothelial dysfunction, sympathetic system and hypothalamic-pituitary-adrenal axis [2]. Untreated PRES can cause permanent neurologic deficits due to cerebral ischemia, haemorrhage, and herniation [3]. The neuroimaging study of choice is MRI due to its high sensitivity [1]. It is possible that there is a higher prevalence of PRES associated with drug use than currently documented. Early recognition and meticulous treatment are important to prevent permanent neurological sequelae and to advise the patient of risk of recurrence.

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29. High mortality (13%) in a five-year follow-up after acute gamma-hydroxybutyrate (GHB) poisoning in Gothenburg, Sweden

Kai Knudsen and Mirella Wictoran

Sahlgrenska University Hospital, Gothenburg, Sweden

Objective: Acute overdose with gamma-hydroxybutyrate (GHB) may reflect a propensity for abuse, self-destructive behavior with repeated poisoning and risk of developing severe addiction [1]. The short-term prognosis is good, while the long-term prognosis has not previously been thoroughly examined. We have studied the development of psychiatric comorbidity and mortality after GHB overdose in a five-year follow-up.

Methods: All cases of acute poisoning with GHB admitted during 2010-2015 were recorded in a retrospective observational cohort study. Data was collected from our hospital's electronical medical records. Main outcome measures were sex, age, psychiatric comorbidity, concomitant mood disorder or addiction disorder, mortality, and repetition of poisoning.

Results: A total of 841 patients were treated for acute poisoning with GHB during 2010-2015 in our hospital. In total 376 patients (45%) presented more than once with 2-19 presentations. We recorded 703 (84%) patients with psychiatric comorbidity. A total of 124 (15%) patients were registered with a concomitant mood disorder and 690 (82%) with an addiction disorder. One-hundred and twelve (13%) patients died within five years of follow-up, of which 29 (26%) died within the first year. Patients with a registered psychiatric or mood disorder had a significantly higher risk of death ($p < 0.05$) during follow-up.

Conclusion: Intoxication with GHB is an alarming medical condition in patients with increased risk of repeated poisonings and development of psychiatric comorbidity in the nearby time. These patients have a short-term mortality far beyond the normal population. Follow-up with medical and psychosocial interventions should be made at the same level as in other psychiatric conditions with highly increased risk of death.

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30. Seven year trends in benzodiazepines detected in patients attending emergency departments in the UK after drug misuse

Simon H.L. Thomas[a], Dan Vidler[b], Jane Officer[c], Michael Eddleston[d], Paul I. Dargan[e], Jamie Cooper[f], Simon Hudson[g], Janos Baombe[h], James T. Harnett[i], Mark Pucci[j], Nigel Langford[k], Jonathan Leung[l], George Bailey[m] and Alberto Oteo[n]

[a]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom; [b]Newcastle University, Newcastle, United Kingdom; [c]Scottish Police Authority Forensic Laboratory, Edinburgh, United Kingdom; [d]Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; [e]Guys & St Thomas' NHS Foundation Trust, London, United Kingdom; [f]Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [g]LGC Ltd, Fordham, United Kingdom; [h]Manchester University NHS Foundation Trust, Manchester, United Kingdom; [i]University College London Hospitals NHS Foundation Trust, London, United Kingdom; [j]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [k]University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; [l]East Kent Hospitals University NHS Foundation Trust, Ashford, United Kingdom; [m]Imperial College Healthcare NHS Trust, London, United Kingdom; [n]Health Improvement & Disparities, Department of Health and Social Care, London, United Kingdom

Objective: Benzodiazepines are commonly involved in non-medical drug use and their presence may enhance toxicity associated with other substances, including opioids. In recent years new psychoactive substance (NPS) benzodiazepines have become available and may be supplied by dealers or purchased via the Internet, and are also found in counterfeit medicines. Here we report trends in benzodiazepines detected in the UK Identification Of Novel psychoActive substances (IONA) study for the period March 2015 to October 2021.

Methods: Adults (≥16 years) presenting to participating hospitals with toxicity after suspected drug misuse have been included in the IONA study after informed consent (or agreement of a relative/representative if lacking capacity) since March 2015. Demographic and clinical features are recorded and blood and/or urine samples analysed using high-resolution accurate mass liquid chromatography–mass spectrometry. Inclusion criteria initially required severe toxicity (except in Scotland and according to defined criteria) and suspected NPS exposure, but exposure to non-medicinal opioids was added in 2017. Since January 2020 those using any drug can be included and severe toxicity is no longer required.

Results: By October 2021 analytical data were available for 1199 IONA participants. At least one benzodiazepine was identified in samples from 592 (49.4%) of these. There have been recent increases in the proportion of participants where benzodiazepines were identified. For individual benzodiazepines, increases were observed for diazepam (including potential metabolites such as temazepam and oxazepam), clonazepam, and for the NPS benzodiazepines etizolam, flubromazolam, flualprazolam, bromazolam and clonazolam (Table 1).

Conclusion: Benzodiazepines, including NPS benzodiazepines, have been increasingly involved in episodes of toxicity associated with non-medical drug use requiring emergency department presentation in the UK. Widening inclusion criteria may have affected the patterns of substances encountered, especially traditional drugs of misuse, but are unlikely to account for the increasing detections of NPS benzodiazepines.

Table 1. Selected benzodiazepines (including metabolites) detected in at least one patient sample, showing annual patient numbers (and percentage).

	2015	2016	2017	2018	2019	2020	2021
Total patients	56 (100%)	179 (100%)	225 (100%)	170 (100%)	219 (100%)	193 (100%)	157 (100%)
Diazepam[1,4]	20 (36%)	61 (34%)	106 (47%)	73 (43%)	118 (54%)	124 (64%)	90 (57%)
Lorazepam[1]	6 (11%)	15 (8.4%)	25 (11%)	21 (12%)	26 (12%)	12 (6.2%)	13 (8.3%)
Midazolam[1]	3 (5.4%)	5 (2.8%)	10 (4.4%)	15 (8.8%)	13 (5.9%)	10 (5.2%)	10 (6.4%)
Alprazolam[1]	0	2 (1.1%)	16 (7.1%)	16 (9.8%)	8 (3.7%)	4 (2.1%)	12 (7.6%)
Clonazepam[1]	0	1 (0.6%)	6 (2.7%)	0	5 (2.3%)	9 (4.7%)	7 (4.5%)
Lormetazepam[1]	1 (1.8%)	2 (1.1%)	0	0	2 (5.3%)	0	3 (1.9%)
Clonazolam[2]	0	0	0	0	0	2 (1.0%)	5 (3.2%)
Etizolam[2]	0	2 (1.1%)	0	5 (2.9%)	32 (14.6%)	25 (13%)	37 (24%)
Flubromazolam[2]	0	0	0	0	0	19 (9.8%)	17 (11%)
Bromazolam[2]	0	0	0	0	0	0	9 (5.7%)
Flubromazepam[2]	0	3 (1.7%)	0	1 (0.6%)	2 (0.9%)	1 (0.5%)	1 (0.6%)
Flualprazolam[3]	0	0	0	0	12 (5.5%)	12 (6.2%	10 (6.4%)
Any benzodiazepine	28 (50%)	81 (45%)	128 (57%)	95 (56%)	148 (68%)	137 (71%)	110 (70%)

[1]Controlled via the UK Misuse of Drugs Act (MDA) prior to 2015. [2]NPS benzodiazepines controlled via MDA in May 2017. [3]NPS benzodiazepine not yet controlled via the MDA (Psychoactive Substances Act 2016 applies). [4]Temazepam and oxazepam considered as diazepam metabolites.

31. Clinical features associated with exposure to ADB-BUTINACA in patients attending Emergency Departments in England

Simon H.L. Thomas[a], Mark Pucci[b], George Bailey[c], Simon L. Hill[d], Liza Keating[e], Rebecca Macfarlane[f] and Simon Hudson[g]

[a]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom; [b]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [c]Imperial College Healthcare NHS Trust, London, United Kingdom; [d]Newcastle Hospitals NHS Foundation Trust, Newcastle, United Kingdom; [e]Royal Berkshire NHS Foundation Trust, Reading, United Kingdom; [f]Epsom and St Helier NHS Trust, Epsom, United Kingdom; [g]LGC Ltd, Fordham, United Kingdom

Objective: Synthetic cannabinoid receptor agonists (SCRA) are commonly encountered new psychoactive substances. ADB-BUTINACA is an N-butyl indazole SCRA previously detected in Russia [1] and first reported in Europe (Sweden) in 2019. Here we report its detection in samples from patients attending UK emergency departments with toxicity after suspected drug misuse and describe the clinical features associated with isolated exposure to this compound.
Methods: Patients (≥16 years) presenting to participating hospitals with toxicity after suspected drug misuse have been included in the ethically approved Identification Of Novel psychoActive substances (IONA) study after informed consent (deferred if needed) since March 2015. Demographic and clinical features are recorded and blood and/or urine samples analysed using high-resolution accurate mass liquid chromatography–mass spectrometry.
Results: By October 2021 analytical data were available for 1,199 IONA participants. ADB-BUTINACA was detected in at least one sample from 9 patients (8 males, age range 16-51 median 45 years), including one transferred from a prison, all presenting between March and July 2021. The hospitals involved were located in the English Midlands, (4) South-East (2), North-East (2) and London (1). Smoking spice was reported by 4 patients, 1 had ingested edible "cannabis" gums and 4 reported heroin use (2 intravenous, 1 smoked, 1 route not known). Pregabalin (oral) and crack cocaine (smoked) use were also reported. ADB-BUTINACA was the only substance detected in 3 patients; reduced level of consciousness (minimum Glasgow Coma Score 8, 12 and 13) was documented in all 3, while respiratory acidosis (venous pH 7.27, pCO_2 7.0 kPa, pO_2 2.7 kPa, base excess -2.7 mmol/L, lactate 1.2 mmol/L), metabolic acidosis (arterial pH 7.04, pCO_2 6.0 kPa, pO_2 8.3 kPa, base excess -18.1 mmol/L, lactate 16 mmol/L), seizures, hallucinations, tachycardia (106/min) and confusion were each reported in one patient. All 3 patients recovered with supportive care alone and were discharged within 25 hours of presentation. The 6 patients with multiple substances detected (including ADB-BUTINACA) also recovered to be discharged (2) or left hospital before medical clearance (3). One was transferred to psychiatry for treatment of pre-existing depression.
Conclusion: ADB-BUTINACA has recently emerged as a drug of misuse in England. Clinical features of toxicity, not previously reported for this compound, are consistent with those of other SCRA and include reduced level of consciousness, respiratory and/or metabolic acidosis, seizures, confusion and hallucinations.

Reference

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32. Clinical features associated with exposure to SL-164 in two patients attending an Emergency Department in England

Simon H.L. Thomas[a], Liza Keating[b], Shauna Bartley[b], Sabi G. Rai[b], Simon L. Hill[c] and Simon Hudson[d]

[a]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom; [b]Royal Berkshire NHS Foundation Trust, Reading, United Kingdom; [c]Newcastle Hospitals NHS Foundation Trust, Newcastle, United Kingdom; [d]LGC Ltd, Fordham, United Kingdom

Objective: Methaqualone (Quaalude, Mandrax) is a $GABA_A$ agonist previously misused due to its sedating and euphoric effects. SL-164 is a methaqualone analogue developed in Japan in the late 1960s but never marketed as a medicine. Following a recent case report of SL-164 misuse in Germany [1], we report the detection of SL-164 in samples taken from 2 patients who consented to inclusion in the Identification Of Novel psychoActive substances (IONA) study. IONA has been collecting clinical data

and analysing samples (high-resolution accurate mass liquid chromatography–mass spectrometry) from adults presenting to participating hospitals with toxicity after suspected drug misuse since 2015.
Case series: Two males presented to the same hospital in the South East of England on the same day in June 2021 after reported acute oral use of "methaqualone", purchased via the Internet. Case 1 (24 years) reported also ingesting "carisoprolol". He was agitated, confused, clammy, pale, tachycardic (130/min) and hypertensive (164/102 mmHg) with mydriasis and myoclonus. Blood tests were normal other than a raised creatine kinase (567 IU/L). He was sedated with lorazepam, admitted to the High Dependency Unit for 72 hours and discharged from hospital with no sequelae after 85 hours. Admission bloods contained SL-164 with etizolam, diazepam and metabolites, alprazolam and lormetazepam but not carisoprolol. Case 2 (27 years) reported using no other substances. The only feature reported was haematuria, which resolved. Renal function, X-rays and ultrasound were normal. He was discharged from hospital after 2 days, refusing further investigations. Admission bloods contained SL-164 with nitrazepam, alprazolam, diazepam and metabolites, etizolam and lormetazepam.
Conclusion: SL-164 can be purchased via the Internet and cause toxicity. The tachycardia, delirium and myoclonus experienced by Case 1 and the published case [1] are unlikely to be caused by co-ingested benzodiazepines and also occur with methaqualone toxicity, which has also caused hypotension, hypertonia, increased tendon reflexes, respiratory depression, hallucinations and cardiac arrest [2]. Case 2 had undiagnosed haematuria; haemorrhagic cystitis has been described with methaqualone [3] but a link with SL-164 is unproven.

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33. Feasibility of a phenobarbital-based protocol in benzodiazepine and Z-drug detoxification

Simone Sartori[a], Giada Crescioli[b], Valentina Brilli[a], Sara Traversoni[a], Cecilia Lanzi[a], Alfredo Vannacci[b], Guido Mannaioni[a] and Niccolò Lombardi[b]

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

Objective: Given the increase in benzodiazepine (BZD) and Z-drug (ZD) abuse and dependence, this study assessed the use of phenobarbital (PHB), alone or in combination with long half-life BZD, in BZD-ZD detoxification.
Methods: A 15-year observational retrospective cohort study was performed on BZD-ZD use disorder patients detoxified with a PHB mixed protocol at the Medical Toxicology Unit of Careggi University Hospital (Florence, Italy). The probability of protocol failure ("dropout") was estimated during hospitalisation considering both demographic (sex, age, employment, psychiatric comorbidities, alcohol or drug co-abuse, and maintenance therapy) and pharmacological (PHB equivalents at admission, number of abused substances, plasma half-life, formulation, administration route, and supportive therapy) characteristics. "Hospitalisation length" (>7 days), "PHB discharge dose" (>100 mg/day), and "BZD-ZD free status" at discharge, were evaluated. Multivariate logistic regression was used to estimate the odd ratios (ORs) and 95% confidence interval (CI) of the four outcomes.
Results: There were 355 patients (57% of men), with mean age of 42.9 (SD ±10.7) years; 271 patients (76.3%) had psychiatric comorbidity, 120 (33.8%) had alcohol co-abuse history, while 103 (29.01%) had other drugs co-abuse. In total, 107 (30.14%) patients were under maintenance therapy with buprenorphine or methadone. The majority of them abused only one BZD (n = 257, 72.4%), 12 (3.4%) only one ZD, and 13 (3.7%) both BZD and ZD. The 3 most frequently abused substances were lormetazepam (39.2%), lorazepam (25.1%), and alprazolam (16.6%). Accordingly, intermediate half-life substances resulted in the most abused drugs (74.7%). Drop formulations (52.4%) and oral route (94.1%) were preferred. During detoxification, only 20 (5.6%) were considered as "dropout"; 19 were discharged against medical advice or due to misbehavior, and only one for PHB-related non-serious skin rash. Logistic regression showed a higher probability to be BZD-ZD free at discharge for patients with employment (OR 2.29, CI 1.00-5.24), for those who abused BZD-ZD in drop formulations (OR 2.16, CI 1.30-3.59), and for those concomitantly treated with PHB, BZD and trazodone (OR 2.86, CI 1.14-7.17) during hospital stay. The risk of having a hospitalisation of >7 days was observed for patients with a maintenance therapy (OR 2.07, CI 1.20-3.58) for substance use disorder, and for those treated with more than 300 mg/day of PHB equivalents at hospital admission (OR 1.68, CI 1.03-2.72).
Conclusion: Despite not being a recent detoxification option, our study suggests that PHB can be used safely in clinical practice. Further research should evaluate its effectiveness compared to other existing protocols both in achieving a rapid detoxification and maintaining long-term abstinence.

34. The impact of vitamin D concentration on detoxification and usage in patients with prescription opioids and benzodiazepines

Gabija Laubner[a] and Sigute Miskinyte[b]

[a]Center of Toxicology, Republican Vilnius University Hospital, Vilnius, Lithuania; [b]Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Objective: To confirm or refute the hypothesis that vitamin D has an impact on prescription opioid or benzodiazepine detoxification and usage.
Methods: A retrospective review of patients that underwent rapid elective opioid or benzodiazepine detoxification in the years 2018-2021, the groups were analyzed separately. All opioid doses were converted to oral morphine equivalents and benzodiazepine doses to diazepam equivalents. Patients were divided into 3 groups based on vitamin D concentration with deficiency (< 50 nmol/L), insufficiency (50-75 nmol/L) or normal (75-250 nmol/L). Statistical analysis was carried out using MS Excel and IBM SPSS v25.0.
Results: Table 1. There was a statistically significant different outcome of benzodiazepine detoxification while comparing the groups ($p < 0.05$), but no differences of benzodiazepine dose or duration of use ($p = 0.442$ and $p = 0.978$, respectively). There were no statistically significant differences of opioid drug dose

Table 1. Comparing vitamin D status, duration of use and dose and outcome in patients undergoing rapid opioid or benzodiazepine detoxification.

Patients with prescription opioids (n = 19, M/F 6/13)				
	Vitamin D deficiency group, n = 10 (52.6%)	Vitamin D insufficiency group, n = 5 (26.3%)	Normal vitamin D levels group, n = 4 (21%)	P value
Average morphine equivalent dose, *mg*	70.42 ± 59.7	84.72 ± 72.44	75.8 ± 76.22	0.926
Average duration of opioid use, *years*	6.16 ± 5.64	10.8 ± 8.76	5.52 ± 6.83	0.408
Completed detoxification, *n (%)*	8 (80%)	5 (100%)	3 (75%)	0.561
Length of stay in hospital, *days*	8.4 ± 4.03	12.2 ± 3.7	9.5 ± 4.12	0.247

Patients with prescription benzodiazepines (n = 16, M/F 6/10)				
	Vitamin D deficiency group, n = 5 (31.3%)	Vitamin D insufficiency group, n = 5 (31.3%)	Normal vitamin D levels group, n = 6 (37.5%)	P value
Average diazepam equivalent dose, *mg*	19 ± 18.08	28 ± 13.04	17.5 ± 10.37	0.442
Average duration of benzodiazepine use, *years*	6.85 ± 7.34	7 ± 5.43	6.33 ± 3.5	0.978
Completed detoxification, *n (%)*	4 (80%)	–	3 (50%)	**0.03**
Length of stay in hospital, *days*	9.8 ± 3.11	6 ± 4.36	10.5 ± 1.38	0.073

(p = 0.926), duration of use (p = 0.408), outcome of detoxification (p = 0.561) or duration of stay in hospital (p = 0.247) between the groups. There was no statistically significant correlations between age and the outcome of detoxification (p = 0.837) and length of stay in hospital (p = 0.271).

Conclusion: Vitamin D concentration has an impact on the outcome of rapid benzodiazepine detoxification. A larger study needs to assess the possible impact of vitamin D deficiency or insufficiency on the development, course and treatment of addiction. This is a relevant hypothesis as in our study the patients had vitamin D deficiency in 78.9% in the opioid group and 62.6% in the benzodiazepine group, similar to the 70.3% overall prevalence rate of vitamin D deficiency [1]. Moreover, previous studies have found a significant influence of vitamin D concentrations on patients with prescription opioid use [2].

References

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35. Calls concerning drugs of abuse to the Finnish Poison Information Center in people under 25 years old during years 2011-2020

Johanna L. Tikkanen[a] and Tuomas O. Lilius[b]

[a]Poison Information Center, Department of Emergency Medicine and Services, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [b]Poison Information Center, Department of Emergency Medicine and Services, Helsinki University Hospital and University of Helsinki; Department of Pharmacology and INDIVIDRUG Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland

Objective: While the total number of deaths due to poisoning has been steadily decreasing in Finland, a marked increase in deaths by illicit drug overdose in people under 25 years of age has raised an alarming signal during the last three years. Our objective was to investigate trends in the calls to the Finnish Poison Information Center (FPIC) concerning drugs of abuse in people under 25 years.

Methods: We analysed calls from the FPIC database concerning people under 25 years with an acute intentional poisoning related to a drug of abuse during the years 2011–2020.

Results: Over the study period, the FPIC received 1486 calls concerning acute poisonings caused by drugs of abuse; 92% (n = 1361) of these calls were intentional poisonings. The age of the victim was known in 61% (n = 830) of these calls and 54% (n = 445) of these concerned people aged under 25 years (range 12-24 years). The majority of the calls (57%, n = 252) came from healthcare professionals. This finding was even more pronounced in children under 15 years, where 85% (n = 29/34) of the calls were from healthcare professionals. Of the calls that concerned persons under 25 years, amphetamine accounted for 26% (n = 114), cannabis for 16% (n = 69), 3,4-methylenedioxymethamphetamine (MDMA) for 12% (n = 55), gamma-hydroxybutyric acid and related agents for 8% (n = 35) and lysergic acid diethylamide (LSD) for 7% (n = 30). The remaining 22% (n = 98) consisted of substances which were mentioned less than fifteen times. The drug was unknown in 10% (n = 44) of the calls. In addition to these calls, there were 32 cases with medicinal buprenorphine being the drug of abuse (9 of them in 2020). We were unable to differentiate other medicinal opioids from the data. We observed a trend for increase in calls concerning children under 15 years during the last two years (at most 4 calls/year between 2011-2018, 12 in 2019 and 8 in 2020).

Conclusion: We observed only slight variations in the number of calls concerning drugs of abuse in people aged under 25 years in the last 10 years. Amphetamine remains the most frequently queried drug of abuse in Finland in people in this age group, while buprenorphine is the most common cause of death in drug overdose in Finland. A large number of the calls related to drugs of abuse come from healthcare professionals especially when concerning children. A particularly worrying signal is the emergence of queries regarding children under 15 in the last two years, suggesting that drug abuse begins at a younger age.

36. Altered mental status at the emergency department. Clinical management of acute tetrahydrocannabinol (THC) oral exposure by the Florence Poison Control Center: a case series

Cecilia Lanzi[a], Giacomo Baldereschi[b], Haifa Ounalli[b], Giulia Borgioli[b], Sara Traversoni[a], Brunella Occupati[a], Alessandra Pistelli[a], Andrea Missanelli[a], Alessandra Ieri[a] and Guido Mannaioni[b]

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

Objective: Cannabis is a widely abused substance. Accidental and voluntary intake of cannabis derivatives are becoming more frequent [1], probably due to ready availability in both the illegal and legal market. In this case series, we describe a syndromic pattern of alternating sedation and psychomotor agitation after ingestion of cannabis derivatives.
Case series: Case 1: A 28-year-old woman presented to the Emergency Department (ED) for sensory impairment following a Bedrocan (medicinal cannabis) overdose. She was unresponsive to stimuli, displaying myoclonus and markedly hyperactive osteotendinous reflexes (OR), mild hypoxia and elevated lactate 2.1 mmol/L. Electrocardiogram (ECG) and electroencephalogram (EEG) were normal. Case 2: A 28-year-old woman presented with hallucinations after eating a meat stew. She cooked the dish herself and blended it with some wine found in the apartment she rented. She denied substance use. She appeared somnolent and confused, with brisk OR and abnormal EEG. Brain imaging was negative. The patient's boyfriend, who ate the same stew, reported episodes of vomiting and paranoid thoughts. The "wine" had a greenish color and a smell of cannabis. Case 3: A 20-month-old girl was referred for drowsiness and unresponsiveness to stimuli alternating with agitation. The mother reported probable ingestion of "something brown" the child found in a public garden. Clinical neurological involvement was excluded. Case 4: An 11-month-old girl was referred to the ED for an alternating state of drowsiness and irritability. ECG was normal, except for sinus tachycardia. Organic causes were excluded. Case 5: A 12-month-old girl was referred after witnessed ingestion of tetrahydrocannabinol (THC) at a public garden. She was asymptomatic with the exception of generalized myoclonus. All cases were managed with hydration and symptomatic therapy until clinical resolution. All patients, including patient 2's partner, showed isolated positivity for THC on urinary toxicological screening. The "wine" was also positive for THC.
Conclusion: All the cases of THC ingestion managed by our Poison Control Center (PCC) displayed common clinical features of alternating sedation and hyperexcitability. Awareness of such a syndromic pattern, along with PCC involvement in the management of such cases might limit invasive tests in hemodynamically stable patients with altered mental status.

Reference

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37. Body fillers: complications from injection of synthol for esthetic reasons

Benedetta Brolli, Davide Lonati, Lucia Bernasconi, Valentina Negrini, Cristina Grazioli and Carlo A. Locatelli

Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy

Objective: Synthol is an oil composed of medium-chain triglycerides, lidocaine and alcohol available online. It was created by Christopher Clark in 1990 and is particularly popular among body builders to enhance muscle appearance and dimension. It is administered by local subcutaneous injection mainly in the biceps, triceps, and gastrocnemius. Moreover, Synthol (and oil injections) are also used for cosmetic/esthetic reasons and to "correct" defects of parts of the body (e.g. breast, nose, etc.). We report a case of Synthol injection in the breast in order to augment volume/dimension with local and systemic severe complications.
Case report: A 56-year-old woman was admitted to emergency department for coma associated with diffuse hypertonia. At physical examination multiple subcutaneous nodules at breast level were noted associated with multiple diffuse petechiae (mainly on the lower limbs). The first clinical suspicion was postictal seizure state. Emergency medical services (EMS) found her at home with a syringe and a bottle of Synthol. Toxicological urinary screen was negative, and hematological tests and biochemistry were normal. Electroencephalography (EEG) showed a diffuse suppressed activity without epileptic focus. Cranial magnetic resonance imaging (MRI) scan showed signs of multiple bilateral ischemic stroke. Endocarditis was excluded and investigations for vasculitis were inconclusive. A "fat embolism like-syndrome" associated with granulomatous disease was the diagnosis. After 10 days the patient was discharged for rehabilitation. A plastic surgical evaluation was requested for multiple breast subcutaneous nodules and granulomas.
Conclusion: Products like paraffin oil, Vaseline®, and sesame oil have been used to improve esthetic qualities or to correct perceived defects of the body. The esthetical result is temporary and the risk of side effects goes beyond any benefits. Synthol can be accidentally injected into vessels increasing the risk of embolism, heart attack, and ischemic stroke. There is also a high risk of ulceration and infections. A correlation between oil injection and autoimmunity has been reported and cases of myositis from oil injection have been described. This kind of practice is just a dangerous cosmetic shortcut with many complications that can be life-threatening. It is important to alert health personnel and sports communities about the risk of these practices.

38. Poisoning with novel dissociative drugs in Slovenia

Mark Jovanović and Miran Brvar

University Medical Centre Ljubljana, Ljubljana, Slovenia

Objective: Dissociative drugs cause distorted sensory perceptions or feelings of disconnection and detachment from the environment and self. Phencyclidine (PCP) and its derivative ketamine were the first recognized dissociative drugs. In the last decade

novel synthetic analogues of phencyclidine and ketamine have been recognized. The aim was to evaluate the epidemiology of poisonings with dissociative drugs in Slovenia and present the case of poisoning with 2-OXO-PCE (O-PCE).
Methods: A retrospective review of the Slovenian register of intoxications, an electronic database that includes 13,960 reported cases (up to October 2021).
Results: There were 1840 (13%) cases of poisoning with illicit drugs, which included 19 (1%) involving dissociative drugs. There were 8 cases of poisoning with ketamine, 4 with phencyclidine and 7 cases of poisoning with novel dissociative drugs: 2 with N-ethyldeschloroketamine (2'-OXO-PCE, O-PCE), 1 with *2*-fluorodeschloroketamine (2-F-DCK), 3 with 3-methoxyphencyclidine (3-MeO PCP) and 1 with 3-methoxyeticyclidine (3-MeO-PCE). In one case, a 20-year-old male returned home at the evening and talked normally with his parents. Two hours later he started yelling and crying. He held his hand in front of his forehead and did not recognize his father. He did not respond to vocal stimulus and did not answer questions. He lost consciousness for approximately 10 seconds. At the arrival of paramedics, he saw monkeys around him. He was sweating and agitated. The paramedics administered 10 mg of midazolam intravenously and he calmed down. They found a drug in the patient's pocket labeled O-PCE. On admission at the Emergency Department, he was somnolent with tachycardia. The laboratory results revealed mild leukocytosis and rhabdomyolysis. The patient was hydrated intravenously. On the next day, he was conscious and admitted taking 2'-OXO-PCE, which was confirmed in his blood sample by liquid chromatography-tandem mass spectrometry (LC-MS/MS).
Conclusion: Dissociative drugs represent 1% of illegal drug poisonings in Slovenia. Novel dissociative drug have become more common in recent years. 2-OXO-PCE is a novel dissociative drug closely related to deschloroketamine. Therapy is symptomatic and supportive with benzodiazepines as the mainstay treatment.

39. A case of challenging acute and chronic treatment of new psychoactive substance addiction

Azzurra Schicchi[a], Eleonora Buscaglia[a], Davide Lonati[a], Valeria M. Petrolini[a], Pietro Papa[b], Antonella Valli[b], Lucia Bernasconi[a], Benedetta Brolli[a], Valentina Negrini[a], Cristina Grazioli[a] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]Laboratory of Analytical Toxicology, Clinical Chemistry Service, IRCCS Policlinico San Matteo Foundation, Pavia, Italy

Objective: The treatment of abusers of new psychoactive substances represents a new challenge and a new disease both in the acute and in chronic setting. Due to the difficulty in diagnosis and in clinical management, NPS-abusers force clinicians to search for a better way to manage poisoned patients. To manage acute intoxication, addiction and possible psychiatric associated disorder a multidisciplinary approach is mandatory. NPS addiction associated with psychiatric diagnosis, in particular, is frequently treated as an organic psychiatric disease, but this is associated with therapeutic failure. We describe a case of a drug user taking different NPS presenting with severe acute toxic effects and long-term psychiatric consequences.
Case report: The clinical course of a 19-year-old male with history of pregabalin (450-600 mg/day), phenibut (1.6 g/day), clonazolam (1 mg/day), flualprazolam (1 mg/day), 4-methylphenidate (20-40 mg/day), and baclofen abuse is described. Over 2 years (2020-2021) the patient was hospitalized (on ICU and/or psychiatric wards) 6 times for severe acute intoxication due to NPS abuse (3/6) and for attempted suicide (3/6). The length of stay of each hospitalization varied from 2 days to 2 weeks. During NPS abuse hospitalizations the main clinical manifestations were urinary retention, confusion and seizures. Drugs detected in biological samples during these hospitalizations were flualprazolam, pregabalin, phenibut, 4-methylphenidate, and deschloroketamine. During this period the patient tried to follow the prescribed detoxification treatment (chlordiazepoxide, pregabalin, diazepam, bupropion) but was unsuccessful. In particular, when trying to reduce the dose of the daily of NPS he manifested a severe depressive syndrome resulting in 3 hospitalizations for attempted suicide in a period of 6 months. On these occasions, he ingested baclofen, amitriptyline and olanzapine. During attempted suicide hospitalizations, the main clinical manifestations were coma, seizures and withdrawal symptoms; in 2/3 of these episodes he needed ICU hospitalization with mechanical ventilation.
Conclusion: The NPS-addicted patient brings different problems compared to the classic substance abuser. NPS-related psychosis shows peculiar clinical aspects, and seems to be less responsive to standardized pharmacological treatments. As future perspectives, a multidisciplinary collaboration is necessary in order to identify an optimal and appropriate detoxification treatment. To better understand all the crucial aspects of these novel toxicological diseases, experimental and clinical research on acute and chronic toxicity of NPS are needed.

40. Enquiries to the UK National Poisons Information Service (NPIS) involving sodium-glucose co-transporter-2 (SLGT2) inhibitors, 2015-2021

Emma J. Moyns[a], Mark Pucci[b], Euan A. Sandilands[c], Laurence A. Gray[d], Ruben H.K. Thanacoody[e] and Sally M. Bradberry[a]

[a]National Poisons Information Service (Birmingham Unit), Birmingham, United Kingdom; [b]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [c]National Poisons Information Service (Edinburgh Unit), Edinburgh, United Kingdom; [d]National Poisons Information Service (Cardiff Unit), Cardiff, United Kingdom; [e]National Poisons Information Service (Newcastle Unit), Newcastle, United Kingdom

Objective: Sodium-glucose co-transporter-2 (SLGT2) inhibitors (e.g. dapagliflozin, empagliflozin and canagliflozin) are used to improve glycaemic control in adults with type 2 diabetes mellitus (T2DM) and to reduce the risk of hospitalisation for heart failure in adults with T2DM and cardiovascular disease. NHS Digital prescription data demonstrate a significant rise in the number of primary care prescriptions for SLGT2 inhibitors in England from 645,735 in 2015 to 2,767,543 in 2020 [1]. We investigated whether this was mirrored in the number of enquiries to the UK NPIS.
Methods: A retrospective analysis of UK NPIS enquiry data between 1 January 2015 and 31 July 2021 for enquiries relating to SLGT2 inhibitors.
Results: There were 139 enquiries involving 134 patients. There were 6 enquiries in 2015 with an increasing trend ($R^2 = 0.73$) to a peak of 34 in 2020; with an additional 22 enquiries in the first seven months of 2021. Seventy-four (55%) patients were female; 60 were male. The median age was 56 years (range 1-88 years) with 127 enquiries in adults and 7 in children ($\leq$18 years). The circumstances of exposure were therapeutic error (n = 88, 65.7%),

intentional (n = 32, 23.9%), accidental (n = 12, 9%) and unknown in two enquiries. Fifty enquiries involved only SLGT2 inhibitors whilst the remaining 84 were polypharmacy exposures. SLGT2 inhibitors involved in single agent enquiries were empagliflozin (n = 22, 42.3%), dapagliflozin (n = 18, 34.6%) and canagliflozin (n = 10, 19.2%). There were no enquiries involving ertugliflozin. The median dose (range) ingested was canagliflozin 900 mg (200–3000 mg), dapagliflozin 20 mg (5-40 mg) and empagliflozin 50 mg (20-100 mg). Features reported following ingestion of SLGT2 inhibitors alone were polyuria (n = 2), malaise (n = 2), fatigue (n = 1), headache (n = 1), thirst (n = 1) and weight loss (n = 1). The Maximum Poisoning Severity Score [2] at the time of enquiry for enquiries involving SLGT2 inhibitors only was none (n = 44), minor (n = 5) and moderate (n = 1; thirst, polyuria and weight loss after triple daily dose of canagliflozin for five weeks).
Conclusion: Telephone enquiries to the NPIS involving SLGT2 inhibitors have gradually increased over the past six years in line with the increase in prescriptions issued. Serious toxicity involving SLGT2 inhibitors was not reported and minor or moderate toxicity was rarely reported with many patients being asymptomatic at the time of the enquiry.

References

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41. Toxic epidermal necrolysis: a case series

Julia V. Radenkova-Saeva and Rayna D. Stoyanova
Clinic of Toxicology, University Hospital for Emergency Medicine "N.I. Pirogov", Sofia, Bulgaria

Objective: Toxic epidermal necrolysis (TEN), or Lyell's disease is a severe life-threatening adverse drug reaction with a high mortality rate, described for the first time in 1956 by Alan Lyell. It is characterized by erythematous or violaceous patches, bullae, erosions and skin detachment. Etiopathogenetically, it results from the combination of drug and host genetic factors, resulting in a delayed-type hypersensitivity reaction. The aim of this study was to investigate the causative agents, clinical characteristics, complications, treatment and mortality rate of all patients with the diagnosis of TEN, who were admitted to the Toxicology Clinic, UHEM "Pirogov", for the period January 2018 to September 2021.
Case series: We present a case series of 17 patients with Lyell's disease, treated in our Clinic over that period of time. Most of them were female (13, 76.5%; male 4, 23.5%). The age of the patients ranged from 30 to 86 years. The offending drugs in our patients were non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics (clindamycin, vancomycin), colchicine, allopurinol, or multiple drugs. The condition displays an acute onset and manifests with an "influenza-like" prodromal phase, followed by painful cutaneous and mucous membrane lesions, with subsequent generalized epidermal sloughing, positive Nikolsky sign, persistent fever, and other systemic symptoms. The TEN cases were treated with fluid and electrolyte replacement, systemic corticosteroids, antihistamines, antibiotic, vitamins, H_2 blockers, and topical care of mucosal changes. Thirteen patients (76.5%) survived with good outcome. Evolution was satisfactory with epidermalization and these patients were discharged from hospital. Four patients (23.5%) died due to extensive skin involvement, complicated by sepsis and multiorgan failure.
Conclusion: TEN is a severe, life-threatening disease. The mortality rate is highly dependent on the quality of care and rapidity with which treatment is initiated.

42. Accidental methanol poisoning: a case series

Julia V. Radenkova-Saeva and Ralitza B. Atanasova
Clinic of Toxicology, University Hospital for Emergency Medicine "N.I. Pirogov", Sofia, Bulgaria

Objective: To examine methanol poisoning cases and to define the demographic features, clinical characteristics and the outcome of intoxication.
Case series: The records of the Toxicology Clinic, Emergency Hospital "N.I. Pirogov" were reviewed retrospectively for all methanol poisonings from 1 January 2019 to 30 September 2021. The patients were characterized according to age, sex, clinical features, blood test results, including methanol concentration, presence of anion-gap acidosis, treatments received and outcome. There were eight patients, hospitalized in the Clinic due to methanol poisoning during the study period. The reason for ingestion in all cases was accidental. There were two men (25%) and six women (75%). The age of the patients ranged from 28 to 94 years. The blood methanol concentrations ranged from 0.68 to 3.50 g/L. All patients had evidence of an extreme or moderate metabolic acidosis. Symptoms, varying in severity, included dizziness, headache, nausea, vomiting, difficulty walking, and in some patients agitated behavior, difficulty breathing, blurred vision, pupil dilation, and low blood pressure. Conventional treatment of methanol intoxication was used including supportive care, correction of acidosis, administration of ethanol as an antidote, hemodialysis. Four (50%) patients died and four (50%) were discharged with visual impairment.
Conclusion: Methanol poisonings are usually severe and with extremely high lethality. Rapid analysis, early adequate treatment and antidotal therapy are important for a favorable outcome.

43. Shit happens! Accidental human coprophagia in northern Germany

Martin Ebbecke
GIZ-Nord Poisons Centre, Göttingen, Germany

Objective: The accidental consumption of faeces plays a minor role in the advisory activities of GIZ-Nord poisons centre (≈1‰ of all inquiries). For the first time, data in this context were evaluated and published by a poisons control centre (PIC).
Methods: For the period 1996-2021 all cases with human accidental ingestion of animal and human excrement in northern Germany were identified (n = 879). The zoologic sources of droppings, age distribution of affected persons and severity of intoxication were analysed.
Results: The age of persons who ingested excrement was documented in 64.5% of all cases and distributed in following age groups: < 1 years 29%, 1-4 years 63%, 5-9 years 2%, 10-14 years <1% and adults 6%. The zoologic source of the droppings could not be determined in 32% of the inquiries. In 68% of all cases at least the zoologic class was available. Of these, 61% belonged to the class Mammalia and 39% to Aves (birds). One exception was the faeces of a chameleon (class: Reptilia). The distribution among mammal excrements was as follows: cats 43%, dogs 23%, humans 8%, mice 6.9%, rats 5.2%, hares and/or rabbits 3.8%,

hedgehogs 3.6%, and martens 1.9%. The remaining mammal species (<1% each) consisted of hamsters, bats, sheep, goats, ferrets, foxes, cows, roe deer, guinea pigs, raccoons and chinchillas. The bird group showed the following picture: in 75% a bird species could not be identified by the inquirer. The remaining 25% consisted of: 14% pigeons, 4% chickens, 1.3% ducks, 1.3% seagulls and 1.3% budgerigars. Geese, ducks, parrots, swallows, cockatiels, crows and canary birds were less than 1% each. The severity of intoxication according to the Poisoning Severity Score (PSS) was as follows: 86% were asymptomatic, 6% showed minor symptoms and in 0.5% symptoms were moderate (severity was not documented 7.5%).

Conclusion: These PIC data reflect the extent of human-animal relationship and can be a valuable source for researchers in various fields.

44. Characteristics of adult poisoning at Copenhagen University Hospital Bispebjerg over a 2.5-year period

Anja J. Huusom[a], Tonny S. Petersen[b], Søren Bøgevig[b] and Poul Frost[a]

[a]Department of Occupational and Environmental Medicine, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark; [b]Department of Clinical Pharmacology, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark

Objective: Poisoning is prevalent but not well described in Denmark despite valid national person registers. We aimed to describe the characteristics of the adult poisonings at a Danish metropolitan acute hospital over a 2.5-year period.

Methods: A retrospective observational cohort study consecutively collected all poisoning cases (n = 3136) at Bispebjerg Hospital (BBH) where the National Poison Centre is located from 1 January 2018 to 30 June 2020. For each group of exposures, the distribution of sex, age group, type of contact and length of stay (LOS) was examined.

Results: We found an even male:female distribution of poisonings. Overall, non-drugs and ethanol were more frequently used (Table 1), whereas paracetamol and opioids were the most prevalent medicinal poisonings. There was a female overrepresentation among the exposures involving weak analgesics, paracetamol, antiepileptics, antipsychotics, antidepressants, other drugs and non-drugs. Paracetamol was the most prevalent medicinal poisoning among females. Poisoning in males was dominated by opioids, central stimulants and ethanol. Almost half (46%) of the poisonings occurred in the under 40-year-olds and the commonest medicinal poisonings in the young were central stimulants and paracetamol. Opioids were widely used in all age groups but dominated the medicinal poisonings among the over 60s. Overall, non-drug exposures were the commonest cause of hospital contact in all age groups whereas ethanol dominated primarily in the 17-59-year-olds. Poisoning with non-drugs, hallucinogens, central stimulants, other drugs, and ethanol were primarily managed in the Emergency Department (ED) whereas all other exposures were more likely to be admitted >12 hours. Ethanol, opioids and paracetamol dominated the group with LOS >37 hours.

Conclusion: We found an even distribution of poisonings among sexes with an overrepresentation of the youngest age group, 17-39 years, whom were mainly exposed to non-drugs, ethanol, central stimulants and paracetamol. Paracetamol was the commonest medicinal exposure followed by opioids.

Table 1. Characteristics of adult poisoning cases at Bispebjerg Hospital, Copenhagen, over a 2.5 year period.

	Weak analgesics	Paracetamol	Opioids	Hallucinogens	Antiepileptics	Central stimulants	Antipsychotics	Antidepressants	Cardiovascular drugs	Drug, other	Ethanol	Non-drugs	Unknown
n	35	248	213	110	160	190	71	21	14	211	825	709	329
Sex (%)													
Female	77	70	39	25	59	31	76	67	50	61	33	54	49
Male	23	30	61	75	41	169	24	33	50	39	67	46	51
Age groups (%)													
17-39 years	57	59	23	71	41	90	59	48	36	37	38	54	67
40-59 years	26	23	34	23	29	9	31	14	7	28	46	27	22
60-79 years	14	15	31	5	23	1	10	33	36	22	15	16	9
80-101 years	3	3	12	1	6	0	0	5	21	12	1	3	2
Contact (%)													
Emergency Department	20	5	23	61	21	58	20	10	14	36	56	84	42
Inpatient	80	95	77	39	79	42	80	90	86	64	44	16	58
Length of stay (%)													
0-12 h	40	10	32	72	38	75	37	29	21	49	57	90	56
13-24 h	29	31	17	4	29	15	44	43	29	20	14	6	21
25-36 h	26	30	9	6	6	4	7	5	0	7	5	2	10
37-791 h	6	28	42	18	26	5	13	24	50	24	23	3	13

45. Spectrum of acute poisoning in north India

Ashish Bhalla, Ashok Pannu, Deba P. Dhibar, Navneet Sharma and Surjit Singh

Postgraduate Institute of Medical Education and Research, Chandigarh, India

Objective: To describe the prevalence of the various types of poisoning and associated case fatality in our tertiary care center in north India.
Methods: We performed a prospective cohort study in patients aged 13 years and above admitted with acute poisoning to the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh (India), for 15 months from December 2016 to December 2017 and from September 2019 to December 2019. The demographic details of the study population, types of poisoning, the circumstances and the outcome were recorded. The results were compared to our previously published experience.
Results: In total, 402 cases were enrolled during the study period (median age 28 years; 63.2% males). Ingestion (97.3%) was the most common mode of exposure and the primary intention was self-harm (78.1%). The major types of acute poisoning were pesticide (65.7%), drug overdose (19.2%), and corrosive ingestion (7.7%). Pesticides included insecticides (36.3%), cholinesterase inhibitors (22.6%), rodenticides (24%, including aluminum phosphide 18.9% and coumarin derivatives 5.0%) and herbicides (5.5%; paraquat). Benzodiazepines ($n = 33$) and opioids ($n = 25$) were frequent causes of drug overdose. The in-hospital case fatality rate was 17.3% ($n = 58$).
Conclusion: When compared to our previous published experience, herbicide and opioid overdose emerged as new threats with a little decline in organophosphate and aluminum phosphide poisoning. The overall case fatality rate remains similar.

46. Acute poisonings in geriatric population in a one year period

Natasha Simonovska, Zanina Perevska, Aleksandra Babulovska, Afrodita Berat-Huseini, Kristin Kostadinovski and Kiril Naumovski

University Clinic of Toxicology, Clinical Centre, "Mother Teresa", Medical Faculty, Ss Cyril and Methodius University in Skopje, Skopje, North Macedonia

Objective: The aim of this study was to assess the intent and most common substances involved in acute poisoning in geriatric patients.
Methods: This was a descriptive study over a period of one year (2019) in which 92 geriatric patients aged $\geq$65 years were enrolled. Data from the national patient electronic system "My term" and from the Poisoning Information Center, University Clinic of Toxicology was used. Variables including gender, age, type of substance, route of substance administration, intent of acute poisoning, duration of hospitalization were analyzed. Severity of poisoning was made using the Poison Severity Score (PSS).
Results: The participants were divided in two groups depending on the intention of acute poisoning: patients with intentional (attempted suicide 45.7%) and unintentional (abuse 26.1% and accidental 28.3%) toxin exposure. The majority of patients were male (52.2%). The mean age was 73.1 ± 6.3 years. The average length of hospitalization was 6.9 ± 8.3 days. There was a significant relationship between gender and intention of poisoning ($p < 0.001$) with a higher prevalence of poisoning in women with suicidal intent (69%) compared to men (31%). There was statistical significance in mixed toxin exposure ($p = 0.001$) in favour of the group with intentional poisoning and alcohol ($p < 0.001$) and gases ($p = 0.035$) in favour of the group with unintentional poisoning. The most frequent toxins were corrosives (26.1%), followed by patients who were exposed to multiple substances (21.7%). Most patients (55.4%) had minor effects and only 9.8% had severe poisoning. Six patients had a fatal outcome (four with intentional and two with unintentional poisoning). Severity of acute poisoning was statistically different between the two exposure type groups, with a higher PSS in the intentional poisoning group ($p = 0.023$).
Conclusion: Unintentional poisonings are more frequent in the geriatric population and the most common are acute poisonings with alcohol, followed by corrosives and medicines. With intentional suicidal poisoning mixed toxin exposure was most common, followed by corrosives and medicines.

47. Circumstances of accidental poisonings in the elderly - a 12 year retrospective analysis from Estonia

Ruth Kastanje, Riina Koltšanova and Mare Oder

Estonian Poisoning Information Centre, Estonian Health Board, Tallinn, Estonia

Objective: Elderly people can be more severely affected by accidental poisonings than younger adults due to worsening health. This study aims to better understand causative factors in accidental poisonings in Estonia's older population in order to determine strategies to minimize the hazards of such poisonings and who should be the main target of prevention work.
Methods: Calls about people aged 65 years and over to the Estonian Poisons Information Centre (EPIC) from January 2009 to December 2020 were analysed in age groups 65-69, 70–74, 75–79, 80-84, 85–89 and 90 and more years old. Data collected included who called, how long after the incident they called, whether the person lived alone or with someone; main reason behind the accident; where the accident occurred and what kind of agent was involved; the toxscore of the patient; and the advice given about further action.
Results: In total 1038 calls were found. Suicide attempts (116) and general questions (172) were excluded leaving 669 calls. Most calls in all age groups where made by the patient themselves (76%), commonly 5-24 hours after the incident (84%). Symptoms were mild in most cases (toxscore 0-1 96%, only 5 cases had a toxscore of 3). In total 25% of patients were referred to hospital, and the others were advised to observe at home. Common reasons for the accident were mistaking it for something similar 54% and forgetting medication had already been taken 39%. Inappropriate storage was less important. Mental confusion became more important after age 75. Incidents mostly happened at home: 100% from age 80. The most common agents causing poisoning were medications (there was no difference between prescription or over the counter medications). The second most common substances were caustic/corrosive chemicals followed by alcohols, cosmetic products and food supplements. Poisonings by plants or mushrooms were very rare.
Conclusion: Most poisoning accidents happen to elderly people living alone, taking care of themselves. The most common reasons for accidents are forgetting about medication already taken, careless handling of different substances and not checking what is in the bottle or package before using it, plus mental confusion. Also, it often takes a dangerously long time to call for specialist help. Knowing this, we can better target our prevention work to

the elderly themselves about medication, chemical safety and help them understand what kind of help is available from the EPIC and encourage them to call sooner. Also, relatives should be informed about possible hazards.

48. Poison center referral patterns in accidental pediatric cannabinoid exposures

Avery Michienzi[a], Natasha Tobarran[b], Andrew Chambers[b], Peter Vandersteenhoven[a], Caleb Martin[a], Kirk Cumpston[b], Brandon Wills[b] and Nathan Charlton[a]

[a]Department of Emergency Medicine, University of Virginia, Charlottesville, United States; [b]Department of Emergency Medicine, Virginia Commonwealth University Health System, Richmond, United States

Objective: To evaluate referral patterns of two US poison centers (PC) for unintentional pediatric exposures to cannabinoids, to determine the rate in which PC advice was followed and understand how non-compliance with PC recommendations affect emergency services.
Methods: This was a retrospective chart review of accidental pediatric cannabis exposures reported to two regional PCs from 1 January 2010 to 31 December 2020. The electronic database, Toxicall™, from each PC was searched using generic codes for marijuana, cannabidiol (CBD) and tetrahydrocannabinol (THC). Inclusion criteria: $\leq$ 10 years; unintentional exposure; single substance exposure. Exclusion criteria: intentional exposure; patient at healthcare facility at the time of call; polysubstance exposure; confirmed non exposure. Data was collected by investigators from the information entered into Toxicall™ by the certified Specialists in Poison Information (CSPIs).
Results: Over the study period 179 cases were identified, and 87 cases were included. Average age of exposure was 3 years (range 3 months to 10 years). Products of exposure included THC/hemp/CBD edibles (57/87), dronabinol/nabilone (2/87), cannabis bud/joint (15/87), CBD oil/cream (9/87), and THC/CBD vape cartridges (4/87). Of the 87 cases, 34 were monitored at home and 53 were referred to the hospital. Of those referred to the hospital, 20 callers did not follow recommendations and a welfare check by police was initiated by the PC for 3 cases. Local police were unable to locate two of the callers, the third caller was found but the child was asymptomatic and not transported to the hospital. Of those referred to the hospital, 15/34 (44%) were symptomatic. Of those monitored at home, 8/54 (15%) were symptomatic.
Conclusion: Pediatric exposure to cannabinoids has increased in the US since marijuana has been decriminalized and legalized in many states [1]. Referring all exposures to the hospital may increase the burden on the healthcare system and parents fearing legal repercussions may fail to follow PC referral advice. Based on data from two regional PCs, the decision to refer pediatric patients to the hospital after unintentional cannabis exposure varies greatly. As cannabis products become legalized in the US, more research regarding the appropriate triage and monitoring of unintentional exposures is needed to appropriately utilize both hospital and pre-hospital resources.

Reference

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50. Monitoring intentional self-poisoning exposures reported to the New Zealand National Poisons Centre in 2018-2021: a retrospective study

Eeva-Katri Kumpula[a] and Adam C. Pomerleau[b]

[a]National Poisons Centre, Dunedin, New Zealand; [b]National Poisons Centre, University of Otago, Dunedin, New Zealand

Objective: Poison centres may provide a first point of contact with health services in cases of poisoning, and their datasets can be used to monitor for emerging trends in exposures reported to them. Recently in New Zealand, there has been concern about increasing prevalence of mental health problems among adolescents, and the country's high youth suicide rate [1]. This study aimed to investigate intentional exposures reported to the New Zealand National Poisons Centre (NZNPC) free 24/7 telehealth service, to assess whether there was any evidence of an increase in self-poisoning incidents over time.
Methods: Contacts to the NZNPC from January 2018 to September 2021 were analysed. Records of human patients who had "Intentional" or "Self-harm – Intentional" coded as the reason for the exposure incident were combined as the "Intentional" pool, and all other reasons were combined as an "Other reason" pool. Quarterly numbers of records over time were analysed for both pools, and records were also characterised by age (groups: 13-19, 13-15, 16-17, 18-19, 20-29, 30-39, 40-64, 65 years and over, unknown adult, unknown age) to investigate any age-group specific trends. The quarterly proportion of "Intentional" records of all within the quarters of the investigated years were determined to take into account overall changes in contact numbers over time.
Results: There were 5,811 "Intentional" and 31,394 "Other reason" records identified. No significant changes in the quarterly proportion of "Intentional" was observed for all age groups as a pool, nor for those aged 20 and over, of unknown age, or unknown adults. Records for 13-19 year olds showed an increasing total number and proportion of relevant quarterly records over time. Particularly the "Intentional" proportion of quarterly contacts for those aged 13-15 increased from 33% in Q1 2018 to 56% in Q3 2021, and from 32% to 62%, respectively, for those aged 16-17 years.
Conclusion: There appeared to be an increase in youth intentional self-poisonings reported to the NZNPC over the study period. Reasons underlying this apparent trend are speculative and likely multifactorial; the influence of large societal changes like the COVID-19 pandemic and the increasing use of social media could play a role. The NZNPC should continue to monitor this trend and consider interventions and stakeholder engagement that could help mitigate self-poisoning among adolescents.

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51. The cure may harm - risk of serious poisoning with antidepressants

Johan Hallengren, Lovisa Östberg and Johanna Nordmark Grass

Swedish Poisons Information Centre, Stockholm, Sweden

Objective: Depression increases the risk of self-harm/suicide, including overdose. Overdose of antidepressants may be life-threatening and are healthcare consuming. The objective of this study was to evaluate if different types of antidepressants differ in risks of serious complications in overdose.
Methods: Hospital calls to the Swedish Poisons Information Centre concerning overdoses of antidepressants during 2020 were evaluated. The number of serious cases for each substance were compared to the total number of serious cases concerning antidepressants. Serious cases were defined as cases with severe symptoms (e.g. deep coma, convulsions, respiratory/circulatory failure and death) as well as cases where advanced monitoring was recommended due to risk of developing serious symptoms (considering ingested dose and/or presenting symptoms). In addition, the number of patients treated with each antidepressant per 1000 inhabitants were collected from the national board of health and welfare. A risk index number was defined; the ratio of serious cases was compared to the percentage (for each substance) of the total number of patients treated with antidepressants per 1000 inhabitants. The number 1 (weighted mean) thus indicates that the risk of developing serious symptoms when overdosing on a specific antidepressant is on the average while a number above 1 indicates increased risk.
Results: The total number of cases concerning antidepressants was 1964. Of these 1158 (59%) were defined as serious. The ratio (number) of serious cases of the different antidepressants were: sertraline 24.1% (n = 279), venlafaxine 22% (n = 255), bupropion 14.9% (n = 173), amitriptyline 12.4% (n = 141), mirtazapine 5.4% (n= 62), clomipramine 5.2% (61), escitalopram 4.5% (n= 52), fluoxetine 3.9% (n = 45), citalopram 3.6% (n = 42), and duloxetine 1.8% (n = 21). A total of 125.5 patients/1000 inhabitants were prescribed antidepressants. The risk index numbers for the different antidepressants were: 5.4 (clomipramine), 4.1 (bupropion), 3.1 (venlafaxine), 1.2 (amitriptyline), 1 (sertraline), 0.8 (fluoxetine), 0.4 (escitalopram), 0.4 (duloxetine). 0.3 (citalopram), and 0.3 (mirtazapine).
Conclusion: Serious cases with bupropion, venlafaxine and tricyclic antidepressants (especially clomipramine) were overrepresented in calls to the poisons center when compared to the treatment ratio in the population. This might be caused by an increased toxicity of these drugs and/or a more frequent use in more serious depression. When prescribing antidepressants, the risk of serious complications of overdosing should be considered.

52. Belgian Poison Centre: annual overview 2020

Dominique Vandijck, Jonas Van Baelen, Jonas Moens, Eline Bekaert, Evelien De Smet, Pamela Selway, Régine Pire, Pascale Wallemacq and Anne-Marie Descamps

Belgian Poison Centre, Brussels, Belgium

Objective: This study provides an overview of the number and type of calls received by the Belgian Poison Centre (BPC) in 2020.
Methods: Data of all calls to the BPC (1 January to 31 December 2020) were collected and analyzed using appropriate statistics (SAS).
Results: The BPC received 65,308 calls in 2020 (60,668 in 2019, $p < 0.05$), of which 56,106 (86%) (involving 57,523 victims) were due to an exposure, and 9,202 (14%) were an information request. Despite a minor decrease of 2.3% (21,151 in 2019 versus 20,666 in 2020, $p > 0.05$), the vast majority (35.9%) of exposures were drug-related, of which paracetamol represented 8.2%. Drugs within the category "nervous system" (e.g. antipsychotics, antidepressants, etc.) were most frequently involved (39.6%). There were 11,836 in 2019 versus 12,247 in 2020 ($p > 0.05$). Relating to chemical household products, in the battle against the coronavirus, people bought large quantities and often highly concentrated products, especially products for personal hygiene and cleaning. Poured into smaller containers such as water or soft drink bottles, this led to accidents in which people accidentally drank from the drink container. In an effort to improving cleaning or disinfection, people also started (accidentally) combining or mixing products, with the risk of releasing irritating vapours. Irritation of the mucous membranes and severe shortness of breath were not uncommon. The BPC received 46.1% more calls for bleach and bleach-containing products than in 2019 (835 calls in 2019 compared to 1,220 calls in 2020, $p < 0.05$). A 12.3% increase of cosmetic- and food-related exposures was noted (8,291 in 2019 versus 9,308 in 2020, $p < 0.05$), of which a stable number of exposures (877 in 2019 versus 876 in 2020, $p > 0.05$) were due to essential oils. Exposures to type 1 biocides significantly increased from 322 in 2019 to 1,676 in 2020 ($p < 0.05$), and exposures to type 2 biocides from 406 to 902 ($p < 0.05$). Finally, a 28.2% increase in exposures related to the group "plants, mushrooms and animals" was observed, with 3,256 in 2019 and 4,175 in 2020 ($p < 0.05$).
Conclusion: In its history, the BPC has never received as many calls as in 2020, demonstrating its added value in today's and future healthcare. Trends in both, number and type of exposures were impacted by the COVID-19 pandemic.

53. Epidemiology study of baclofen enquiries to the National Poisons Information Centre of Ireland

Niamh C. Walsh, Sinead Doyle and Edel Duggan

NPIC Ireland, Dublin, Ireland, Republic of Ireland

Objective: To characterise the epidemiology and type of baclofen enquiries to the National Poisons Information Centre (NPIC) in Dublin.
Methods: This study retrospectively examined all cases involving baclofen reported to the NPIC from 1 January 2004 to 31 August 2021, inclusive. Information on enquiry source, circumstance and patient data were collated.
Results: Over 17 years, 196 calls about baclofen were received, involving 179 patients; 54% of enquiries originated from hospitals, 27% from General Practitioner surgeries, 10% from members of the public, 2.5% from nursing homes, 2% from pharmacies, 1.5% from both carers and schools, and 1% from other/support services. The majority of circumstances were intentional (37%). Therapeutic error accounted for 28% and accidental exposures 26%. Almost half of the enquiries (48%) concerned baclofen only, 43% of enquiries were mixed drug overdose (excluding alcohol), 6% were mixed drug overdoses with alcohol and 2% were baclofen and alcohol only. Most exposures were acute (76%), 16% were acute-on-therapeutic exposures, 3.5% were unknown exposure type, 2.5% were staggered, 1.5% were chronic exposures and

<0.5% were subacute. The total number of patients involved was 179; 27.5% of cases were children under 16 years of which 57% were males and 41% were females. In this group 24% were symptomatic; 2 (4%) of these patients had PSS =3 and both recovered fully. These were accidental exposures of baclofen only. Most cases (72%) involved patients aged ≥16 years of which two thirds (67%) were females; 66% were symptomatic. 21% had a PSS =3 and one death was reported. The predominant symptom was somnolence (34 patients) followed by coma (25 patients) and cardiovascular instability (21 patients), with tachycardia and hypotension.
Conclusion: The National Poisons Information Centre in Dublin received 196 baclofen related calls between 2004 and 2021. The majority of calls were acute overdoses in those over 16 years of age. Somnolence was the most common observed feature with in 1 in 7 patients lapsing into a coma.

54. Chronic methanol toxicity through topical and inhalational routes presenting as vision loss: a case report

Wenceslao Kiat
St. Luke's Medical Center, Quezon City, Philippines

Objective: Ingestion is the most common form of toxicity; however, dermal and inhalational exposures also occur but are documented rarely. While acute intoxication is commonly encountered, chronic exposure to methanol should also be highlighted. We report a case of chronic, inhalational exposure to methanol.
Case report: A 57-year-old female presented to the emergency room with progressive dyspnea, metabolic acidosis with high anion gap, and metabolic encephalopathy. After emergency hemodialysis, the patient complained of vision loss in both eyes. Initial non-contrast cranial magnetic resonance imaging (MRI) revealed restricted diffusion of the intraorbital segment of both optic nerves. A thorough history revealed that for more than year she had been applying a clear colorless liquid bought online all over her body for alleged pruritus. The syndrome of metabolic acidosis with high anion gap, metabolic encephalopathy, vision loss, and laboratory findings led us to suspect a diagnosis of chronic methanol poisoning with an acute component. The liquid in question was sent for chemical analysis and was found to be 95.5% methanol.
Conclusion: This case highlights the need for a high index of clinical suspicion for methanol toxicity in the absence of oral consumption, the complications of chronic methanol intoxication, and the uncommon radiologic findings seen in diffusion-weighted imaging (DWI).

55. Auto-intoxication by intravenous administration of a cleaning product: a rare cause of disseminated intravascular coagulation

Lieven De Smedt and Wim Van Paesschen
AZ Sint-Blasius, Dendermonde, Belgium

Objective: Vim Scouring Powder is a cleansing product containing calcite [1], a carbonate mineral and the most stable form of calcium carbonate. Disseminated intravascular coagulation (DIC) is a systemic process in which coagulation and fibrinolysis are disturbed and abnormally activated, thus potentially leading to thrombosis and/or bleeding. It is a dynamic process and has different presentations ranging from an acute life-threatening condition to a subclinical or chronic state. Identification of DIC and the underlying cause are critical for proper management. DIC is diagnosed based on clinical and laboratory findings. Therapy is largely dependent on clinical presentation and the underlying cause [2]. This case report presents a first case of intravenous Vim injection and outlines the importance of understanding the mechanism of action of the injected product.
Case report: A 19-year-old female was admitted to the emergency department after she self-injected 30 mL of Vim (©Spotless Benelux) in a vein of the left forearm as a suicide attempt. At admission she reported a tenderness at the injection site. The only clinical abnormality was a localized redness. Laboratory findings revealed an unmeasurable low fibrinogen (< 0.30 g/L), a prolonged activated partial thromboplastin time (69.6 seconds), a prolonged prothrombin time (International Normalized Ratio 1.52) and significantly increased D-dimer (greater than 2000 ng/mL). She was observed for 24 hours because of the likely diagnosis of disseminated intravascular coagulation (DIC) and supportive therapy was given. After repeated laboratory tests with normalization of coagulation screening tests after 24 hours, she was discharged with psychological follow-up planned.
Conclusion: We presume the Vim induced DIC in this patient. As calcite is converted to bicarbonate, it theoretically could be a cause of disturbance of acid-base homeostasis [3]. Since there was no measurement of arterial blood gas in this patient, we only presume this influence of calcite on the acid-base balance. Intravenous calcite injection can be a rare cause of DIC but following a low dose it could be considered as a self-limiting condition, as illustrated in this case report.

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56. Clinical features and investigative workup following corrosive ingestions in a 10-year cohort

Gopi Mann, Sandakalani Abeywickrama, Tania Lam and Samoda Mudalige
Western Sydney Tox Service, Sydney, Australia

Objective: Our main goal was to determine significant morbidity and mortality in our study cohort comprising corrosive exposures.
Methods: This was a retrospective cohort study of all corrosive ingestions from two toxicology units over a 10-year period (2010 – 2020). Demographic, clinical and investigative data was obtained from two toxicology admission databases.
Results: There were a total of 100 corrosive exposures with a median age of 30 years (range 4 months to 95 years). This study

included 20 exploratory pediatric ingestions (< 16 years). The majority of the exposures involved household bleach products (88%). Overall, 56 patients were symptomatic (oropharyngeal symptoms 28/56, vomiting 25/56 and epigastric pain 20/56). Computerised tomography (CT) scans (chest/abdomen) was carried out in 7 patients and endoscopy in 11 patients (with 3 patients undergoing both). We identified 3 strong acid cases (2 patients exposed to hydrochloric acid and 1 patient exposed to phosphoric acid) and 3 strong alkali cases (2 patients exposed to lye and 1 patient exposed to sodium hydroxide 55%). Five patients underwent intubation (due to airway swelling) of whom 1 required insertion of a feeding jejunostomy tube. Total parenteral nutrition was provided to 3 patients but the majority received supportive care. There were no deaths recorded in this study.
Conclusion: In our study, no patient died from corrosive ingestion over a 10-year period in the two tertiary toxicology units. There were no recorded esophageal perforations and the majority of the patients were managed supportively in parallel with domestic exposures. Only a handful of patients required CT scanning and endoscopy.

57. Accidental methanol poisoning with reversible vision loss in Republic Vilnius University Hospital Toxicology Center

Gabija Valauskaite[a], Haris Jakavičius[b] and Robertas Badaras[b]

[a]Department of Intensive Care Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [b]Clinic of Anaesthesiology and Intensive Care, Faculty of Medicine, Vilnius University; Centre of Toxicology, Republic Vilnius University hospital, Vilnius, Lithuania

Objective: Methanol is a toxic alcohol that is found in industrial and various household products. Severe intoxication with this agent can cause blindness and death [1]. We present and analyse the first ever case of accidental methanol poisoning with reversible vision loss in the Republic Vilnius University Hospital Toxicology Center.
Case report: A 50-year-old man was admitted to the emergency department severely blind after ingesting alcohol and a full bottle of disinfectant fluid with suspected methanol. The patient was conscious, arterial blood pressure 140/97 mmHg, heart rate 108 beats per minute, peripheral oxygen saturation 97%, body temperature 36.7 ^{0}C. Blood biochemistry performed on admission revealed a plasma sodium 136.3 mmol/L, potassium 5.03 mmol/L, glucose 6.56 mmol/l and urea 3.56 mmol/L. Arterial blood gases revealed acidosis with a pH 7.14, PO_2 140 mmHg, PCO_2 10.7 mmHg, bicarbonate 8.0 mmol/L, and base excess -24.5. The blood ethanol concentration was 0.01 g/L. A brain computerised tomography (CT) scan was normal. He was immediately hospitalized to the Toxicology Intensive Care Unit (ICU) and treated by intravenous ethanol and folic acid, and bicarbonate-based dialysis was performed for 6 hours. Arterial blood gases after dialysis were pH 7.367, PO_2 334 mmHg, PCO_2 39.7 mmHg, bicarbonate 22.3 mmol/L, and base excess -2.8. He was discharged from the ICU 28 hours later with stable vital signs. The patient was reviewed by an ophthalmologist, and hemorrhage of the retina, and suspected atrophy of the optic nerve was diagnosed. Later the patient was treated by one session of 1 atm and 4 sessions of 2 atm pressure hyperbaric oxygen therapy. He was discharged from hospital 8 days later in good health and with no clinical evidence of blindness.
Conclusion: We present a successfully treated case of methanol poisoning with no residual clinical symptoms. This case suggests that hyperbaric oxygen therapy could be an effective treatment of methanol-induced optic neuropathy and should be considered in severe intoxication [2].

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58. Neurotoxicity of diethylene glycol in an animal model

Kenneth McMartin, Courtney Jamison, Areli Cuevas-Ocampo, Ashley Flowers, Mary McKinney and Brian Latimer

Louisiana State University Health Sciences Center, Shreveport, United States

Objective: Diethylene glycol (DEG) has produced numerous mass poisonings through its use in error as a solvent in liquid medicines. DEG poisonings are characterized predominately by acute kidney injury (AKI), but also by delayed neurological sequelae such as decreased reflexes, facial drooping and limb weakness. Characterizing the poorly understood peripheral neuropathy of DEG poisonings in an animal model could create a clearer picture of overall toxicity. Although diglycolic acid (DGA) is responsible for the renal toxicity, its role in the neuropathy is not known.
Methods: Wistar Han rats were administered by oral gavage doses of 4-6 g/kg DEG every 12 or 24 hours for 7 days. Endpoint blood and cerebrospinal fluid (CSF) were collected for kidney biomarker and total protein estimation, respectively. Motor function tests were conducted before and after treatment. Kidney, brain, and spinal cord tissue were harvested after euthanasia for pathology analysis.
Results: Of the 43 animals that were treated with DEG, 11 developed AKI primarily in animals dosed every 12 hours. Hematoxylin and eosin (H&E) staining of kidney cortical tissue showed significant necrosis in animals that developed AKI. Renal and brain DGA content markedly increased in animals that developed AKI compared to animals without AKI. Total protein content of CSF in animals with kidney injury was significantly higher compared to control and to animals without AKI, indicating evidence of nervous system damage. Significant decreases in grip strength as well as decreases in locomotor and rearing activity were observed in animals with AKI but not in animals without AKI. Examination of spinal cord tissue revealed demyelination in the dorsal and lateral white matter; no other pathologic changes were noted in nervous system tissue.
Conclusion: These studies indicate that neurotoxicity can be produced in an animal model, that kidney injury needs to occur in order for neurological symptoms to be observed and that accumulation of DGA is important for the peripheral neuropathology.

59. Multiorgan failure after ingestion of acetic acid

Anton Gustafsson[a], Helen Olofsson[b] and Johanna Nordmark Grass[a]

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

Objective: After ingestion of acid compounds the main problem is usually caustic injuries in the gastrointestinal tract. In addition, hypotension may occur, but has usually been considered secondary to severe gastrointestinal trauma. We present a case of multiorgan failure after acetic acid ingestion despite, relatively, mild gastrointestinal injury.
Case report: A 56-year-old female with a history of gastric bypass and hypertension presented at the emergency department 11 hours after ingesting 500 mL of 24% acetic acid. She was awake, cold and clammy. Her blood pressure was 140/118 mmHg, her heart rate 127 and her respiratory rate 36 (beats and breaths per minute, respectively). Venous blood gas analysis upon arrival showed a combined metabolic acidosis and respiratory alkalosis (partly compensatory): pH 7.42, $PvCO_2$ 2.6 kPa, base excess - 9.4 mEq/L, and lactate 4.5 mmol/L. During the following hours, the acidemia worsened, she became hypotensive and developed a respiratory failure requiring 10 L of oxygen. Six hours after hospitalization she was intubated and emergency gastroscopy was performed showing epithelial damage compatible with acid exposure. She remained severely hypotensive requiring norepinephrine and argipressin. Echocardiography showed good cardiac function and she was considered to have a distributive shock. This resolved and 53 hours after intake she was weaned off vasopressors. A follow up computerised tomography (CT) scan showed intestinal inflammation without perforation or ulceration. In addition, she developed hemolysis (haemoglobin 75 g/L, haptoglobin <0.1 g/L) and renal failure demanding dialysis during and after intensive care. Eventually she improved and was discharged from the hospital without further need for renal replacement.
Conclusion: Distinctive for this case is the severe hypotension that, together with the acute hemolysis, may have contributed to the renal failure. However, the caustic injuries were considered too mild to cause the severe multiorgan failure. The patient had a gastric bypass, and this might have caused a faster absorption of acetic acid than expected. Acetate is known to cause hypotension when added to dialysate solutions. Proposed mechanisms involve vasodilatory effects by adenosine and nitric oxide (NO). Adenosine increases as acetic acid is metabolized. Simultaneously, both endothelial and inducible NO-synthetase may be stimulated [1]. In line with these findings, the severe course of this case, may have been mediated by toxicologic effects of acetate.

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60. Exposures to liquid laundry detergent capsules in adults

Anna Celentano, Marcello Ferruzzi, Fabrizio Sesana, Giovanni Milanesi and Francesco Scaglione

ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

Objective: Liquid laundry detergent capsule (LLDC) contains 15/32 mL of highly concentrated surfactants in easy dissolvable polymer membranes. Sometimes the capsules adhere to each other, and in an attempt to detach them, adults can accidentally be exposed to the contents. LLDCs are very attractive to elderly people because they can look like bonbons or fruit juice. We investigated exposure to these products in adults.
Methods: We analyzed our LLDC adult exposures from July 2010 to July 2021 by adult identification, call site, route of exposure, LLDC (by type, colour and accessibility), circumstances of exposure, presented symptoms, management site and medical outcome. Every case was followed up by one or more recalls depending on the severity of the patient and the healing time.
Results: Over the study period, 113 adult exposures to LLDC were collected. Of them, 73 were female, 30 male and 10 were unknown. In 98 cases, follow up was performed; complete follow up could not be obtained for 15 cases. The age distribution was as follows: 29 cases 18-39 years, 17 cases 40-59 years, 21 cases 60-79 years, 26 cases 80-96 years and age unknown in 13 adults. The circumstances of exposure were: the capsule dissolved in the hand (n = 35), while they were separating two or more capsules that were adherent (n = 17), adults with dementia (n = 39), the capsule was cut open (n = 7), intentional exposure (n = 5), and other circumstances (n = 10). Exposure to LLDCs occurred mainly as a result of ingestion alone (n = 48, 42.5%), oral mucosa alone (n = 11, 9.7%), eye contact alone (n = 22, 19.5%), skin contact alone (n = 23, 20.4%), or inhalation (n = 4, 3.5%). Multiple routes of exposure were involved in 4.4% of cases (n = 5). The most frequently reported clinical effects were vomiting, diarrhea, cough, pharyngodynia, ocular pain and inflammation. No symptoms were present in 29 cases; minor symptoms were present in 46 cases, moderate symptoms in 16 cases, severe symptoms in 5 cases and 2 cases were not evaluable. Three elderly patients died.
Conclusion: This study showed that exposures to LLDC present a risk of poisoning not only for children but also for elderly people that ingest the liquid content in larger quantities. LLDC exposures required hospital evaluation more often than other laundry detergent products due to more severe clinical effects. To reduce the risk of elderly accidental exposure it is important to keep the LLDC in a safe place out of sight and reach of elderly people.

61. Orellanus syndrome: a case series with toxicological confirmation in biological matrices

Nathalie Paret[a], Christine Tournoud[b], Nathalie Jarrier[a], Guillaume Grenet[a] and Estelle Flament[c]

[a]Poison Control Center of Lyon; Hospices Civils de Lyon, Lyon, France; [b]Poison Control Center of Nancy; University Hospital, Nancy, France; [c]Laboratoire LAT LUMTOX, La Voulte-sur-Rhône, France

Objective: Orellanus syndrome may lead to the development of irreversible renal failure. We describe three cases of *Cortinarius* mushroom poisoning in August 2021 in France. For each case, the presence of orellanine in biological matrices was been confirmed by analytical evidence.
Case series: Case 1: A 44-year-old woman was admitted to the Emergency department (ED) with acute renal failure (ARF) (blood creatinine 1100 μmol/L) and anuria occurring 4 days after eating *Cortinarius* instead of edible mushrooms. The patient had experienced severe vomiting and diarrhea at 12 hours. She was treated (from Day 5) with hemofiltration then hemodialysis 3 days a week without improvement of renal function. Persistent anemia (6 g/dL) required erythropoietin administration and blood transfusion. Hemodialysis was still ongoing 2 months later for chronic renal failure (CRF). Case 2: A 41-year-old man was admitted to the ED along with his wife (case 1) for dysuria occurring at Day

4. Abdominal pain and vomiting had started at 25 hours. At admission, blood creatinine concentration was 1200 μmol/L. Hemodialysis was performed for a total of 7 sessions until Day 12. Two months later, renal failure was persisting (creatinine 295 μmol/L; glomerular filtration rate (GFR) 22 mL/min). Case 3: A 72-year-old woman was hospitalised with ARF (creatinine 1540 μmol/L; potassium 6.8 mmol/L) 13 days after eating mushrooms confounded with *Cantharellus cibarius*. Renal biopsy revealed tubulointerstitial nephritis that is consistent with orellanus syndrome. The patient experienced anorexia, vomiting and oligoanuria. She was discharged one month later with chronic renal failure (creatinine 968 μmol/L; GFR 3 mL/min). Hemodialysis, performed 3 days a week since hospitalization, was continued. Analytical analysis: In order to confirm the diagnosis of orellanine poisoning, whole blood, plasma and urine samples from these patients were analysed using a liquid-chromatography method with high-resolution mass spectrometry detection. This analytical method, validated in the three human biological matrices mentioned above, allowed orellanine identification in all samples for each case presented except in whole blood in case 2 (not detected). Concentrations of orellanine were very low (near or below the lower limit of quantification) because of the long latency period of the syndrome that induced a long lapse of time between the ingestion of the mushrooms and the sampling.
Conclusion: Orellanus syndrome is a rare but lesional mycotoxidrome that can lead to severe poisoning with sequelae as in our patients. The method of detection of orellanine is the first validated in biological matrices.

62. Two cases of severe *Taxus baccata* poisoning treated with extracorporeal membrane oxygenation (ECMO)

Angelika Holzer[a], Kinga Bartecka-Mino[a], Tara Arif[a], Philipp Vyhnanek[b], Martin Röggla[c] and Dieter Genser[a]

[a]Poisons Information Centre, Vienna, Austria; [b]University Hospital St. Pölten, St. Pölten, Austria; [c]Vienna General Hospital, Medical University of Vienna, Intensive Care Unit, Vienna, Austria

Objective: Yew (*Taxus baccata*) is an evergreen tree native to Europe. All parts of the plant are poisonous, except for the red pulp of the "berry". The yew alkaloids, taxines, are primarily cardiotoxic. There are few therapeutic options for severe *Taxus baccata* poisoning, and we report two cases with cardiac arrest and resuscitation, that were treated with extracorporeal membrane oxygenation (ECMO).
Case reports: Case 1. An 18-year-old man attempted suicide by ingesting 60 g of yew needles after searching the Internet for a lethal dose. Feeling uncomfortable, he called the ambulance and was taken to the nearest hospital. During the transport, he developed a broad complex tachycardia and resuscitation was started. He needed several defibrillations and was intubated. In the emergency room he was treated with gastric lavage and activated charcoal. His condition gradually worsened. He showed a broad complex bradycardia and was brought to a specialised hospital for ECMO. A venous-arterial extracorporeal membrane oxygenation (VA-ECMO) was implanted quickly in the right femoral vein and artery. Initially the patient received high doses of catecholamines. After several hours he developed a broad complex bradycardia again, with a hyperkalaemia of 6 mmol/L, so a hemofiltration catheter was implanted over the right jugular vein. The patient stabilised as the potassium concentration normalized. The next day he had sinus rhythm again with prolonged QRS duration of 160 ms. Catecholamines were reduced, and the ECMO flow was reduced. The following day, ECMO was explanted and the patient extubated. After 5 days, he was transferred to a psychiatric unit. Case 2. A 27-year-old woman boiled and drank 115 g of yew needles in a suicide attempt. She was found comatose and was transported to the hospital. In the emergency room she developed arrhythmias and had to be resuscitated. A LUCAS® CPR device (mechanical chest compression device) could not be used because the patient was too slim and VA-ECMO was implanted. A temporary pacemaker was installed because she developed various arrhythmias. On the following day the ECMO thrombosed and had to be explanted. The circulation normalised, and she had a good neurological outcome.
Conclusion: In severe yew poisoning cardiac complications often cause a fatal outcome. Arrhythmias may be refractory to the usual symptomatic treatment. As shown in these cases, ECMO is a promising therapeutic option to bridge the period of the most severe cardiac arrhythmias for a few days.

63. Cooperation in antidote administration in a case of death cap (*Amanita phalloides*) mushroom poisoning

Marianne E.C. Leenders, Henneke N. Mulder-Spijkerboer and Dylan W. de Lange

Dutch Poisons Information Center/University Medical Center Utrecht, Utrecht, Netherlands

Objective: We report a case demonstrating good cooperation between the poisons center and the treating physician involving the use of silibinin in the management of amatoxin poisoning.
Case report: A healthy 18-year-old male, in an institution, took a bite of a death cap mushroom while on an evening walk. He knew the mushroom and confessed he ate it intentionally. From pictures of the consumed mushroom a mycologist confirmed it was *Amanita phalloides*. At the institution, vomiting was induced and he was admitted to a hospital. On admission, he complained of abdominal pain. The attending physician contacted the Dutch Poisons Information Center (DPIC), who advised immediate administration of activated charcoal with laxative and N-acetylcysteine (NAC). Silibinin was recommended and ordered through the DPIC. NAC was not started since a bolus dose of 470 mg silibinin could be given that night at 2:45 a.m. (day 1). He then received silibinin by continuous infusion (2000 mg/24 h, 20 mg/kg/24h). Next day he still had abdominal pain, but no liver function abnormalities. The DPIC was contacted again and advised continuing the silibinin for at least 48 hours because of the known delay in liver function deterioration in amatoxin poisoning. The DPIC advised renewed administration of activated charcoal with laxative. On consecutive days, the DPIC was contacted and antidote dispatched twice more. In total 28 ampoules (9800 mg) of silibinin were sent, of which the patient received approximately 8000 mg in 96 hours. The severe abdominal pain improved and liver abnormalities resolved (Table 1). There were no coagulopathy. After 5 days he was transferred to the psychiatric ward.
Conclusion: Though the intake was limited and the patient vomited, this case shows a clear picture of amatoxin toxicity. Close contact between the DPIC and the hospital physician about the dose and duration of silibinin administration lead to a favorable outcome.

Table 1. Laboratory parameters in a patient with *Amanita phalloides* poisoning treated with silibinin.

	Day 2 morning	Day 2 evening	Day 3 morning	Day 3 evening	Day 4 morning
Alanine aminotransferase	420	898	1151	1071	858
Aspartate aminotransferase	324	576	504	374	233
Lactate dehydrogenase	371	604	462	322	226
Alkaline phosphatase	92	–	–	–	–
Gamma-glutamyl transferase	17	–	16	–	–
Bilirubin	–	–	29	25	20
Prothrombin time	–	15	16	17	–

64. Anticholinergic poisoning associated with frozen spinach

Silvia Plackova, Blanka Caganova, Olga Otrubova, Erik Puchon and Igor Batora

National Toxicological Information Centre, Department of Occupational Medicine and Toxicology, University Hospital Bratislava, Faculty of Medicine Comenius University, Bratislava, Slovakia

Objective: In some countries the Thursday before Easter is called Green Thursday according to the Christian calendar, and in this tradition, a green meal should be eaten on this day to ensure good health throughout the coming year. A few days before Easter the National Toxicological Information Centre (NTIC) registered an increased number of toxicological consultations following consumption of deep-frozen spinach puree which was sold in retail chains throughout Slovakia. Symptoms were characteristic of tropane alkaloid intoxication and experts suspected the spinach was contaminated with Jimson weed (*Datura stramonium*).
Methods: A retrospective analysis of all telephone calls concerning frozen spinach products from the database of the NTIC from 1 March 2021 to 30 April 2021 was conducted.
Results: The NTIC received 93 telephone calls from people who had consumed frozen spinach, of which 64 people (7 children) had mild symptoms of intoxication (PSS1) and 5 moderate poisoning (PSS2). The most commonly reported symptoms were malaise, dizziness, dry mouth, mydriasis and blurred vision that appeared within 1 to 2 hours after ingestion. Patients with moderate symptoms of intoxication were confused, disoriented and had hallucinations. The symptoms disappeared spontaneously within 48 hours. The country was in a state of emergency that had been declared before Easter due to COVID-19 and people were afraid to attend hospitals. Therefore, only 7 out of 69 people with symptoms arrived in hospital. Only 3 patients were hospitalised. Treatment was symptomatic, without the administration of an antidote physostigmine. The other patients were treated at home. Unfortunately, an increased number of consultations was recorded on Good Friday afternoon, when it was very difficult to initiate a wide scale alert informing the public through the media. Over the Easter weekend, the NTIC alerted the public to avoid the contaminated spinach via social media and the NTIC website. The State Veterinary and Food Administration of the Slovak Republic arranged analyses of contaminated frozen spinach samples in an accredited laboratory and this confirmed the presence of atropine and scopolamine.
Conclusion: *Datura stramonium* grew with spinach in the field as a weed and contaminated the spinach due to insufficient entry and exit controls. As a result of promptly spreading information and informing the public about the contaminated spinach product in the media, further cases of poisoning over the Easter holidays were successfully averted.

65. Characteristics of emergency department presentations following *Taxus baccata* ingestion

Vanessa A. Bütler[a], Alexandra M. Braunshausen[b], Jolanta Klukowska-Rötzler[b], Stefan Weiler[a], Aristomenis K. Exadaktylos[b] and Evangelia Liakoni[a]

[a]Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [b]Department of Emergency Medicine, Inselspital, University Hospital Bern, University of Bern, Bern, Switzerland

Objective: Yew (*Taxus baccata*) poisoning can cause cardiotoxicity through calcium and sodium channel blocking mediated by the plant's alkaloids (taxines), with fatal cardiogenic shock in some cases [1]. Current knowledge regarding poisoning characteristics and treatment options is limited to few case reports and post-mortem analyses. We investigated emergency department (ED) presentations after yew poisoning to identify risk groups and contribute to optimizing treatment and prophylactic measures.
Methods: Retrospective analysis of cases ($\geq$ 16 years of age) presenting at the ED of the University Hospital of Bern, Switzerland, from May 2012 to May 2020 following yew exposure. Cases were retrieved from the electronic patient database using full-text terms.
Results: During the study period 55 cases (11 patients presenting 1-36 times) of the 350,381 ED attendances were included. Eight patients (73%) were <30-years-old (median age at presentation 20 years, range 16-48) and all were female. In intentional cases (n = 54, 98%) all patients had a documented psychiatric disorder and the reported median ingested amount (n = 40) was 193 leaves (range 7-1000). Common symptoms were gastrointestinal disturbances (n = 31), neurological (n = 8) and cardiovascular symptoms (n = 5); the most frequent clinical findings were tachycardia (n = 20) and hypotension (n = 14). Pathological electrocardiogram (ECG) findings were documented in 3 of the 23 cases in which an ECG was performed. There were no cases with allergic or anaphylactic reactions. In 52 cases (95%) gastroscopic extraction of the leaves was performed, with application of activated charcoal in 22 of these and one additional case (42% total). There were no fatalities. One patient developed severe polymorphic ventricular arrhythmia and subsequent cardiac arrest after ingestion of approximately 150 yew leaves within a 3 hour period and was treated with activated charcoal, sodium bicarbonate, intravenous lipid emulsion, gastroscopic extraction of few leaves 4 hours after the last ingestion, cardiopulmonary resuscitation and extracorporeal membrane oxygenation. The majority of patients (n = 40) were observed in the ED and then admitted to a psychiatric institution (n = 35) or discharged (n = 5). Fourteen were observed in intensive care then admitted to a psychiatric institution (n = 5) or discharged home (n = 4) or to an unspecified location (n = 5). One patient was discharged

home without observation or treatment (after ingestion of one leaf).
Conclusion: ED presentations after yew intoxication appear to be rare, but potentially life-threatening and commonly observed in the context of suicidal attempts by young female patients with underlying psychiatric diseases. In this case series, gastroscopic extraction and activated charcoal application were commonly performed and there were no fatalities.

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66. Intentional self-poisoning with plants: a 19-year-retrospective from the Marseille Poison Control Center

Romain Torrents[a], Julien Reynoard[b], Mathieu Glaizal[b], Corinne Schmitt[b], Katharina von Fabeck[b], Audrey Boulamery[b], Luc de Haro[b] and Nicolas Simon[a]

[a]Aix Marseille Univ, APHM, INSERM, IRD, SESSTIM, Hôpital Sainte Marguerite, Clinical Pharmacology and Poison Control Centre, Marseille, France; [b]APHM, Hôpital Sainte Marguerite, Clinical Pharmacology and Poison Control Centre, Marseille, France

Objective: In some areas of the world, intentional plant poisoning causes high morbidity and mortality [1,2]. We wanted to check if this was the case, especially with local plants found in southern France. The aim of the study was to describe plant poisoning through the Marseille Poison Control Center (PCC) experience from 2002 to 2020.
Methods: A retrospective study of enquiries compiled by the Marseille PCC between January 2002 and December 2020. Our center covers the entire French Mediterranean coast, Corsica and Indian Ocean. In all cases, severity was evaluated using the Poison Severity Score (PSS).
Results: There were 275 cases (Table 1). The most common plant was *Nerium oleander* which was involved in more than half of the cases. Other common plants were *Datura* sp. and *Ricinus communis*. There were 4 fatal cases, all involving *Nerium oleander*. Almost all patients were hospitalized, but few of them had serious clinical features and only 19 received antidotal therapy.
Conclusion: *Nerium oleander* is a widely distribution endemic Mediterranean plant containing cardiac glycosides. There are no guidelines for antidote use in *Nerium oleander* poisoning, but it would be useful to develop protocols for the management of *Nerium oleander* poisoning.

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67. Identification of mushrooms from pictures by mycologists versus an online identification tool: a comparison

Jonas Moens, Jonas Van Baelen, Dominique Vandijck and Anne-Marie Descamps

Antigifcentrum, Neder-Over-Heembeek, Belgium

Objective: The objective of this study was to verify if mushrooms responsible for exposure calls to the Belgian Poison Centre and French Poison Centres could be identified with pictures taken by the victim himself or by bystanders using an online identification tool (OIT).
Methods: The original pictures were first identified by a mycologist and then by an OIT (i.e. www.waarnemingen.be). The OIT identified the mushrooms in the pictures in a first phase without further editing and in a second phase after resizing the pictures in order to optimize identification. If the OIT yielded an identification with a certainty of 66.7% or more, the identification was considered to be reliable. The study was performed from 10 to 24 October 2020.
Results: From the original pictures, 162 mushrooms, of which 38.9% (n= 63/162) are known to be toxic, were included. Without editing the pictures, 8.0% (n = 13/162) of the mushrooms yielded a reliable identification, which was correct for 76.9% (n = 10/13) of all identified mushrooms. After resizing of the pictures, 31.5% (n = 51/162) of the mushrooms yielded a reliable identification, which was correct for 52.9% (n = 27/51) of all identified mushrooms. If the mushroom was known to be toxic, 28.6% (n = 18/63) yielded a reliable identification and 50.0% (n = 9/18) of these mushrooms were correctly identified along with 44.4% (n = 8/18) that were incorrectly identified as a non-toxic or an edible mushroom. One toxic mushroom was wrongly identified as another toxic mushroom. Of the mushrooms known to be non-toxic, 33.3% (n = 33/99) yielded a reliable identification with 72.7% (n = 24/33) correctly identified as well as 27.3% (n = 9/33) that were incorrectly identified. One of these was wrongly identified as a toxic mushroom.
Conclusion: This study confirms the added value of mycologists, in addition to the toxicological experts working at a Poison Centre, in the correct identification of mushrooms in case of an exposure. Although an OIT might be helpful in some cases, risk assessments based only on the identification of mushrooms by

Table 1. Main characteristics of the plants involved in self-poisoning reported by the Marseille PCC between January 2002 and December 2020.

Plants involved	N (%)	Symptomatic cases	Severe poisoning (PSS =3)	Fatal (PSS =4)	Antidote use
Nerium oleander	172 (62.6%)	134	33	4	19
***Datura* species**	11 (4%)	10	3	0	1
Ricinus communis	10 (3.6%)	5	1	0	0
Taxus baccata	5 (1.8%)	1	0	0	0
Digitalis purpurea	4 (1.3%)	2	0	0	0
Aconitum napellus	4 (1.3%)	4	1	0	0
Myristica fragrans	4 (1.3%)	4	0	0	0
Pyracantha coccinea	3 (1.1%)	2	0	0	0
Other plants (maximum 2 each)	63 (23%)	14	1	0	0
Total	**275**	**176**	**39**	**4**	**20**

an OIT can be misleading. Good relations, mutual appreciation and communication between Poison Centres, clinical toxicologists and mycologists should therefore be strongly encouraged and supported.

68. *Cortinarius rubellus* poisoning in Estonia: a case series

Vladislav Mihnovitš[a], Kristiina Põld[b] and Raido Paasma[c]

[a]Tartu University Hospital, Tartu, Estonia; [b]North Estonia Medical Centre, Tallinn, Estonia; [c]Pärnu Hospital, Pärnu, Estonia

Objective: *Cortinarius rubellus* is a mushroom containing the nephrotoxic substance orellanine, which is stable at high and low temperatures. Orellanine is highly selective to renal tissue and ingestion of only few mushrooms seems to be enough to make victims depend on dialysis for the rest of their lives. The toxin had been shown to inhibit synthesis of macromolecules, such as proteins, RNA, and DNA, interrupt the production of ATP and produce free radicals and therefore oxidative stress [1]. We report 7 cases of orellanine toxicity due to *Cortinarius rubellus* ingestion in Estonia in August 2020 (Table 1).
Case series: Four foreign workers (Cases 1-4) were sequentially hospitalized with acute kidney injury (AKI) caused by ingestion of mushrooms, later identified as *Cortinarius rubellus*. Three of them were hospitalized with weakness, stomach pain, diarrhea, and oligoanuria 6 to 11 days after ingestion. The first symptoms appeared 3-4 days after ingestion. Blood tests revealed AKI, hyperkalemia and metabolic acidosis. Treatment with intermittent-hemodialysis (IHD) was initiated. To this date their renal function has not recovered necessitating regular renal replacement therapy (RRT). The fourth coworker was asymptomatic, but was hospitalized for evaluation. Her blood test also revealed AKI, but she had normal diuresis and did not require RRT. At the same time, in a different hospital, a married couple (Cases 5 and 6) was hospitalized a week after ingestion with weakness, vomiting, diarrhea, and oligoanuria lasting for 4 days. Their blood tests also revealed AKI, hyperkalemia and metabolic acidosis. Treatment with IHD was started. A 58-year-old woman needed RRT for 5 months and her 66-year-old husband for 6 months before their renal function stabilized. Lastly, a 33-year-old male (Case 7) presented with similar symptoms: weakness, vomiting and stomach pain, 5 days after eating *Cortinarious rubellus* mushrooms. His blood tests also revealed AKI, hyperkalemia and metabolic acidosis. Treatment with IHD was started and lasted for 10 months before the renal function stabilized.
Conclusion: *Cortinarius rubellus* is a mushroom containing orellanine, a substance that can cause acute and chronic renal injury requiring dialysis or transplantation.

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69. Performance of two mushroom identification applications for pictures of poisonous mushrooms

Sarah Mahonski, Joshua Bloom and William Chiang

Division of Medical Toxicology, Ronald O. Perelman Department of Emergency Medicine, NYU Grossman School of Medicine, New York, United States

Objective: Poison centers are consulted for advice on management of mushroom poisoning [1]. Poisoning results from misidentification of mushrooms during foraging or from unintentional ingestion in children. Mushroom identification is performed through consultation with a mycologist but is not always available in real time. Recently, mushroom identification applications using artificial technology have become available. It is unclear how accurate these applications are on identification of poisonous mushrooms. This study aims to evaluate the accuracy of several mushroom identification applications specifically for poisonous mushroom identification.
Methods: Images of poisonous mushrooms and poison mushroom mimics of toxicological significance were identified in a comprehensive mushroom textbook [2]. Two popular applications in the Apple App Store were used: Picture Mushroom and Mushroom Identificator. These were chosen because they are free and allow for unlimited identification of mushrooms per day. Identification of each mushroom was performed once. Picture Mushroom provides the most likely result, as well as two other options. Mushroom Identificator provides the most likely result and four other possibilities.
Results: Picture Mushroom correctly identified the genus and species as most likely result in 30 out of 76 photos (39%) and

Table 1. Initial blood tests in patients hospitalized after ingestion of *Cortinarius rubellus*.

Case number	Patient age, sex	Serum creatinine (μmol/L) and BUN (mmol/L)	eGFR (ml/min/1,73m^2)	pH and base excess (mmol/L)	Potassium (mmol/L)
Case 1	45, F	S-C 949 BUN 25.3	4	pH 7.289 BE -10.7	4.8
Case 2	47, M	S-C 1600 BUN 31.7	3	pH 7.252 BE -13.4	7.5
Case 3	46, M	S-C 2025 BUN 32.0	2	pH 7.25 BE -16.0	6.2
Case 4	46, F	S-C 243 BUN 14.6	20	N/A	5.3
Case 5	58, F	S-C 1703 BUN 48.4	2	pH 7.41 BE -4.2	4.6
Case 6	66, M	S-C 1927 BUN 58.0	2	pH 7.3 BE -13.6	8.0
Case 7	37, M	S-C 914 BUN 26.6	6	pH 7.3 BE -9.1	5.7

Abbreviations: F female; M male; BUN blood urea nitrogen; eGFR estimated glomerular filtration rate; BE base excess; N/A not available; S-C serum creatinine.

the correct genus in 62/76 photos (81%). The correct genus and species were listed as a possibility in 44 out of 76 (57%) and correct genus only in 69/76 (91%). Mushroom Identificator identified the correct genus and species as the most likely result in 26 out of 76 (34%), and the correct genus only in 52 out of 76 (68%). Within all the possibilities, Mushroom Identificator identified the correct genus and species in 38 out of 76 (50%) and genus only in 63 out of 76 (83%). Genus was identified correctly in highly concerning species containing cyclopeptides, including *Amanita bisporigera, Amanita phalloides, Amanita virosa,* and *Galerina autumnalis*. When these mushrooms were misidentified, suggested species also contained cyclopeptide toxins.
Conclusion: Both Picture Mushroom and Mushroom Identificator performed poorly for prediction of the correct genus and species. Both applications were able to identify at least the correct genus as a possible result with over 80% accuracy. Picture Mushroom was superior compared with Mushroom Identifier.

References

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70. Is there a risk of severe morel poisoning? A retrospective study from the French Poison Control Centres between 2010 and 2020

Laurine Le Visage[a], Laurène Dufayet[b], Dominique Vodovar[c], Hervé Laborde-Castérot[d], Weniko Caré[e], French PCC Research Group[a], Robert Garnier[a] and Jérôme Langrand[d]

[a]Centre Antipoison de Paris, Fédération de Toxicologie (FeTox), APHP, Hôpital Lariboisière-Fernand-Widal, Paris, France; [b]Urgences Médico-Judiciaires, Hôtel-Dieu, APHP; INSERM UMR-S 1144, Université de Paris; UFR de Médecine, Université de Paris, Paris, France; [c]Centre Antipoison de Paris, Fédération de Toxicologie (FeTox), APHP, Hôpital Lariboisière-Fernand-Widal; INSERM UMR-S 1144, Université de Paris; UFR de Médecine, Université de Paris, Paris, France; [d]Centre Antipoison de Paris, Fédération de Toxicologie (FeTox), APHP, Hôpital Lariboisière-Fernand-Widal; INSERM UMR-S 1144, Université de Paris, Paris, France; [e]Service de Médecine Interne, Hôpital d'Instruction des Armées Bégin, Saint-Mandé, France

Objective: In France, mushrooms and in particular morels are very frequently consumed [1]. In 2020, the Paris Poison Control Centre (PCC) reported two cases of lethal poisoning with morels. In these cases, the incriminating agent was dehydrated morels from Asia. As such severe clinical presentations have never been reported before [2,3], it was decided to carry out a retrospective study of morel poisoning reported to French PCCs between 2010 and 2020.
Methods: Cases of morel exposure were extracted from the French National Database of Poisonings (FNDP) between 2010 and 2020. We reviewed all cases of morel exposure in order to find similar severe clinical presentation, using the Poison Severity Score (PSS) [4] to grade severity.
Results: During the study period, 446 cases of morel exposure were reviewed. For 43% of them, the origin of the morel was harvesting compared to 37% of commercial origin. All harvesting cases were classified as PSS1 or PSS2, corresponding to a mild symptomatology with a favorable evolution. Ten cases (2%) were classified as PSS3 or PSS4 (severe symptoms or death). Of these 9/10 of them concerned cases were the origin was commercial, and one was undetermined. The majority of severe cases present a similar symptomatology: profuse diarrhea and vomiting, sometimes associated with gastrointestinal injury, followed by hypovolemic shock that may lead to death.
Conclusion: These severe morel intoxications appeared in parallel with the arrival of imported morels from Asia into French territories [5]. Moreover, for 3/10 severe cases, a certainty on the Asian origin of the morels was confirmed. For three other cases, there is a strong suspicion on the origin because of the dehydrated form of the mushrooms. These data raise the question of toxicity specific to this new morel cultivation process and would require further investigation to ensure the safe consumption of these cultivated morels.

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71. Severe gastroenteritis without acute hepatitis in three patients after *Amanita phalloides* ingestion

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

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

Objective: Since historical times, ingestion of *Amanita phalloides* (death cap) and other amatoxin-containing mushrooms have been well known to cause severe poisoning with acute hepatitis and potentially lethal liver failure. It is said that Julia Agrippina, Caligula's sister and Nero's mother, poisoned her third husband, emperor Claudius, with a meal of *A. caesarea* (Caesar's mushroom) served with *A. phalloides* juice. After intestinal absorption, organic anion–transporting polypeptide OATP1B3 and bile acid Na+-taurocholate cotransporting polypeptide (NTCP) are the transporters of amanitins (bicyclic thermoresistant octapeptides) in the liver. Their toxic mechanisms include RNA polymerase II inhibition and oxidative stress generation, leading to hepatic cell apoptosis and necrosis. One mushroom (about 10 g) can be lethal for a 70 Kg patient.
Case series: A cluster of three patients (75-year-old female, 44-year-old male and 43-year-old female; mother, son and daughter) arrived at our Emergency Department with acute gastroenteritis 20 hours after ingestion of cooked mushrooms, peppers and

potatoes. The two mushrooms were collected, for the first time, by the mother in the woods near home. Emesis and diarrhea appeared after 7 hours in the mother, and 12 hours in brother and sister. In hospital only diarrhea was still present for all patients. Aggressive treatment with gastric lavage, multiple-dose activated charcoal and high-volume infusions (100 mL/Kg/day) was immediately started. No antidotes are used in our protocol. Urine was collected for amanitins before starting the infusion, and were positive with 40, 22 and 26 ng/mL respectively. Mycological evaluation confirmed *A. phalloides*. Mild increases in arterial pressure with tachycardia were observed in all three. Laboratory tests showed neutrophil (80-90%) leukocytosis (14.27 to 14.92 x 10^9/L) and hemoconcentration (hematocrit 49.3 to 53.6%). Coagulation, hepatic and renal tests were normal. In the following three days, the diarrhea completely resolved, and only a mild elevation of ALT (70, 65 and 151 U/L, respectively) and AST (66, 50 and 144 U/L, respectively) were observed. The patients were discharged home 4 days after the ingestion of a potentially lethal dinner.

Conclusion: Our case report describes a very lucky evolution after ingestion of *A. phalloides* mushrooms. The severe gastroenteritis and the minimal hepatic effect can be possibly explained with a low dose of amanitins even with moderate urinary concentrations. Otherwise, genetic polymorphism of hepatic transporters or RNA polymerase II, or interfering substances (e.g. amanullin) in the meal could be an alternative hypothesis. In any case, aggressive treatment is essential for amanitins poisoning management.

72. Three episodes of aconitine poisoning in one patient over the course of one week

Henning Wimmer[a], Mari A. Bjørnaas[b], Rami Abushaar[c], Arne Helland[d], Merete Vevelstad[e] and Dag Jacobsen[f]

[a]Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [b]The Norwegian CBRNE Centre of Medicine, Department of Acute Medicine, Oslo University Hospital, Oslo, Norway; [c]Department of Acute Medicine, Oslo University Hospital, Oslo, Norway; [d]Department of Clinical Pharmacology, St. Olavs University Hospital, Trondheim, Norway; [e]Department of Forensic Science, Oslo University Hospital, Oslo, Norway; [f]National Poisons Information Centre, Norwegian Institute of Public Health, Oslo, Norway

Objective: Aconitine is a highly toxic plant toxin, and ingestion of aconitine-containing plants may induce severe or fatal poisoning with mainly neuro- and cardiotoxic effects. Due to variable aconitine content in different plants, it is difficult to estimate the toxic dose when these plants are ingested. We present a self-poisoning case with ingestion of increasing amounts of Carmichael's monkshood (*Aconitum carmichaelii*), with different clinical presentations during the same week.

Case report: An 18-year-old female was admitted to hospital 4 hours after ingestion of 3 leaves of Carmichael's monkshood. She presented asymptomatic except for transient nausea. The electrocardiogram (ECG) was normal. She refused activated charcoal. She developed bradycardia (40/min) with SA-block but stable blood pressure 13 hours after ingestion. After ECG normalization 30 hours after ingestion, she was referred to the psychiatric department. She was readmitted three days later due to a renewed ingestion of 6 leaves of another plant of the same species. She was administered 30 g of activated charcoal 90 minutes after ingestion. No neurological or cardiovascular features occurred, apart from an initial QRS of 93 ms compared to 80 ms on earlier ECGs. She was discharged the next day but on the day of discharge she ingested a whole Carmichael's monkshood plant leading to readmission to our intensive care unit (ICU). She refused all treatment and was therefore sedated and intubated on vital indication. Some plant residue was removed by gastric lavage, and activated charcoal was administered. About 14 hours after ingestion she developed AV-block (3rd degree) requiring a temporary pacemaker, which was removed the next day. She recovered without sequelae. Aconitine was detected in the urine but not in the blood sampled 2.5 hours after ingestion on the 2nd admission. The failure to detect aconitine in blood may be due to spontaneous degeneration during a long transport time of the sample.

Conclusion: Aconitine poisoning may induce serious cardiovascular manifestations up to 14 hours after ingestion with need for ICU treatment. Our patient developed bradycardia and SA-block after ingestion of 3 leaves while she was asymptomatic after ingestion of 6 leaves. This might be related to activated charcoal given early after the 2nd ingestion, or to varying aconitine content in different plants. Detection of aconitine in blood depends on early sampling and prompt analysis due to its short half-life and instability, while it seems to be detectable in urine for a longer period of time.

73. Circulating miRNAs as early markers of amatoxin-containing mushroom poisoning

Marco Cirronis[a], Elisabetta Bigagli[b], Francesca Luceri[c], Nicoletta Cini[c], Lorenzo Cini[b], Mario D'Ambrosio[b], Valeria M. Petrolini[d], Guido Mannaioni[b] and Cristina Luceri[b]

[a]Poison Control Center and National Toxicological Information Center, Maugeri IRCCS Clinical Scientific Institutes, Pavia, Italy; Department of NEUROFARBA, University of Florence, Florence, Italy; Bergamo Poison Control Center & Teratology Information Service, ASST Papa Giovanni XXXIII Hospital, Bergamo, Italy; [b]Department of NEUROFARBA, University of Florence, Florence, Italy; [c]General Laboratory, Department of Services, Careggi University Hospital, Florence, Italy; [d]Poison Control Center and National Toxicological Information Center, Maugeri IRCCS Clinical Scientific Institutes, Pavia, Italy

Objective: Amatoxin-containing mushrooms (ACM) are responsible for 90% of death following mushrooms poisoning. ACM poisoning is suspected when gastrointestinal symptoms arise at least 6 hours after mushroom ingestion and it is confirmed by detection of α-amanitin in urine. However, symptoms are not specific, mushrooms are seldom recognized and analysis of α-amanitin is not readily available in all laboratories [1]. We investigated whether urinary microRNA (miRNA) analysis can be used in early diagnosis of ACM poisoning.

Methods: In a first phase, 11 miRNAs associated with liver injury were analyzed in serum and urine of 6 ACM poisoned patients and 6 healthy control subjects. In the experimental phase of the study, HepG2 human hepatocarcinoma cells were treated with a sub-toxic concentration of α-amanitin with evaluation of cytotoxicity, changes in viability and cell cycle after 24, 48, 72 and 96 hours of exposure.

Results: Two circulating miRNAs, miR-320 and miR-155, were over-expressed in samples collected from poisoned patients, and poorly expressed or absent in the serum/urine of the control group. The two miRNAs were investigated in a second group of cases, in 14 sera and 10 urine samples from patients with ACM poisoning and confirmed the same trend observed in the first phase. The HepG2 cells show a notable decrease in vitality after

24 hours of exposure to α-amanitin, a decrease which remained constant for up to 96 hours; after 24-48 hours of exposure, about 25-30% of the cells died and after 72-96 hours, the number of live cells was almost completely reduced. Cytotoxicity data suggest that after 24-48 hours of exposure to α-amanitin, the cells go into arrest, but remaining alive, but when the exposure is prolonged they are unable to survive. The two miRNAs identified in the human study were measured both in the cells and in the culture medium, after 24 and 48 hours of exposure, associating the results obtained with the gene expression profiles of the cells in order to identify the biological processes controlled by the two miRNAs.
Conclusion: miR-320 and miR-155 appear to be good candidates for the diagnosis of ACM poisoning. Inflammatory processes and the corresponding miRNA, prevail in the early stages when hepatocytes go into arrest but are still alive following amatoxin exposure. Treatment should start within 48 hours of ingestion of amatoxins to avoid irreversible cells death, hence measurement of miRNAs could help in early diagnosis.

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74. Comparing bedside coagulation assays for detecting venom-induced consumption coagulopathy following viper bites in Sri Lanka

Supun Wedasingha[a], Geoffrey K. Isbister[b], Sisira Siribaddana[a], Kanishka Seneviratne[c] and Anjana Silva[a]

[a]Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura, Sri Lanka; [b]Clinical Toxicology Research Group, School of Medicine and Public Health, University of Newcastle, New South Wales, Australia; [c]Emergency Treatment Unit, Teaching Hospital Anuradhapura, Anuradhapura, Sri Lanka

Objective: Practical bedside tests for detecting venom-induced consumption coagulopathy (VICC) are important in developing settings, due to unaffordability of standard laboratory clotting tests. We compared the well-known whole blood clotting test (WBCT) to the simpler capillary blood clotting test (CBCT) for detection of VICC in viper envenoming.
Methods: All confirmed snakebite patients admitted to a Sri Lankan tertiary care hospital from July 2020 to June 2021 were included. On admission, 15, 20, 25 min WBCT (WBCT-15, WBCT-20 and WBCT-25), and 5, and 10 min CBCT (CBCT-5 and CBCT-10) were performed. For CBCT-5 and CBCT-10, a 1 cm long capillary blood column (from a finger prick) was collected in two capillary tubes. These were then kept horizontally undisturbed for 5 and 10-min respectively. For WBCT-15, 20 and 25, 1 mL of venous blood were placed vertically undisturbed in 5 mL uniform glass tubes for 15, 20 and 25 min separately. At the conclusion of all tests, tubes were checked for stasis of blood. Non-stasis of blood was considered a positive test. Blood was collected simultaneously for prothrombin time (PT)-International Normalized Ratio (INR) and plasma fibrinogen. VICC was defined as an INR >1.5.
Results: Overall, 272 patients were recruited, with median age of 42 years (interquartile range: 30- 53y); 189 (70%) were males. There were 41 specimen-confirmed Russell's viper (RV) bites and 87 hump-nosed viper (HNV) bites. On admission, 159 (58%) had VICC. This included 82 having partial VICC (INR 1.5-2.9) and 77 having complete VICC (INR ≥3). Sixty-six (24%) had plasma fibrinogen <2 g/L which included 11 with zero fibrinogen. The WBCT-15 had the best sensitivity of 47% in diagnosing VICC and a specificity of 87%. The CBCT-10 was least sensitive. No difference in sensitivity of WBCT-20 and WBCT-25 was noted. All tests had improved sensitivity in detecting complete VICC, with the WBCT-15 improving up to 67%, while all other tests ranging from 57% to 61%. Although WBCT-15 was marginally better, it still missed 25/77 patients with complete VICC and 2/11 patients with zero fibrinogen. Five patients (2 RV, 1 HNV, 2 unknown snakebites) with a negative WBCT20 on admission, received delayed antivenom and developed acute kidney injury (AKI).
Conclusion: None of the bedside tests used was sufficiently sensitive, giving false negative results in some patients with coagulopathy and AKI. Quick, accurate and cost-effective alternative tests are urgently required. The decision to give antivenom should not depend wholly on bedside clotting tests, and must consider other clinical and laboratory evidence.

75. Psychostimulant drug co-ingestion in emergency department patients with opioid overdose: a multi-center ToxIC Collaboration

Siri Shastry[a], Kim Aldy[b,e], Jeffrey Brent[c], Paul Wax[b], Alex F. Manini[d] and On Behalf of The Toxicology Investigators Consortium Fentalog Study Group[e]

[a]Icahn School of Medicine at Mount Sinai, New York, United States; [b]University of Texas Southwestern Medical Center; American College of Medical Toxicology, Dallas, United States; [c]University of Colorado School of Medicine, Aurora, United States; [d]Icahn School of Medicine at Mount Sinai; Elmhurst Hospital Center, New York, United States; [e]American College of Medical Toxicology, Phoenix, United States

Objective: In 2017, psychostimulant deaths involving cocaine and methamphetamine both increased by more than 30% from the years prior. Opioid co-exposure with psychostimulants is a major driver of this increase in overdose deaths. Furthermore, the prevalence of fentanyl analog (fentalog) positivity among urine drug test results positive for cocaine or methamphetamine in non-fatal exposures is becoming increasingly more common. Characterization of clinical outcomes in patients with exposure to fentanyl/fentalogs and psychostimulants is critical but few studies have examined outcomes in this patient population. This study aims to investigate outcomes in patients with exposure to fentanyl and psychostimulants and compare outcomes in patients with fentanyl/psychostimulants to those with fentanyl/fentalogs only.
Methods: This was a secondary analysis of a prospective consecutive cohort of emergency department (ED) patients with opioid overdose presenting to 9 participating sites within the ToxIC network from 6 October 2020 to 17 August 2021. ED patients age 18+ with presumed opioid overdose and available waste blood specimens for analysis were enrolled. Exclusion criteria included age <18 years, non-toxicological diagnosis, prisoners and trauma/burn patients. Waste blood specimens from enrolled patients were sent to the Center for Forensic Science Research and Education and liquid chromatography quadrupole time-of-flight mass spectrometry were paired with clinical data for analysis. The primary study outcome was total naloxone bolus dose administered. Secondary outcomes included endotracheal intubation, cardiac arrest and troponin elevation within 4 hours of ED arrival and presenting vital signs. We performed t-test and chi-

squared analyses to compare demographics and outcomes between groups.
Results: Of 378 patients enrolled, 207 (51.8%) were found to have both psychostimulants and fentanyl present on assay. Patients in the fentanyl only group were significantly older than the fentanyl/stimulant group (mean 45.2 years versus 40.6 years, $p < 0.01$). Patients in both groups were predominantly male. Patients in the fentanyl/stimulant group had significantly higher total naloxone dose requirements (mean total dose 3.56 mg versus 2.85 mg, $p = 0.01$). There was no significant difference in presenting vital signs or rates of intubation, cardiac arrest, and troponin elevation.
Conclusion: We identified a high rate of co-exposure to psychostimulants and fentanyl. Patients in the fentanyl/stimulant group had significantly higher naloxone dose requirements, suggesting potential greater severity of overdose. Fentanyl/stimulant patients and fentanyl only patients had similar rates of endotracheal intubation, cardiac arrest, and myocardial injury. Further, powered studies are needed to fully evaluate the impact of psychostimulant co-exposure on outcomes in fentanyl/fentalog overdose.

76. Evaluation of a decontamination solution, Diphoterine®, for chemical burns: a systematic review

Nassime Belkhiri[a], Romain Mouchel[b], Laure Fayolle-Pivot[c], Jules A. Vaucel[d], Rania Jebri[e] and Guillaume Grenet[a]

[a]Poison Control Center, Lyon, France; [b]Ophthalmology Center, Edouard Herriot Hospital, Lyon, France; [c]Burn Center, Edouard Herriot Hospital, Lyon, France; [d]Poison Control Center; Emergency Department, Bordeaux, France; [e]Emergency Department, Hospices Civils de Lyon, Lyon, France

Objective: Diphoterine® is a decontamination solution commercialized for cutaneous and ocular chemical exposure in humans. Previous reviews reported conflicting results, and new studies are now available. We aimed to update the assessment of the evidence level of Diphoterine® for the decontamination of cutaneous and ocular chemical burns in humans.
Methods: We performed a systematic review, searching PubMed (27 January 2021) and Embase (19 March 2021) without time restriction, as well as Google and the manufacturer's website in February 2021. We included all English and French-language studies comparing Diphoterine® to water or physiological solution for cutaneous and ocular chemical burns decontamination in humans, assessing any criteria clinically evaluating burn severity (burn depth, duration of disability, etc). Qualitative analysis of internal validity of the studies was performed by assessing the statistical validity and the risk of bias for each study.
Results: We identified 1020 records, from which seven studies were included, involving approximately 1200 patients in total. There were 2 studies related to ocular burns, 3 to cutaneous burns, and 2 related to both. The main findings claimed for the use of Diphoterine® were reductions in the risk of serious burn, healing delay, the length of hospital stay and of time off work. Regarding statistical validity: studies showed multiple comparisons, without adjustment for multiple testing reported. Regarding selection bias: none of the studies were randomized. In two studies, type of decontamination was allocated differently depending on the time to presentation, in favor of Diphoterine®. Three studies used a before/after design. Regarding measurement bias: all studies were open-label design, without blinded adjudication of efficacy outcomes reported. Regarding confounding factors: decontamination characteristics and chemical agents were rarely reported between groups. In three studies, time to decontamination was shorter in the Diphoterine® group. Regarding conflicts of interest, they were reported in two studies.
Conclusion: Available studies showed a high risk of false positive results, and a high risk of bias. Our review displayed several limits: only one reviewer analyzed the studies, we did not use a validated tool for risk of bias assessment. The superiority of Diphoterine® over water or physiological solution has yet to be demonstrated, with more methodologically robust studies required.

77. Occupational accidents reported to the Dutch Poisons Information Center: an alarming increase

Anja P.G. Wijnands, Saskia J. Rietjens, Robbert B.T. Verkooijen, Dylan W. de Lange and Irma de Vries

Dutch Poisons Information Center, University Medical Center Utrecht, University Utrecht, Utrecht, Netherlands

Objective: Insight into the prevalence and circumstances of workplace accidents involving hazardous substances is important for occupational health and safety management. Poisons Information Center records are an important source of information.
Methods: A retrospective study of all enquiries from 2015-2019 on acute occupational exposures. Data on enquirer, patient characteristics (age, gender), exposure (substance, route), reported symptoms and treatment advice, were extracted from the database and analysed.
Results: The number of acute occupational intoxications reported to the Dutch Poisons Information Center (DPIC) increased 132%, from 375 in 2015 to 871 in 2019. In 2985 enquiries a single patient was involved, whereas multiple patients

Table 1. Occupational accidents reported to the Dutch Poisons Information Center, 2015-2019.

	Inhalation (n, %)	**Dermal** (n, %)	**Ocular** (n, %)	**Oral** (n, %)
Unknown	51 (4%)	63 (6%)	88 (11%)	31 (8%)
No symptoms	560 (40%)	282 (27%)	136 (17%)	169 (43%)
Mild to moderate effects	727 (52%) e.g. mucous membrane irritation, cough, dyspnea	548 (52%) e.g. skin irritation, itching, pain, edema	558 (69%) e.g. pain, redness, lacrimation	184 (47%) e.g. mucous membrane irritation, nausea, vomiting, diarrhoea
Severe effects	52 (4%) e.g. bradypnea, hypoxemia, chemical pneumonitis	166 (16%) e.g. chemical burns, necrosis	23 (3%) e.g. corneal abrasion	5 (1%) e.g. mucous membrane damage
Number of patients	1390	1059	805	389

were involved in 277 enquiries. Enquirers were mostly general practitioners (69%), followed by emergency departments (11%) and ambulance workers (4%). The victims were mainly males (75%; age range 13-85 years). Inhalation was the most common route of exposure (43%), followed by skin contact (32%), eye contact (25%) and ingestion (12%). Patients were often exposed via multiple routes. Acids (444 accidents), alkalis (255 accidents), and gases (247 accidents) were often involved. The majority of patients reported mild to moderate health effects. Severe symptoms were reported infrequently (Table 1). In 43% of the accidents, a wait-and-see-policy seemed sufficient, whereas in 52% the DPIC advised clinical assessment of the patient and monitoring the course of the intoxication. In 5% of the accidents, hospital admittance was recommended.
Conclusion: The number of acute occupational accidents involving hazardous substances reported to the DPIC has more than doubled in the period 2015-2019. In most cases, mild to moderate symptoms were reported. Although retrospective data provide valuable information, more detailed information about the nature and circumstances of accidental occupational poisoning is needed to advise on preventive measures. Therefore, a prospective follow-up study was started in 2020.

78. Case studies of chemical accidents: National Poison Control Centre lessons learned

Slavica Vucinic, Jasmina Jovic Stosic, Vesna Kilibarda, Tomislav Rezic and Dragana Djordjevic

National Poison Control Centre, Medical Faculty University of Defense, Military Medical Academy, Belgrade, Serbia

Objective: Exponential growth of chemical industries at the global level and the diversity of chemicals with different classes of danger on the market increase the risk of chemical accidents. Providing effective medical care depends on the nature of the accident, duration of exposure and toxicity of the chemical, the number of victims affected, the availability of medical care, the co-ordination of rescue teams and the medical treatment provided.
Methods: Evaluation of the circumstances of the event and medical histories of patients from three major chemical accidents [1].
Results: On 27 May 1998 in the vicinity of Belgrade, a tank with 2.5 t of ammonia exploded, causing spread of a toxic cloud over a vast area, and mass exposure of the local population. The National Poison Control Centre (NPCC) was informed about the accident 45 minutes later, when Emergency Medical Teams, fire crews and police were already at the scene of the accident. The total number of patients treated at the NPCC was 143, and 54 were hospitalized. Most had irritation of the respiratory tract and eyes, and 9 developed acute respiratory distress syndrome (ARDS). In 2006 in Jagodina Brewery, during conflict, workers were splashed with acetic acid, and remained in an enclosed space for at least an hour; 21 people were hospitalized for irritation of respiratory tract and chemical burns of the skin. On 6 April 2008, in a pesticide factory in Belgrade, fire and explosion involving containers of dimethoate, caused exposure of local workers, security and fire crews. Concentrations of sulfur oxides, nitrogen oxides, carbon monoxide and, volatile hydrocarbons were above normal limits. Overall, 73 patients were treated and 27 were hospitalized. Fire, explosion, toxicity and the experience of traumatic events were identified as potential basic injury mechanisms in chemical accidents, and common symptoms were irritation of respiratory tract, eyes and skin, chest pain, headache, and anxiousness even in mild cases. Multispecialized teams at the NPCC Military Medical Academy (MMA) were engaged in the treatment of hospitalized patients. NPCC advice to the public was to shut windows and stay indoors.
Conclusion: The major role of the NPCC, besides risk assessment and providing accurate information about the toxicity and effects of chemicals, and treatment, is co-ordination of activities with the Responsible Authorities. Communicating risks to the press and public should not be delayed.

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80. ToxNet 2: Judgement Day

Tobias Zellner[a], Hendrik Burwinkel[b], Matthias Keicher[b], David Bani-Harouni[b], Nassir Navab[b], Seyed-Ahmad Ahmadi[c] and Florian Eyer[a]

[a]Division of Clinical Toxicology and Poison Control Centre Munich, Department of Internal Medicine II, TUM School of Medicine, Technical University of Munich, Munich, Germany; [b]Computer Aided Medical Procedures, TUM Department of Informatics, Technical University of Munich, Munich, Germany; [c]German Center for Vertigo and Balance Disorders, Ludwig-Maximilians-Universität München, Munich, Germany

Objective: Previously we presented the artificial intelligence (AI) "ToxNet", a machine-learning based computer-aided diagnosis (CADx) system, which predicts poisons based on patient symptoms and metadata. Its accuracy in a set of 10 different toxins from 8,995 patients was 66% (F1 micro score). It was significantly superior to naïve literature matching and the machine learning baselines ($p < 0.005$) and outperformed our physicians experienced in clinical toxicology. We expanded the dataset to 28 substance classes, including the most common substances in Poison Control Center (PCC) consultations, and tested if the accuracy was still acceptable.
Methods: The CADx system was re-trained using data from 36,033 patients extracted from the PCC database from 2001-2019. All cases were mono intoxications. The substance classes included ACE-inhibitors/sartans, acetylsalicylic acid (ASA), acetaminophen, antidepressants (SSNRI, SSRI and tricyclic), benzodiazepines, beta-blockers, calcium-channel-inhibitors, (dihydropyridine type and class IV), cetirizine/loratadine, cocaine, diphenhydramine/doxylamine/dimenhydrinate, ethanol, gamma-hydroxybutyrate/gamma-butyrolactone (GBH/GBL), levetiracetam, lithium, methylphenidate, antipsychotics (atypical and typical), NSAIDS (excluding ASA and acetaminophen), opiates (buprenorphine and full μ-agonists), pregabalin/gabapentin, stimulants, tetrahydrocannabinol (THC), valproic acid and Z-drugs. Patient symptoms and meta-information (e.g. age group, sex, etiology, toxin point of entry, weekday, etc.) were provided. Prediction was optimized using graph convolutional networks.
Results: Our CADx system was able to predict the correct toxin with an overall performance of 27% ± 1 (F1 micro score). It was especially good at predicting ethanol (n = 2,767, 70% ± 2 F1 micro score), opiates (n = 1,622%, 49% ± 2), THC (n = 467, 48% ± 4), lithium (n = 1,026, 45% ± 5), GHB (n = 979, 45% ± 3) and stimulants (n = 914, 44% ± 3). It had difficulties with substances that appeared rarely, such as class IV calcium-channel blockers (n = 85, 7% ± 3), cetirizine/loratadine (n = 161, 7% ± 1), levetiracetam (n = 97, 1% ± 1) or valproic acid (n = 308, 1% ± 2). Substances with unspecific symptoms like NSAIDS (n = 2216, 5% ± 1) were also hard to predict.

Conclusion: Our AI trained on a large PCC database and also works on an increased number of substance classes, although it loses some of its accuracy. It performs especially well in common intoxications but has difficulty with rare substances or substances with non-specific symptoms.

81. Detection of isotonitazene in two patients during a cluster outbreak of patients with acute opioid toxicity

Klara S.C. De Baerdemaeker[a], Alison M. Dines[a], Simon Hudson[b], Lachland J. Sund[a], Mitchell L. Waters[a], Laura J. Hunter[a], Matthew S. Blundell[a], John R.H. Archer[c], David M. Wood[c] and Paul I. Dargan[c]

[a]Clinical Toxicology, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; [b]LGC Forensics, Fordham, United Kingdom; [c]Clinical Toxicology, Guy's & St Thomas' NHS Foundation Trust; Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom

Objective: Isotonitazene is a novel psychoactive substance (NPS), an opioid, which was first identified in Europe on the illicit drug market in Belgium in August 2019. We describe two cases of acute opioid toxicity in which isotonitazene was detected.
Case series: During August 2021 there was an increase in presentations with acute opioid toxicity to our Emergency Department (ED) in central London, UK. To further investigate, we obtained patient consent for analysis of serum-samples from two patients; qualitative analysis was undertaken on a Thermo-XRS ultrahigh-performance liquid-chromatography interfaced to a ThermoQ Exactive high-resolution accurate mass-spectrometer. Patient 1: A 43-year-old male on buprenorphine replacement therapy collapsed on the street after smoking heroin. He received 2 mg intramuscular naloxone from staff of a neighbouring homeless shelter. When the ambulance arrived 10 minutes later, he was alert with heart rate 115/min, blood pressure 148/95 mmHg, respiratory rate 22/min, and oxygen saturations 95% (room air). On arrival in the ED, he was alert and observations remained normal. He was observed overnight and discharged with no sequelae. Analysis of a presentation serum sample detected cocaine (and metabolites), buprenorphine (and metabolites) and isotonitazene. Patient 2: A 41-year-old male with previous cannabis and crack-cocaine use, but no reported previous opioid use was found collapsed after smoking a new powder. On ambulance arrival he was in respiratory arrest, heart rate 108/min and blood pressure 135/85 mmHg. He received bag-mask ventilation and was given a total of 0.8 mg intramuscular naloxone with improvement in respiratory rate to 12/min. On arrival in the ED he had a Glasgow Coma Score (GCS) 13/15, pin-point pupils, respiratory rate 16/min, oxygen saturations 100% on 15 L oxygen via non-rebreather mask, heart rate 88/min and blood pressure 110/75 mmHg. Forty-six minutes after prehospital naloxone administration, he deteriorated and needed 0.8 mg intravenous naloxone (given in 4 incremental titrated doses); 2 hours later his respiratory rate dropped again and he was started on a 480 μg/hour naloxone infusion. Twelve-hours later the naloxone infusion was stopped, he remained well and was discharged 21 hours after ED presentation with no sequelae. Analysis of a presentation serum sample detected buprenorphine metabolites, parent cocaine and isotonitazene.
Conclusion: We report two cases of acute opioid toxicity in which isotonitazene was detected. The extent to which isotonitazene contributed to the clinical presentations is limited by the detection of other drugs in both cases, however, it would appear that isotonitazene is associated with a typical opioid toxidrome responsive to naloxone.

82. Exposures to combustion products of lithium-ion batteries reported to the National Poisons Information Center

Arjen Koppen, Tim Verbruggen, Maxim Carlier, Anja P.G. Wijnands, Antoinette J.H.P. van Riel and Dylan W. de Lange

Dutch Poisons Information Center, UMC Utrecht, Utrecht, Netherlands

Objective: The use of rechargeable lithium-ion (Li-ion) batteries has increased dramatically over the last decade with their omnipresence in consumer goods, electric bikes and cars. Li-ion batteries can auto-ignite when misused or damaged, resulting in a so called "thermal runaway". During this process high concentrations of hazardous chemicals can be emitted, including hydrofluoric acid and lithium hydroxide. The health effects related to exposure to the combustion products of Li-ion batteries are unclear. We therefore performed a prospective follow-up study of incidents reported to the National Poisons Information Center (NPIC).
Methods: Exposures to Li-ion combustion products reported to the NPIC were followed-up during 1 year by telephone questioning of patients. Patients were questioned about the causes, circumstances and duration of exposure, the clinical symptoms and medical treatment. A standardized questionnaire was used.
Results: Seven cases were included involving 9 people exposed to Li-ion battery combustion products. In two cases the NPIC consulted the treating physician. All exposures took place indoors. The batteries were from smartphones (n = 3), e-bikes (n = 2) and e-smokers (n = 2). Batteries combusted spontaneously (n = 2), after (forced) disassembly of smartphones (n = 2), during charging (n = 1), during battery change (n = 1) or after an electrical short circuit (n = 1). In most cases the duration of exposure was <2 minutes. Symptoms after inhalation of smoke were usually mild and consisted of cough (n = 4), sore throat (n = 3), chest pain (n = 2), dyspnea (n = 1) and oral irritation (n = 1). In 3 cases skin was exposed to combustion products due to the ignition/explosion of a battery nearby. All three patients had skin burns, which were classified as $2^{nd}/3^{rd}$ degree in two patients. The burns were mainly thermal after ignition/explosion of a battery nearby. Interestingly, in these two patients a high pH had been observed in the wounds. In one of these patients wound rinsing was performed with mineral oil, to wash away water-reactive metals, followed by water.
Conclusion: Inhalation of combustion products of Li-ion batteries as found in e-smokers, smartphones and e-bikes can result in mild respiratory symptoms. In case of ignition/explosion of Li-ion batteries near the skin, $2^{nd}/3^{rd}$ degree skin burns can occur, as a result of a combination of heat and chemical exposure. The pH of such burns can be elevated. Removing metal debris before rinsing with water is recommended following ignition or explosion of a Li-ion battery.

83. Endogenous ethylene glycol production in monozygotic twins

Marc Ghannoum[a], Joe Rigley[b], Dean Hickey[c], Sylvie Robichaud[c], Danielle K. Bourque[d] and David Skidmore[e]

[a]University of Montreal, Montreal, Canada; [b]Miramichi Hospital, Miramichi, Canada; [c]Bathurst Hospital, Bathurst, Canada; [d]Children's Hospital of Eastern Ontario, Ottawa, Canada; [e]IWK Health Centre, Halifax, Canada

Objective: We describe endogenous ethylene glycol (EG) production in twin sisters.
Case series: The case involved two 37-year-old monozygotic twin sisters with no relevant medical or psychiatric history. From May 2019, Sister 1 presented to the emergency room 69 times with symptoms of malaise, altered consciousness, occasional seizures, and lactic acidosis. A plasma EG concentration of 2.7 mmol/L was noted in December 2019. From February 2020, Sister 2 presented 43 times with the same clinical picture (except seizures). Both denied ingestion of EG. No household members became sick during the study period. Serum EG (by gas chromatography and/or high-performance liquid chromatography), bicarbonate and anion gap on presentation are presented in Table 1. On several occasions, EG concentration increased and acidemia worsened during hospitalization. Ethanol, isopropanol, and acetone concentrations always remained negative. A positive serum methanol concentration (1.2 mmol/L) was found once on 6 May 2021 in Sister 2. For both, oxalate, lactate, glycolate, glyoxylate, and glycine were detected in blood and urine, as well as calcium oxalate crystals in urine. Blood pyruvate, total/free carnitine, amino acids, methylmalonate, acetoacetate, ß-hydroxybutyrate, ammonia, D-lactate, and creatinine always remained within normal limits. Genetic testing (whole exome sequencing) did not identify an underlying cause, such as mitochondrial disease or methylmalonic/propionic aciduria. When admitted, they were treated with fomepizole, pyridoxine, and intravenous bicarbonate, but without hemodialysis. Chronic hemodialysis was initiated in June 2021 and both are doing well. Since hemodialysis initiation, only 2/28 EG assays were positive.
Conclusion: Endogenous EG production is not described in humans. Propionic acid misidentified as EG and many complex 1 mitochondrial diseases have been excluded. The short-term plan is to arrange hospitalization to exclude concealed ingestion and to organize toxicokinetic studies and full metabolomic profiling. Reanalysis of the exome sequencing data is underway with hopes of possible identification of a novel genetic cause for endogenous EG production.

84. Contribution of imaging in the diagnosis of cerebral thrombosis related to snakebite envenoming by *Bothrops lanceolatus* in Martinique: a report of 25 cases

Dabor Resiere[a], Jonathan Florentin[a], Remi Neviere[b] and Hossein Mehdaoui[a]

[a]Critical Care Unit, University Hospital of Martinique (French West Indies), Fort-de-France, France; [b]Department of Cardiology, University Hospital of Martinique, Fort-de-France, France

Objective: Snakebites due to *Bothrops lanceolatus* represent a frequent medical morbidity requiring admission to the emergency department and intensive care unit, with an average of 25-30 cases per year. Any bite by this unique snake in Martinique may result in severe thrombotic complications such as cerebral infarction, pulmonary or myocardial events, which may have functional sequelae or be a risk to life. The composition of the venom and the lesion mechanisms are currently being assessed. A specific antivenom immunotherapy (AVI), Bothrofav® 2, available since 2011, has resulted in a significant reduction in mortality and morbidity including ischemic strokes induced by envenoming. The aim of this study was to evaluate the contribution of imaging in the diagnosis of cerebral thrombosis in envenomation by *Bothrops lanceolatus*.
Methods: We conducted an observational, retrospective study over a period of 10 years between 2011 and 2021, including all successive patients admitted to the department of emergency medicine and intensive care at the University Hospital of Martinique for *Bothrops lanceolatus* snakebite. The radiological data were completed and analyzed, via medical records using emergency software, Dx Care, X-plore and Cyberlab.
Results: Two hundred and thirty one (231) patients were included in this study, 165 men and 76 women. Among these patients, 52 were grade III or IV only and 25 had magnetic resonance imaging (MRI). No thrombotic cerebrovascular accident was noticed.
Conclusion: The indication to carry out a cerebral MRI systematically in the management of snakebites by *Bothrops lanceolatus* remains questionable. This study showed that patients who received early Bothrofav2 antivenom do not develop thrombosis.

Table 1. Laboratory values from multiple presentations until initiation of chronic hemodialysis in monozygotic twins with endogenous ethylene glycol production from an unknown cause.

Laboratory parameters	Sister 1 (76 measurements from 69 admissions and 6 follow-ups)	Sister 2 (49 measurements from 43 admissions and 6 follow-ups)
Serum ethylene glycol concentration (mmol/L)*		
Median	2.3	3.5
Q1, Q3	1.3, 4.9	2.7, 4.8
Range	0-12.8	0-14.8
Serum bicarbonate concentration (mmol/L)		
Median	17	20
Q1, Q3	14, 23	20, 22
Range	8-28	10-27
Anion gap ($Na + K - HCO_3 - Cl$, mmol/L)		
Median	17.9	16.8
Q1, Q3	14.9, 20.3	14.9, 18.5
Range	8.9-24.1	13.0-26.1

*Note that EG was not measured every time (41 for Sister 1, 32 for Sister 2)

Due to our underpowered study with methodological limitations, MRI should be limited to patients with grade 3 or 4 envenomation by *Bothrops lanceolatus*.

85. When drugs break your heart. Takotsubo syndrome in addiction medicine: a case series

Simone Sartori[a], Valentina Brilli[a], Cecilia Lanzi[b], Francesco Gambassi[b] and Guido Mannaioni[a]

[a]Department of Neuroscience, Psychology, Pharmacology and Child Health (NEUROFARBA) Department, University of Florence, Florence, Italy; [b]Toxicology Unit and Poison Control Center, Careggi University Hospital, Florence, Italy

Objective: To highlight the need for more careful monitoring of toxicological patients both in overdose or withdrawal due to the high risk of stress cardiomyopathy.
Case series: Case 1[1]: A 54-year-old woman was hospitalized for repeated seizures after forgetting her benzodiazepines (BZD) supply at home during a weekend at the seaside. Multiple electroencephalograms did not show any evidence of epileptic activity. The initial electrocardiogram (ECG) showed T-wave alterations compatible with Takotsubo syndrome (TTs), which was later confirmed by apical ballooning appearance at the cardiac ultrasound with a 30% ejection fraction (EF). The following negative coronarography ruled out any other etiologies. Withdrawal therapy with phenobarbital controled both her withdrawal and neurological symptoms. She was discharged after 10 days with improved EF. Case 2: A 60-year-old man was admitted for thoracic pain during alcohol withdrawal, following a sub-acute pancreatitis which stopped him from drinking alcohol for 4 days. A heart ultrasound was performed due to ST-segment and T-wave alterations on the ECG, showing apical akinesia and a 35% EF. Coronarography later found a non-critical calcific stenosis of the anterior interventricular artery. Withdrawal therapy with chlordiazepoxide was started and at one month follow-up, heart ultrasound showed a 56% EF. Case 3: A 45-year-old woman was admitted to the emergency room after being found unconscious at home with some syringes, a pack of white powder and puncture marks on her neck. A computerised tomography (CT) scan was performed and showed signs of aspiration pneumonia. A toxicologic urine screen (due to suspicion of cocaine use) and a heart ultrasound were performed. A 35% EF with apical ballooning and a negative coronarography confirmed TTs. Positivity for opioids, cannabinoids, methadone and benzodiazepines was found. The patient later acknowledged the use of heroin. She continued her therapy with alprazolam and methadone and after 9 days she recovered with a 50% EF.
Conclusion: Toxicological etiology is not addressed in the current guidelines for diagnosis and clinical characteristics of TTs [2]. Addiction and emergency specialists should be aware of this possible complication easily detectable with routine investigations.

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86. Lethal methanol poisoning: an outbreak in the Kaunas region, Lithuania

Marius Perminas[a], Jonas Surkus[a], Linas Darginavicius[a], Dalius Banionis[b], Vilma Traskaite-Juskeviciene[a], Egle Belousoviene[a], Ruta Leksiene[a], Donatas Cibulskis[a], Karolina Buozyte[a], Akvile Vasiliauskaite[a] and Greta Kaminskaite[a]

[a]Lithuanian University of Health Sciences, Kaunas, Lithuania; [b]The State Forensic Medicine Service, Kaunas, Lithuania

Objective: Methanol poisoning causes severe morbidity and mortality. Mortality is high when patients arrive at the emergency department with severe clinical symptoms. In the Kaunas region of Lithuania in 2021 there was an outbreak of severe methanol poisoning, accounting for at least 17 confirmed deaths.
Methods: A retrospective analysis of patients presenting during the outbreak to medical facilities. Demographical data, clinical presentation with laboratory studies, treatment results and post-mortem analysis was performed.
Results: In the summer of 2021 two Kaunas hospitals admitted several severely ill patients; some had been found unconscious at home or on the street. Almost all patient case histories were unobtainable. Neurologic disease was suspected and detailed neurological examinations were performed. Blood analyses revealed profound acidosis (pH 6.46-7.29 (in two cases blood pH was unmeasurable, so $<$7.3), low bicarbonate concentration and negative base excess). Gathering the information led to the suspicion of illegal alcohol ingestion and methanol poisoning was suspected. Antidotal treatment with ethanol and hemodialysis were provided. In most cases continuous venovenous hemodiafiltration was given due to the presence of shock. This treatment combined with supportive care was unsuccessful in most cases. Out of 19 patients with confirmed methanol poisoning only 2 survived; one survivor is permanently blind. Methanol concentration in blood ranged from 0.3-5.04 g/L and in urine from 1.42-7.72 g/L. The total number of people affected by the outbreak is not known as the investigation is on-going. The police shut down many illegal trading places and confiscated huge amounts of alcohol. Unfortunately, the exact amount of illegal alcohol in possession of potential users is unknown and poisoning cases are still occurring.
Conclusion: Patients presented to the emergency department with decreased level of consciousness and an adequate case history was unobtainable. Profound metabolic acidosis with severe symptoms of intoxication are poor prognostic factors for the methanol-intoxicated patient.

87. Infant botulism treated with heptavalent botulinum antitoxin: a case series

Cristina Grazioli[a], Davide Lonati[a], Fabrizio Anniballi[b], Azzurra Schicchi[a], Lucia Bernasconi[a], Concetta Scalfaro[b], Valentina Negrini[a], Benedetta Brolli[a], Francesca Zaffino[c], Giulia Scaravaggi[a] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]National Reference Centre for Botulism (NRCB), Department of Veterinary

Public Health and Food Safety, National Institute of Health (ISS), Roma, Italy; [c]Scorta Nazionale Antidoti e Farmaci (SNAF), Direzione Generale della Prevenzione Sanitaria, Ufficio 3, Ministry of Health, National Health System, Roma, Italy

Objective: Infant botulism (IB), differs from foodborne botulism, and is due to *in situ* neurotoxin production by *Clostridia* colonizing the intestinal lumen in infants (<1-year-old). IB is an underdiagnosed disease mainly due to the insidious clinical onset [1]. The clinical syndrome is a floppy baby. Severe IB cases may require ventilatory support and specific antitoxin treatment. The antidote varies in several countries as previously reported [2]. Since October 2018, in our country HBAT [heptavalent equine Fab/F(ab')2] is available. Our aim is to evaluate the clinical response to HBAT and the safety profile in infants with this rare form of botulism.
Case series: All clinically suspected (and/or laboratory confirmed) cases treated with antitoxin IB cases collected from October 2018 to October 2021 were evaluated concerning demographics, circumstances, clinical manifestations, toxin-type, laboratory results, acute/delayed adverse reactions, and outcome. Six patients were studied (mean age 15.6 ± 8.4 weeks, body-weight 3200 to 4050 g). No specific sources of spores were identified (honey ingestion in 2 cases). Severe constipation was the "alert" symptom at ED admission in all cases. One baby was breast-fed. Main clinical manifestations were: constipation and difficult suckling (100%), severe hypotonia (5/6, 83.3%) and dysphagia (4/6, 66.6%). Due to progressive worsening of clinical manifestations (severe hypotonia and dysphagia) antitoxin was administered as soon as a suspicion of botulism was made. HBAT was administered intravenously at 10% of adult dose regardless of body weight without acute adverse reactions. Despite antitoxin treatment 5 babies required intubation and respiratory support to prevent complications and permit adequate nutrition. Intestinal sterilization (with clostridiocidal antibiotic therapy), whole bowel irrigation by gavage and probiotics were administered only after the HBAT administration (to avoid eventual massive toxin absorption). *Clostridium botulinum* type-B (3 cases), type-A (2 cases) were isolated from stool samples of 5 patients. All patients recovered fully and no delayed reactions (e.g. serum sickness) were noted.
Conclusion: HBAT in IB seems to be effective and safe. To date, only 1 case of IB (type-F) was treated with HBAT [2]. Considering the rarity of the disease and the different protocols treatment applied for IB around the world, a multicentre and prospective study is needed.

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88. The increasing problem of intentional ingestion of sodium nitrite: an Italian experience

Benedetta Brolli[a], Valeria M. Petrolini[a], Davide Lonati[a], Franco Tagliaro[b], Lucia Bernasconi[a], Valentina Negrini[a], Cristina Grazioli[a], Azzurra Schicchi[a], Giulia Scaravaggi[a] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]Department of Diagnostics and Public Health - Unit of Forensic Medicine, University of Verona, Verona, Italy

Objective: Sodium nitrite is an inorganic salt used in food industry as a preserving agent. Nitrate/nitrite are potent oxidizing agents that in toxic dose may result in profound life-threatening methemoglobinemia. The intentional use of sodium nitrite has been an emerging problem in 2021. This trend may be the result of ready access to this poison through online vendors' recommendations shared in online communities that sodium nitrite be used as an effective method of suicide. We aimed to evaluate the trend of sodium nitrite intentional ingestion in the last 5 years.
Methods: We designed a retrospective observational study including all patients referred to our Poison Control Centre for sodium nitrite intentional ingestion in the period 2016-2021. For all included patients we collected all clinical and biological parameters on admission and during hospitalization, the observed complications and the outcome.
Results: Nine cases were included: 1 occurred in 2019, 8 in 2021. Seven patients ingested sodium nitrite to attempted suicide, in 2 cases sodium nitrite was used in an attempted homicide. Details

Table 1. Details of patients with intentional ingestion of sodium nitrite.

Case no.	Year	Gender	Age	Consumption modality	Clinical Manifestations at ED-admission	Methemoglobin (%) at ED-admission	Methylene blue administered dose	Outcome
1	2019	M	55	Suicide	Cyanosis, mydriasis, Glasgow Coma Score 10	–	–	Death at ED-admission
2	2021	M	18	Suicide	Cardiac arrest, bradypnea	–	–	Death at ED-admission
3	2021	F	56	Homicide	Diarrhea, dyspnea, cyanosis, lactic acidosis	72.2	2 mg/kg (single dose)	Improvement
4	2021	M	65	Homicide	Syncope, cardiac arrest	–	–	Death at ED-admission
5	2021	M	21	Abuse/Suicide	Syncope, hypotension, lactic acidosis	79.6	2 mg/kg (single dose)	Improvement
6	2021	M	49	Abuse/suicide	Syncope, cyanosis, hypotension, tachycardia, lactic acidosis	not performed at admission	1 mg/kg	Improvement
7	2021	M	29	Suicide	Asymptomatic	0.5	–	Improvement
8	2021	M	42	Suicide	Syncope, coma, cyanosis, scattered tremors at extremities	30	1 mg/kg	Improvement
9	2021	M	33	Suicide	Cyanosis	64	1.5 mg/kg	Improvement

about clinical manifestations at Emergency Department (ED) admission, methaemoglobin level (MetHb), treatment and outcome are described in the table. Nitrite blood concentration level was not available in emergency setting.
Conclusion: An increasing trend of sodium nitrite misuse has been observed in Italy during 2021. Sodium nitrite poisoning could be fatal if not recognized, emergency physicians should be aware of this trend and perform metHb determination in case of syncope/hypotension/peripheral cyanosis. PCC has a crucial role in syndromic surveillance and spread the alert of similar dangerous trend, especially among adolescents. A prompt administration of methylene blue is life saving and for this reason it should be available in every ED.

89. Acute opioid withdrawal following high dose intramuscular naloxone: a prospective prehospital series

Katherine Z. Isoardi[a], Lachlan Parker[b], Keith Harris[a], Stephen Rashford[b] and Geoffrey K. Isbister[c]

[a]Clinical Toxicology Unit, Princess Alexandra Hospital, Brisbane, Australia; [b]Queensland Ambulance Service, Brisbane, Australia; [c]Clinical Toxicology Research Group, University of Newcastle, Newcastle, Australia

Objective: Large doses of intramuscular naloxone are commonly used in the prehospital environment to reverse opioid toxicity, but less commonly in hospital because of concerns about opioid withdrawal. We aimed to determine the frequency of acute opioid withdrawal following a large intramuscular naloxone dose.
Methods: We undertook a prospective study of adult (>15 years) patients treated by an Australian state ambulance service with 1.6 mg intramuscular naloxone for respiratory depression (respiratory rate [RR] < 11 and/or oxygen saturations [sats] < 93% on room air) due to presumed opioid poisoning. Paramedics entered serial observations, including the Sedation Assessment Tool [SAT] score [1] on a preformatted datasheet following naloxone administration. The primary outcome was the proportion of patients with acute opioid withdrawal (any tachycardia (heart rate >100 bpm), hypertension (systolic >140 mmHg), vomiting, agitation, seizure, myocardial infarction, arrhythmia or pulmonary oedema). Secondary outcomes included the proportion of patients with severe agitation (SAT score >1), and the reversal of respiratory depression (RR >10 and sats >92%/Glasgow Coma Score [GCS] 15).
Results: From October 2019 to July 2021 there were 199 presentations in 173 patients with a median age of 41 years (range: 18-80 years); 120 males (69%). The commonest opioids were heroin (132, 66%), oxycodone (15, 8%) and morphine (11, 6%). Opioid withdrawal occurred in 77 presentations (39% [95% confidence intervals [CI]: 32-46%]), with the commonest non-specific features being tachycardia in 35 (18%), hypertension in 32 (16%) and vomiting in 6 (3%). Mild agitation/anxiety occurred in 50 (25%, 95%CI:19-32%) cases and severe agitation in 14 (7%, 95%CI 4-12%). There were no instances of seizure, myocardial infarction, arrhythmia or pulmonary oedema. Three patients (1.5%) received chemical sedation for severe agitation within 1 hour of naloxone administration. A single 1.6 mg dose of naloxone reversed respiratory depression in 194 (97%) presentations.
Conclusion: Acute opioid withdrawal occurred commonly after 1.6 mg intramuscular naloxone, but severe agitation was uncommon and rarely required chemical sedation.

Reference

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90. Moderate neurotoxicity from topically applied lidocaine cream

Darren M. Roberts[a], Giles Flick[b] and Brett McWhinney[c]

[a]Department of Clinical Pharmacology and Toxicology, St Vincent's Hospital, Sydney, Australia; [b]Emergency Department, St Vincent's Hospital, Sydney, Australia; [c]Queensland Health Pathology, Royal Brisbane and Women's Hospital, Brisbane, Australia

Objective: To describe moderate neurotoxicity in a patient who applied lidocaine 10.56% cream to most of his body with an occlusive barrier for analgesia during hair removal.
Case report: A 48-year-old man exited an Uber in a suburban shopping precinct wrapped in a plastic film beneath his clothes. He was disorientated, ataxic, dysarthric, and agitated pulling at the plastic film. Paramedics and police attended, cardiorespiratory vitals were normal, Glasgow Coma Score (GCS) 14/15 and pupils 3 mm bilaterally. He was diagnosed with an "acute mental health episode" and sedated with intramuscular droperidol 10 mg to facilitate hospital transfer. In the Emergency Department his vitals remained stable, he was sedated with eyes closed, shivering with occasional twitching of his limbs. Within 60 minutes GCS improved, but dysarthria, dysphasia, hypertonicity (particularly of lower limbs), brisk knee jerks without ankle clonus, were present. The plastic film was removed. The electrocardiograph was normal (QRS 112 ms). The patient guided doctors to call his partner. She explained that in preparation for laser hair removal, four hours previously, the patient applied >300 g lidocaine cream 10.56% (ordered online) from his ankles and wrists to the neck (excluding groin) and covered it with plastic film to facilitate penetration. He was practiced with doing this, but today applied it a few hours earlier because of a virtual meeting. Clinical toxicology advised dermal decontamination and diazepam 5 mg and hypertonicity quickly resolved. He was admitted for observation including continuous cardiac monitoring. He steadily improved and the electrocardiograph 24 hours later noted QRS 102 ms. Drug assay results noted peak lidocaine concentration 13.2 mg/L (reference range 2-5 mg/L) on admission with a first-order elimination half-life of 5.8 hours. Peak metabolite concentrations were monoethylglycinexylidide 4 mg/L 10 hours post-application, and glycylxylidide 1.4 mg/L 21 hours post-application. On review 4 weeks later he reported feeling "drunk" so he caught an Uber rather than driving; an electrocardiograph noted QRS 98 ms. The clinical features were typical for lidocaine neurotoxicity and dynamic changes in the QRS duration may also reflect mild cardiotoxic effects.
Conclusion: This is amongst the highest lidocaine concentration in the literature from dermal exposure. Topical local anaesthetic use for cosmetic purposes is a risk factor for systemic toxicity. The lidocaine elimination half-life is longer than anticipated (typically 1-2 hours post-intravenous), likely reflecting transdermal pharmacokinetics. Management includes supportive care, skin decontamination and titrated benzodiazepines, and education on the potential hazards of topical medications.

91. Thick and rugged skin, with scales… it is a crocodile!

Juan Ortega Pérez, Catalina Homar Amengual, Francisco Javier García Sola and Bernardino Comas Díaz

Hospital Universitario Son Espases, Palma de Mallorca, Spain

Objective: Krokodil is the street name for the homemade injectable mixture used as a cheap substitute for heroin. The core ingredient is desomorphine, an opioid-analogue that can be easily and cheaply manufactured. People who inject krokodil present a great variety of serious effects, including thrombophlebitis, ulcerations, gangrene, and necrosis, quickly evolving to limb amputation and death. We present a case of Krokodil injection.
Case report: A 33-year-old male, an intravenous drug user came to the emergency room due to poor evolution of ulcers on his right leg. It was very difficult to obtain an adequate history due to a low level of consciousness. According to the family, the patient consumed Krokodil, in addition to cocaine, heroin and cannabis. No fever or dysthermic sensation was present. The patient has a history of tricuspid bacterial endocarditis caused by *Staphylococcus aureus* on several occasions, chronic liver disease, and leg ulcers of years of evolution that have required several admissions for antibiotic treatment. He was not taking any medication chronically. Physical exploration found he was in poor general condition. Cardiac and respiratory auscultation and abdominal examination were normal. He was noted to have venepuncture injuries in both arms and neck. He had an edematous right foot, with a large wet ulcer, bleeding, with an intense red background with purulent exudate, at the anterior level of the lower third. There were multiple surrounding ulcers of different sizes with a pinkish background and surface with fibrin/necrosis which resembled crocodile skin. His vital signs were temperature 38.1 °C, heart rate 92 bpm, and blood pressure 160/102 mmHg. General laboratory tests, blood cultures (negative), right leg X-ray (no sign of osteomyelitis), chest X-ray (normal) and a urine toxin screen (positive for cannabis, cocaine, and opiates) were undertaken. He had leukocytosis with a left shift. Culture of a leg ulcer was positive for oxacillin-sensitive *Staphylococcus aureus*. He received meropenem and vancomycin and was switched to cotrimoxazole treatment after the results of the ulcer culture were received. He had a good clinical evolution and was discharged home in 15 days. He refused transfer to a drug cessation center.
Conclusion: There are reports of the dermatologic sequelae of krokodil use. We found significant swelling and pain in the areas of intravenous or subcutaneous injection, followed by a discolored (greenish-black) scaling and large-scale necrotic ulceration. This can progress to muscle and cartilaginous tissue damage. Finally, skin and muscle decay can cause the skin to slough off, often exposing bones.

92. Exposures to chemicals used in clandestine drug laboratories reported to the National Poisons Information Center

Arjen Koppen, Anja P.G. Wijnands, Antoinette J.H.P. van Riel and Dylan W. de Lange

Dutch Poisons Information Center, UMC Utrecht, Utrecht, Netherlands

Objective: Clandestine drug laboratories (CDLs) and illegal drug waste disposal are an increasing problem in the Netherlands. Since minimal safety measures are usually taken in CDLs, and waste is randomly dumped, there is a high exposure risk to hazardous chemicals for both CDL workers, bystanders and first responders. In this retrospective study an overview is given in order to characterize exposures to CDL chemicals as reported to the National Poisons Information Center (NPIC).
Methods: The database of the NPIC was retrospectively analyzed for cases involving human exposures to CDL chemicals or drug waste in the period 2010-2019. Several search terms for CDL and drug waste were applied. For each included case, information was collected concerning the patient (number of patients involved, age, sex), the exposure (route, identity of the involved chemicals) and the symptoms present at the time of report.
Results: From 2010 to 2019 the NPIC was consulted 24 times about exposures to CDL chemicals. In total 40 people (35 adults, 5 children) were involved, consisting of 19 CDL workers (16 men, 3 women, all adults), 6 police officers and 15 bystanders (including a family of two parents and their 4 children). The most common route of exposure was inhalation (n = 33), followed by skin exposure (n = 3). In 4 people the route of exposure was unknown. Six bystanders stated that they were exposed to CDL chemicals, but the exposure was not confirmed. On 3 occasions methanol was inhaled in a laboratory, involving 8 male employees. These patients showed moderate to severe health effects (including central nervous system depression, severe metabolic acidosis) and one patient died. In another case a CDL worker showed symptoms of sympathomimetic stimulation after exposure to an unknown chemical. In the remaining people (n = 31) mild symptoms, including dizziness, coughing, dyspnea, irritation of the throat, or no symptoms were reported. In all cases except one, the identity of the chemicals involved was initially unknown.
Conclusion: Intoxications caused by CDL chemicals incidentally occur and can lead to severe health effects and even death. Most exposures are due to inhalation. A problem for healthcare workers is that the chemicals involved in the exposures are often unknown, hampering timely therapeutic interventions. More widespread knowledge regarding chemicals present in CDLs could tackle this problem.

93. Occupational poisonings in Germany

Nina Glaser, Michael Reuser and Herbert Desel

German Federal Institute for Risk Assessment (BfR), Berlin, Germany

Objective: In Germany, all poisonings at the workplace (including local effects of chemical agents) must be notified to the German Federal Institute for Risk Assessment (BfR) by the statutory accident insurance on a legal basis. All cases notified to the 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) and product categories are assigned to all noxae recorded according to the Toxikologischer Dokumentations- und Informationsverbund (TDI) Kategorie System (TKS) category system of the German Society for Clinical Toxicology. BfR prepares annual workplace poisoning reports that are distributed to competent stakeholders. For this study, BfR analysed workplace poisoning cases notified over the recent decade.
Methods: All cases submitted by statutory accident insurances between 2011 and 2020 were merged and analysed for industry branch, categories of products involved, patient data, route of exposure and the clinical course.

Results: Between 2011 and 2020, the statutory accident insurances notified 50,648 cases of poisoning to BfR. Of these, 2,222 cases were medically treated because of a poisoning concern but no symptoms were reported (4.4%). The majority of patients suffered only minor symptoms (81.2%). The proportion of medium or severe cases was 7.7%. A particularly large number of poisonings occurred in the construction (12.8%) and agriculture industries (10.0%). Animals (especially wasps, bees, oak processionary moth caterpillars (*Thaumetopoea processionea)*), chemical products for construction (binders, fillers, adhesives) and exhaust gases were most often involved in poisonings. In 54.9% of cases the eyes were involved (irritation and more severe chemical burn). The proportion of eye exposures was particularly high in health services (84.9%) and agricultural settings (68.6%), while inhalative poisoning was mainly reported by fire brigade staff (96.6%) and personnel in the transport sector (92.6%). About twice as many reports concerned men (31,264 cases) in comparison to women (15,226 cases). The proportion of manifest poisoning cases was also more than twice as high among men (9.8%) in comparison to women (3.9%).
Conclusion: The analysis presented here allows a cross-sector overview of an evaluation of over 50,000 cases of occupational poisoning from all professional sectors. The documentation of poisonings in the database of BfR facilitates identification of critical exposure scenarios at work. The annual statistical feedback may help the statutory accident insurances to improve well-targeted safety measures.

94. Lead poisoning as a difficult diagnosis?

Ildiko Urban and Istvan Elek

Peterfy Hospital, Clinical Toxicology Department, Budapest, Hungary

Objective: Lead is highly toxic heavy metal following acute or chronic exposure. Lead poisoning is rare, its symptoms are nonspecific, but it can be life-threatening and cause long-term health problems. Due to the nonspecific multiorgan symptoms misdiagnosis can occur. We report two cases in which the patients suffered acute lead exposure by inhalation, and correct diagnosis of poisoning required comprehensive investigations [1].
Case series: Case 1. A 40-year-old male self-presented to hospital because he developed stomach ache, sore throat, chest discomfort and fever. On admission, his general condition was satisfactory. In the previous two days he had been removing paint from an iron column without protective equipment. Medical history revealed gastric surgery 10 years ago. His diagnoses were as follows: virus infection, peptic ulcer, other abdominal diseases, metal fume fever. He was referred to his general practitioner. One day later he returned to our department due to aggravated abdominal cramp, vomiting, and constipation. His vital signs were stable, electrocardiogram (ECG) was normal. Laboratory results showed elevated (mainly indirect) bilirubin and liver function tests, hyponatremia, and anemia. Chest X-ray was normal, abdominal X-ray and ultrasound showed meteorism, and gastroscopy showed chronic gastritis. Despite fluid supplementation, antispasmodic, analgesic and laxative treatment, his abdominal pain did not improve significantly. Based on clinical symptoms and analytical data acute abdominal, cardiac and pulmonary diseases were excluded, due to these and proven exposure lead poisoning was probable. Whole blood lead concentration was 105.8 μg/dL. He was treated with chelation therapy, which resulted in prompt improvement of clinical symptoms. Case 2. A 33-year-old male was admitted to the emergency department due to spasmodic abdominal pain, constipation, nausea, fatigue, anorexia, weakness and arthralgia. On admission he had fever, leukocytosis, moderate anemia, and hypertension. Ultrasound and abdominal X-ray showed no abnormality, and surgical consultation did not recommend acute surgery. He was treated with fluid resuscitation and analgesia, but his abdominal pain did not improved. Finally, he said that he had worked with lead-containing material for five days. Repeated laboratory results showed normocytic anemia with basophilic stippling and elevated zinc protoporphyrin. In our department supportive therapy was continued, the whole blood lead concentration was 86.1 μg/dL, and chelation therapy was initiated.
Conclusion: Acute and subacute exposure to lead can cause severe abdominal symptoms and diagnostic challenges. In case of unexplained complaints and proven metal exposure, toxicity should be considered.

Reference

[1] Staudinger KC, Roth VS. Occupational lead poisoning. Am Fam Physician. 1998;57:719–26.

95. Changes in oxidant-antioxidant system indicators in geriatric patients with psychopharmacological drug and corrosive substance acute poisoning

Anastasia Yu Simonova[a], Kapitalina K. Ilyashenko[a], Elena V. Klychnikova[a], Anatolii K. Evseev[a], Maria V. Belova[a], Michail M. Potskhveriya[a], Irina V. Goroncharovskaya[a] and Elizaveta V. Melnik[b]

[a]N.V. Sklifosovsky Research Institute of Emergency Medicine of the Moscow Department of Health, Moscow, Russian Federation; [b]I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation

Objective: To study the oxidant-antioxidant status in the early stage of poisoning in geriatric patients with psychopharmacological drug and corrosive substance acute poisoning.
Methods: An open prospective observational study was conducted. Overall, 80 patients with poisoning of moderate and severe degree were examined: 49 patients aged 72.1 ± 9.6 years with psychotropic drug poisoning and 31 people aged 73.0 ± 10.3 years with corrosive substance poisoning. The control group included 39 conditionally healthy volunteers aged 68.3 ± 6.3 years. The following indicators were evaluated: the concentration of malonedialdehyde (MDA), total antioxidant activity (TAA) in the blood, the content of stable nitric oxide metabolites (nitrite/nitrate, NOx) in the blood, the oxidative stress coefficient ($K_{MDA/TAA}$) on the 1st, 3th and 5th days after admission to the hospital.
Results: It was noted that all patients of geriatric age were characterized by lower values of the studied parameters compared to the control group. In patients with psychotropic drug poisoning, a decrease in MDA on days 1 and 3 by 1.2 times ($p = 0.002$; $p = 0.008$) was observed. NOx decreased at all stages of the study by 1.7 times ($p < 0.001$), $K_{MDA/TAA}$ – by 2.4-2.9 times ($p < 0.001$). In patients with corrosive substance poisoning a decrease in MDA on days 1 and 3 by 1.1-1.2 times ($p = 0.003$; $p = 0.010$) was observed, NOx decreased during the study by 1.4–1.6 times ($p = 0.004$; $p = 0.012$; 0.023), TAA by 1.1-1.3 times, and $K_{MDA/TAA}$ by 2.3-2.4 times ($p < 0.001$). When comparing patients with a favorable and fatal outcome, it was shown that with a favorable course of the disease, by the 5th day, an increase in $K_{MDA/TAA}$ was observed against the background TAA. With a fatal outcome,

$K_{MDA/TAA}$ continued to decrease due to a continued drop in NOx levels, reaching values 2.8-2.9 times ($p < 0.001$) below control values.
Conclusion: It has been established that in geriatric patients with psychopharmacological drug and corrosive substance acute poisoning, an inadequate reaction from the oxidant-antioxidant system is noted, which is manifested by a decrease in the patient blood peroxidation products with normal or slightly reduced content of antioxidant protection components. Oxidative distress results, which when aggravated leads to the development of a fatal outcome.

96. Investigation of the risk/benefit ratio of a new opioid peptide with two different sustained-release hydrogel-based formulations in comparison to morphine: an experimental study in mice

Christian Béaini[a], Lucie Chevillard[a], Patricia Risède[a], Charlotte Martin[b], Steven Ballet[b] and Bruno Mégarbane[a]

[a]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris University, Paris, France; [b]Research Group of Organic Chemistry, Departments of Bioengineering Sciences and Chemistry, Vrije Universiteit Brussel, Brussels, Belgium

Objective: Pain is a major public health issue. Opioid analgesic prescription is regularly increasing, resulting in an increase in consultations related to 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 investigate the antinociceptive and respiratory effects of a new endomorphin-2 analogue, the CM-80 peptide, and its co-formulation with hydrogel SBL-HG-01 or with hydrogel SBL-HG-01D, in comparison to morphine.
Methods: The antinociceptive (using tail-flick test) and respiratory effects (using whole-body plethysmography) were studied in mice after a unique SC administration.
Results: CM-80 induced more prolonged analgesic effects than morphine (7 hour) but with greater respiratory toxicity, while this analgesic effect lasted up to 24 hours with the two co-formulations with a less toxic respiratory profile than CM-80 and morphine. The ratios of the median analgesic effective dose (ED_{50})-to-area under the curve of the minute volume determined using plethysmography and taken as indicator of neurorespiratory toxicity were 0.016 (morphine), 0.0155 (CM-80 peptide), 0.030 (hydrogel SBL-HG-01) and 0.023 (hydrogel SBL-HG-01D).
Conclusion: The CM-80 peptide as well as the co-formulations do not induce an analgesic effect beyond 24 hours, thus showing limited therapeutic value. The deleterious respiratory effects of co-formulations are more limited than the opioid itself.

97. Continuous renal replacement therapy (CRRT) removal capacity of selected pharmaceuticals in high concentrations, a whole blood (swine) *in vitro* model

Lotte C.G. Hoegberg[a], Ditte Hermann[b], Mikkel B. Christensen[c], Troels Riis[d], Jens Hannibal[b] and Søren Bøgevig[d]

[a]Department of Anesthesiology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark; [b]Department of Clinical Biochemistry, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark; [c]Copenhagen Center for Translational Research and Department of Clinical Pharmacology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark; [d]Department of Clinical Pharmacology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark

Objective: Continuous renal replacement therapy (CRRT), hemodialysis (HD) and hemoperfusion exist as treatment modalities for

Table 1. Plasma concentration reductions in CRRT whole blood (swine), *in vitro*. Percent indicates drug fraction removed.

CRRT settings	Normal blood flow/ Low dialysate flow	Normal blood flow/ Moderate dialysate flow	Normal blood flow/ High dialysate flow	High blood flow/ High dialysate flow
Blood flow, Qb, mL/min	200	200	200	400
Dialysate flow, Qd, mL/min (mL/h)	25 (1500)	67 (4000)	116 (7000)	116 (7000)
Time	**Lithium, mmol/L**			
0	5.6 (0%)	5.7 (0%)	5.4 (0%)	5.5 (0%)
5	4.9 (12%)	4.9 (13%)	4.4 (19%)	4.6 (16%)
15	4.5 (20%)	4.0 (30%)	3.4 (38%)	3.2 (42%)
30	4.0 (29%)	2.9 (48%)	2.2 (60%)	2.0 (64%)
60	3.0 (46%)	1.5 (73%)	1.2 (78%)	1.0 (82%)
	Salicylate, mmol/L			
0	NA	3.9 (0%)	4.4 (0%)	4.2 (0%)
5	NA	3.8 (3%)	4.0 (9%)	3.9 (7%)
15	NA	3.7 (5%)	3.6 (18%)	3.6 (14%)
30	NA	3.5 (10%)	3.1 (30%)	3.1 (26%)
60	NA	3.0 (23%)	2.5 (43%)	2.5 (40%)
	Valproic acid mmol/L*			
0	NA	NA	1.38 (0%)	1.50 (0%)
5	NA	NA	1.34 (3%)	1.38 (8%)
15	NA	NA	1.20 (13%)	1.25 (17%)
30	NA	NA	0.97 (30%)	0.99 (34%)
60	NA	NA	0.79 (43%)	0.76 (49%)

*Laboratory valproic acid method limited to therapeutic drug concentrations <2.08 mmol/L.
Qd dialysate flow rates, Qb blood flow rates.

extracorporeal removal of a range of xenobiotics in severe poisonings. The higher extracorporeal removal efficiency of HD outperforms CRRT, but advanced CRRT machines are approaching HD in flow rate parameters. The purpose of this study was to expand our knowledge of modern CRRT machines that are commonly available in the intensive care unit, using optimized settings in dialysate flow rates (Qd), and blood flow rates (Qb).
Methods: We developed an *in vitro* model using CRRT connected to a full-scale (adult) whole blood volume, 4 L, from swine. The blood was collected at a local small-scale abattoir and anticoagulated using heparin to prevent blood clotting during transport and CRRT. The CRRT efficacy (B. Braun Omni® CRRT Machine) was tested using Qb of 200 or 400 mL/min, and Qd of 25, 65 or 117 mL/min along with a continuous venovenous hemodiafiltration (CVVHDF) modus. In a simulated overdose model, high plasma concentrations of three dialysable drugs (plasma lithium 6 mmol/L, plasma salicylate 5 mmol/L, and plasma valproic acid 2 mmol/L) were dialyzed for 1 hour with continuous plasma concentration monitoring.
Results: The extraction fraction of lithium was markedly increased with increased Qd (Table 1). Increasing Qb from 200 to 400 mL/min and additional blood column pressure (CVVHDF modus) only marginally increased the extraction fraction. A similar, less pronounced, pattern was observed for salicylate. With valproic acid there was no increase in extraction fraction with Qb doubling, and data for low and moderate Qd was unavailable due to exceeded quantification limit.
Conclusion: This study emphasizes the importance of high dialysate flow for extracorporeal removal of toxic concentrations of dialysable drugs. Results suggest that modern effective CRRT machines with high dialysate flow settings may be used if HD is not readily available.

98. Investigation of the mineral consequences of repeated lithium exposure in a rat model

Mathieu Klein[a], Lucie Chevillard[a], Nahid Tabibzadeh[b], Morgane Bourmaud[c], Martine Cohen-Solal[c], Pascal Houillier[d] and Bruno Mégarbane[a]

[a]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris University, Paris, France; [b]Renal Physiology Department, Hôpital Bichat, INSERM U1149, Université de Paris, Paris, France; [c]INSERM UMR 1132, Biologie de l'os et du cartilage (BIOSCAR), Lariboisière Hospital, Paris University, Paris, France; [d]INSERM, CNRS, ERL 8228, Sorbonne Université, Université de Paris, Centre de Recherche des Cordeliers, Paris, France

Objective: Lithium, first-line treatment for bipolar disease, is responsible for various mineral impairments in chronically treated patients including hypercalcemia, hypocalciuria, hyperparathyroidism, and reduction in mineral bone density (DMO). These biological impairments suggest alteration in the calcium/parathyroid hormone (PTH), poorly evidenced by the available published experimental models, which delay onset of post-lithium exposure. The exact mechanisms involved are still unknown. The objectives of our study were to develop a rat model able to mimic all mineral modifications observed in humans on lithium therapy.
Methods: Two rat groups on a low-calcium diet (0.01% calcium in food) and two rat groups on normal diet were fed for one month with food with or without lithium (N= 9 rats/group). The mineral metabolism before and post-lithium administration was investigated by measuring blood/urine calcium, sodium, magnesium, creatinine, lithium and PTH (Elisa assay). Mineral bone density was measured in the rat tibias after sacrifice. Comparisons were performed using chi-squared tests, Student t-tests and ANOVA with post-tests and Bonferroni correction, as appropriate.
Results: We observed a significant progressive decrease in blood calcium after day 15 in the control rats ($p < 0.005$), as consequence of the low-calcium diet. By contrast, blood calcium was maintained in lithium-treated rats, with no significant differences in comparison to rats under normal diet. Mineral bone density was significantly decreased in rats under low calcium diet compared to rats under normal diet (control, $p < 0.0001$; lithium, $p < 0.05$). The different urine calcium and PTH profiles observed in the four rat groups suggested lithium-induced increase in tubular calcium reabsorption in the kidneys.
Conclusion: We developed a rat model able to mimic lithium-induced modifications in the mineral metabolism homeostasis as observed in humans early in lithium exposure. Our findings support a rapid-onset increase in tubular calcium reabsorption responsible for the lithium-induced hypercalcemia.

99. The last little push: use of naltrexone microinduction for protracted opioid withdrawal after prolonged buprenorphine tapers

Mayra Rodriguez[a] and Timothy J. Wiegand[b]

[a]Rochester Regional Health & Huther Doyle, Rochester, United States; [b]Department of Emergency Medicine University of Rochester School of Medicine and Dentistry, Rochester, United States

Objective: Tapering buprenorphine can be challenging. As a potent partial agonist, low doses have significant mu activity. Many individuals have protracted symptoms of opioid withdrawal at the end of tapers [1]. We present two cases illustrating effective use of an ambulatory rapid naltrexone microinduction protocol that attenuated withdrawal symptoms after buprenorphine taper.
Case series: A 35-year-old male had been tapering buprenorphine for several months after several years stability of his opioid use disorder, to 0.4 mg/day for several weeks. He felt unable to decrease despite adjunctive medications and various titration strategies and reported fatigue, myalgias, and insomnia if he did not take 0.4 mg buprenorphine 24-48 hours after last dose. Naltrexone microinduction was initiated with adjunctive medications. The patient felt completely "through the withdrawal" within 5 days of starting and transitioned to monthly IM-XR-naltrexone, remaining opioid free. A 46-year-old male stopped SC-buprenorphine monthly injections (10 months/300 mg/month) and planned to "autotaper". He felt fine for 6 months then reported feeling fatigue and paroxysmal sweating, interpreting them as due to opioid withdrawal. He used Kratom for 2 days prior to starting the naltrexone microinduction (36 hours after last Kratom). After the third dose (6 mg) he noticed less fatigue and completed the microinduction in 4 days without adjunctive medications after day 2.
Conclusion: Naltrexone microinduction may help patients transition fully off buprenorphine if protracted withdrawal symptoms after taper, or difficulty with low dose buprenorphine titration occurs. A naltrexone liquid formulation starting at 1 mg/mL dosed at 21:00 with adjunctive medications is included in Table 1. This was completed in an ambulatory setting using a combination of telemedicine and in-person visits over 6 days.

Table 1. Rapid naltrexone microinduction protocol for patients with protracted opioid withdrawal symptoms after buprenorphine taper.

Day	Naltrexone dosing (solution 1 mg/mL) at 21:00 nightly	Adjunctive medication dosed with naltrexone at 21:00 then QID PRN	Adjunctive medication if insomnia despite clonidine, then TID PRN	Follow-up
1	1 mg (1 mL)	Clonidine 0.2 mg with naltrexone and QID PRN (continued to day 5)	Hydroxyzine 50 mg PO/HS PRN and TID PRN anxiety (continued to day 5)	XR-naltrexone 380 mg/month IM after naltrexone 50 mg/day dose
2	3 mg (3 mL)	Clonidine	Hydroxyzine	NA
3	6 mg (6 mL)	Clonidine	Hydroxyzine	NA
4	12 mg (12 mL)	Clonidine	Hydroxyzine	NA
5	25 mg (25 mL)	Clonidine	Hydroxyzine	NA
6	50 mg (tab)	NA	NA	NA

HS hora somni (at bedtime), IM intramuscular, PO per os (by mouth), PRN pro re nata (when required), QID quater in die (4 times a day), TID ter in die (3 times a day), XR extended release

Reference

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100. Characteristics of poisonings in infants up to three months of age: comparison of two ten-year time periods

Mirjam Gessler, Katharina E. Hofer and Cornelia Reichert

Tox Info Suisse, Zürich, Switzerland

Objective: Poisonings in infants ≤3 months old are rare. A study from our poisons centre showed that from 2001 to 2010 only 0.8% of all poisonings in children <16 years occurred in this age group [1]. The aim of this study was to identify poisonings in infants ≤3 months from 2011 to 2020 and to compare the results with the previous study.

Methods: A retrospective case study of all inquiries involving infants ≤3 months reported to our poisons centre from 2011 to 2020 was conducted and the results compared to the data from 2001 to 2010. In cases with written feedback from the treating physician, analysis of poisoning severity was performed.

Results: In the present study 171,895 cases in children <16 years old were registered, 2274 (1.3%) involved infants, while in the former study 136,945 cases with 1096 (0.8%) involving infants were seen (Table 1). In the period 2011-2020 five severe cases were recorded: chloral hydrate, methadone, potassium phosphate, sulfamethoxazole/trimethoprim, *Illicium anisatum* (Japanese star anise). In 2001-2010 six severe cases were seen: cholecalciferol (n = 2), dimenhydrinate (n = 2), digoxin, *Illicium*

Table 1. Comparison of the two data sets from 2001-2010 and 2011-2020 of poisoning in infants up to three months of age.

2001 to 2010			2011 to 2020		
	Number of cases	%		Number of cases	%
Cases					
Total number of cases	1096	100.0	Total number of cases	2274	100.0
Sex (all cases)					
Male	432	39.4	Male	1025	45.1
Female	384	35.0	Female	1128	49.6
Unknown	280	25.5	Unknown	121	5.3
Callers (all cases)					
Laypersons	603	55.0	Laypersons	1528	67.2
Physicians	454	41.4	Physicians	672	29.6
Other health professionals	39	3.6	Other health professionals	74	3.2
Substances (all cases)					
Pharmaceuticals	650	59.3	Pharmaceuticals	1197	52.6
Household products	223	20.3	Household products	485	21.3
Cosmetics	70	6.4	Cosmetics	205	9.0
Food/beverages	47	4.3	Food/beverages	150	6.6
Other agents	106	9.7	Other agents	237	10.5
Top ten substances (all cases)					
Cholecalciferol	154	14.1	Cholecalciferol	215	9.5
Essential oils	108	9.9	Ethanol	146	6.4
Detergents	67	6.1	Essential oils	141	6.2
Smoke gas	55	5.0	Detergents	115	5.1
Paracetamol	40	3.6	Paracetamol	107	4.7
Amidosulfonic acid	19	1.7	Smoke gas	79	3.5
Phytomenadione	18	1.6	Amidosulfonic acid	70	3.1
Chlorhexidine	18	1.6	Acetic acid	53	2.3
Ethanol	16	1.5	Amoxicillin	35	1.5
Amoxicillin	14	1.3	Citric acid	31	1.4
Severity according to Poisoning Severity Score (cases with follow-up)					
Number of cases with feedback	174	100.0	Number of cases with feedback	350	100.0
No symptoms	118	67.8	No symptoms	264	75.4
Mild	41	23.6	Mild	69	19.7
Moderate	9	5.2	Moderate	12	3.4
Severe	6	3.4	Severe	5	1.4
Lethal	0	0	Lethal	0	0

anisatum. Some changes were seen regarding the top ten substances. Exposures to ethanol increased from 1.5% to 6.4%; most cases were due to confusing vitamin D with ethanol-containing disinfection solutions for the umbilical cord. Exposures to acids increased from 1.7% to 6.8%, often due to preparation of baby formulas/nutrition with water containing descaling products.
Conclusion: The results of both studies were similar. Poisonings in infants $\leq$3 months were rare with 0.8% and 1.3% of all pediatric poisonings, respectively. Severe symptoms were infrequent and were mostly due to pharmaceuticals.

Reference

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101. Gastroscopy – a potential role in decontamination: case report of a massive ingestion of isoniazid

Marco Marano, Manuel Murciano, Mara Pisani, Morida Khalil Ramla, Tullio Pelosi, Joseph Nunziata, Gabriella Bottari, Corrado Cecchetti, Biancamaria Goffredo, Sara Cairoli and Filippo Torroni
Bambino Gesù Children Hospital, Roma, Italy

Objective: Incidence of intentional massive drug intakes increased during the pandemic. We describe a teenager treated for a late diagnosed lethal dose of isoniazid with gastroscopy and supportive care, reporting the ineffectiveness of gastric lavage.
Case report: A 15-year-old girl (70 Kg), with Pott's Disease treated with rifampicin and isoniazid for 2 years, presented to the emergency department unresponsive with seizures. She had vomited and her face and lips were stained orange suggestive of rifampicin. Fast intubation and gastric lavage were performed, with removal of dense orange material. According to her father she had taken 2400 mg of rifampicin capsules. Electrocardiogram (ECG) showed sinus tachycardia. Blood gas analysis reported pH 6.95, lactate 15.8 mmol/L, base excess -22 mmol/L, and bicarbonate 10 mmol/L. Cerebral computerised tomography (CT) scan was negative. Subsequently the mother reported she had also taken 30 g of isoniazid. Pyridoxine 4 g intravenously, fluid therapy and sodium bicarbonate were administered. Considering the dose taken and the risk assessment, although 12 hours had passed, a gastroscopy was performed and abundant dense material was removed. At this stage, echocardiogram and electroencephalogram (EEG) showed no signs of seizures. She was extubated 24 hours after the event. Sixty hours after ingestion, she developed increased creatine phosphokinase (CPK) and transaminases (AST, ALT) up to a maximum of 68,190 U/L, 431/194 U/L, and 112 U/L, respectively. These parameters gradually improved and she was transferred to the neuropsychiatry ward on the fifth day where management included: lactate control, hepatic and renal profile with CPK every 8 hours, repeat dose activated charcoal, N-acetylcysteine and hyperhydration with control of diuresis. Isoniazid concentrations on admission and after 48 hours were 93.45 μg/mL and 0.25 μg/mL.
Conclusion: Gastric lavage is often used in cases of massive drug ingestion although its efficacy is reportedly limited [1,2]. Usually, gastroscopy is not considered in decontamination protocols and only anecdotal cases are described. We performed gastroscopy on the basis of clinical deterioration (after gastric lavage) and the dose ingested. Gastroscopy performed (after gastric lavage) for decontamination purposes, 12 hours after taking a massive ingestion of isoniazid and rifampicin, was useful in preventing more severe consequences for this patient.

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102. Toddlers exposed to opioid maintenance treatment 2004-2020

Anita Von Krogh and Mari Tosterud
Norwegian Poison Information Center, Oslo, Norway

Objective: Norway has seen the tragic death of a 2-year-old child due to accidental intake of its parent's medication for opioid maintenance therapy (OMT). OMT medications prescribed in Norway are mainly methadone, buprenorphine and buprenorphine/naloxone. Data from the Norwegian Prescription Database shows that the number of people on OMT has risen from 2700 in 2004 to 8100 in 2020 [1]. Approximately a third of these are women of child bearing age and every year 30-50 children are born to women who are on OMT [2]. We searched our inquiry database that covers 18 years to find what characteristics were prevalent in the cases where toddlers are exposed to this group of medication, and whether these show if there is a potential for prevention.
Methods: Our database was searched combining the codes for OMT and age 0-4 years. The data extracted were scrutinized for data errors. Repeated inquiries about the same case were pooled.
Results: We identified 22 unique cases involving 24 children. Two patients were less than 1 year, the rest 1-4 years old. Fourteen cases involved buprenorphine, 5 methadone and 3 buprenorphine/naloxone. The first enquiry for each case came from the public, day care, or pharmacy in 12 cases, in 10 cases it came from a medical facility or a hospital. Twenty cases were regarding an oral exposure, 15 of these were considered risk for moderate or severe toxicity requiring medical attention. One child was sent to hospital because severe symptoms developed, although the reported exposure was oddly small. This illustrates that in these dialogues, the anamnesis can be confusing and sometimes probably only part of the story is told. In 3 cases the child had found the packaging outdoors, and in 5 cases the child had found the medication at home. In the rest of the cases, it was unknown.
Conclusion: OMT medications are extremely toxic to children. We find that the numbers of accidents where toddlers are exposed to OMT are relatively low, but the risk associated is very high. Information to people using OMT regarding the toxicity and safe storage of the medication, can possibly prevent some future exposures.

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103. A life-threatening pediatric case of *Bufo bufo* toad egg poisoning with a happy ending

Cecilia Lanzi[a], Francesco Gambassi[a], Brunella Occupati[a], Alessandra Ieri[a], Claudia Saffirio[b], Zaccaria Ricci[c], Manuela L'erario[c], Elisabetta Cini[d], Monica Salomoni[e], Alessandra Franco[e] and Guido Mannaioni[e]

[a]Medical Toxicology Unit and Poison Control Centre, Careggi University Hospital, Florence, Italy; [b]Department of Emergency Medicine and Trauma Center, Meyer Children's Hospital, Florence, Italy; [c]Pediatric Intensive Care Unit, Meyer Children's Hospital, Florence, Italy; [d]General Laboratory, Careggi University Hospital, Florence, Italy; [e]Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA) Department, University of Florence, Florence, Italy

Objective: *Bufo* parotid glands and eggs contain bufadienolides. These cardiac glycosides can cause digoxin-like cardiac toxicity by inhibiting the sodium, potassium-adenosine triphosphatase (Na/K-ATPase) pump. *Bufo* poisoning is rare but carries a high mortality risk. Few cases of toad venom poisoning are reported worldwide, none in Europe. We describe the case of a child, on the autistic spectrum disorder, who developed an acute and severe cardiac bradyarrhythmia soon after bathing in a mountain creek.
Case report: On the way home, a boy appeared quieter than usual and vomited a large quantity of small black pearls. The father recognized them as toad's eggs, and he guessed a possible risk of poisoning. Soon after, the child became dizzy and confused. He was evaluated at home by the emergency medical unit showing bradycardia (35/min) with a second-degree atrial ventricular block (AVB). The Florence Poison Control Center (PCC) indicated the use of atropine on while the way to the nearest hospital. In the emergency room, the child showed bradyarrhythmia partially responsive to atropine and potassium blood concentration was 5.6 mEq/L. The Florence PCC suggested external pacing, atropine administration and anti-digoxin fragment antibodies (DigiFab®). Due to the evolving clinical features, the patient was transferred to the Regional Referral Pediatric Hospital (RRPH). At arrival in RRHP's Emergency Department, the patient was drowsy with an initial heart rate (HR) of 70 bpm, rapidly decreasing to 50 bpm associated with a third degree AVB. The potassium concentration had increased to 6.7 mEq/L, and the digoxin blood concentration was 0.68 ng/mL. A vial of DigiFab® was administrated with no effect, followed by another one with insulin and dextrose to correct hyperkalemia. Atropine was given with a fleeting result and pacing was considered. In the intensive care unit drowsiness and second degree AVB persisted, and the child showed a mild lactic acidosis, corrected with sodium bicarbonate. Three more Digifab® vials were administered. The cardiac rhythm finally evolved to sinus rhythm and potassium blood concentration decreased. Afterward, cardiac rhythm remained normal, and the patient was discharged 48 hours after the poisoning. A test, performed by the Pharmacology and Toxicology Laboratory Unit of Careggi University Hospital, confirmed the presence of bufadienolides in toad's eggs collected in the same mountain creek, in the area the child had been bathing.
Conclusion: As far as we know this is the first report of toad egg poisoning in Europe, one of the few worldwide. The administration of Digifab® was useful to revert the bufadienolide cardiac toxicity.

104. Home sweet home: a case of pediatric acrodynia

Fabiana Ursitti[a], Lucia Fusco[a], Mara Pisani[a], Carlo A. Locatelli[b], Anna Ronchi[b], Morida Khalil Ramla[a], Gabriella Bottari[a], Matteo Di Nardo[a] and Marco Marano[a]

[a]Bambino Gesù Children Hospital, Roma, Italy; [b]Maugeri Clinical and Scientific Institutes, Pavia, Italy

Objective: Mercury poisoning is rarely described in children [1,2] considered the most vulnerable population to environmental contaminants, due to differences in their immature detoxification mechanisms, physiology, body growth, lifestyle, and physical activity. We present a case of chronic elemental mercury poisoning with characteristic features.
Case report: A 13-month-old female, 10 kg, with a previous normal development, started showing symptoms of behavioral regression around 12 months of age. Within a few weeks she had lost social smiling and autonomous walking and her play strategies had regressed, as well as her interaction skills. She was drowsy and in bed all day, going from sleep to a state of inactive wake, with poor appetite, poor motor activity and poor language, systemic hypertension, maculo-papular palm plantar skin rash, edema, itching and desquamation. She was admitted to our neurology center. Virological, immunological investigations and brain magnetic resonance imaging (MRI) were negative. Electroencephalogram (EEG) showed irregular high voltage diffuse delta activity when the child was awake and not stimulated and theta-beta desynchronization when the child was sitting up and aroused. Cerebrospinal fluid was normal. Secondary causes of hypertension were excluded. As the EEG and neurological features suggested a secondary encephalopathy with skin signs, acrodynia and hypertension, mercury poisoning was suspected. Her mother reported accidental rupture of sphygmomanometer in the girl's room one month before the onset of symptoms which was only removed after two days. Environmental analysis of the room confirmed the contamination. Mercury blood and urine screening showed values 2.6 μg/L and 4.7 μg/L, respectively. In addition, both parents were also exposed although asymptomatic. The sphygmomanometer was promptly removed from home. No chelation therapy was performed, urinary mercury concentrations were monitored with clinical improvement and resolution of symptoms.
Conclusion: Mercury poisoning can present a non-specific clinical picture. Diagnosis is based on the history, exposure and onset of symptoms, including acrodynia. In case of suspected exposure to mercury, it is necessary to perform environmental testing, measure mercury concentrations in plasma and urine, remove the patient from the source of exposure and if necessary, start chelation therapy. In our case, after infectious and autoimmune causes underlying encephalopathy and hypertension were excluded, and exposure to mercury was suspected early.

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105. Unexpected outcome of an inhalational exposure to the microbial insecticide, *Bacillus thuringiensis*

Jonas Van Baelen, Jonas Moens, Pamela Selway, Dominique Vandijck and Anne-Marie Descamps
Belgian Poison Centre, Brussels, Belgium

Objective: To present a case received by the Belgian Poison centre (BPC) regarding XenTari WG®, a water-dispersible insecticide containing the bacterium *Bacillus thuringiensis* (aizawai strain).
Case report: The BPC was contacted by a professional gardener who had accidentally inhaled a finely dispersed (80 μm) solution of XenTari WG® while working. The man had used a large mobile vaporiser to treat oak trees infested with the oak processionary caterpillar without any personal protective equipment. The weather was windy and regularly blew vapors in his direction. He did not feel any immediate irritation and so continued to work. In the evening, a cough and respiratory tract irritation started and worsened during the night. The next morning, he first called his general practitioner and then contacted the BPC by phone. During the call, the patient mentioned a respiratory tract irritation and a pronounced cough. At the end of the call, the BPC advised him to consult a physician. A follow-up call by a specialized and experienced staff member of the BPC was performed 1 month later. The patient had indeed consulted his general practitioner, who immediately sent him to the hospital after auscultation. There, it was confirmed that the severe cough resulted in a collapsed lung, for which he underwent surgery the same day. He fully recovered.
Conclusion: Although inhalational exposures to *Bacillus thuringiensis* are known to produce mostly minor upper respiratory tract irritation [1,2], this patient developed a more serious effect. It should be noted that a key factor here was the exposure to the finely dispersed solution without any protective measures. It shows that the basic toxicity of a product can be enhanced by various causes. Formulation and route of exposure are important factors that should be considered, even in case of supposedly benign exposures.

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106. Early potassium supplementation as an antidote for barium poisoning

Ágnes Bakos and Ildikó Urbán
Péterfy Hospital and Jenő Manninger National Institute of Traumatology, Budapest, Hungary

Objective: Barium poisoning is a very rare, life-threatening condition characterized by gastrointestinal, neuromuscular, cardiac symptoms and severe hypokalaemia [1]. We reported two cases, one patient was treated successfully, the other patient died.
Case series: Case 1. A 33-year-old woman ingested a few sips of barium-polysulfide intentionally. Abdominal pain, nausea, vomiting, diarrhoea, and headache developed soon after. Gastric lavage was performed at the scene. Dizziness, forearm weakness, drowsiness, head numbness, bradycardia and ventricular extrasystole were detected during transport to the hospital. She was given 13.42 mmol of potassium and fluid replacement. Upon arrival her arrhythmia ceased. She was treated for five days in the intensive care unit (ICU). In addition to supportive therapy continuous parenteral potassium was administered for six days, followed by 1 day of oral dosing. She received a total of 604.02 mmol potassium. Haemodialysis was started 6 hours post-ingestion to eliminate barium. Chest pain occurred several times without cardiac enzyme changes. She received ceftriaxone due to fever and leucocytosis. Otherwise, there were no significant differences in laboratory results. Paralysis, respiratory failure, and fatal arrhythmia did not occur. She recovered completely and was discharged 10 days after admission. Case 2. A 32-year-old man was admitted to our department with hypertension, wide QRS tachycardia, dilated pupils, oral cyanosis, slurred speech and severe muscle flaccid paralysis in all four limbs and neck [1]. He was awake and oriented, confessed drinking alcohol but he denied the consumption of any substances and trauma. The blood gas and laboratory results showed metabolic acidosis, hyponatraemia, elevated serum creatinine concentration and leucocytosis. Chest, cervical spine X-ray and liquor tests detected no pathology. Via inserted nasogastric tube yellow, sulphur-smelling fluid was excreted. Shortly after admission, he developed respiratory failure and he was ventilated. One hour later he suffered a cardiac arrest. After successful resuscitation, he became cyanotic and repeat laboratory examination showed severe hypokalaemia (1.6 mmol/L). His mother found an insecticide containing barium-polysulfide and vomit in their cellar, which confirmed the possibility of barium poisoning. Massive potassium supplementation and haemodialysis was initiated, but he failed to respond and died.
Conclusion: In case of a definite diagnosis, in addition to gastric decontamination, adequate supportive therapy, and haemodialysis treatment, early initiation of potassium supplementation as an antidote can be successful even with a normal serum potassium concentration in barium poisoning.

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107. Toxins in local tissue after cobra envenomation

Jing-Hua Lin[a], Wang-Chou Sung[b], Han-Wei Mu[a] and Dong-Zong Hung[a]
[a]Division of Toxicology, China Medical University Hospital, Taichung City, Taiwan; [b]National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Miaoli, Taiwan

Objective: The cobra (*Naja* species) is one of the most common venomous snakes distributed over a wide geographical area, including Asia and Africa. Envenomation is characterized by muscle paralysis, local necrosis, and chronic musculoskeletal disability. The pathology of devastating tissue destruction, even though specific antivenoms exist, is not fully clear and continues to challenge healthcare providers. Cytotoxins, one of the main

groups of toxins in cobra venom, are thought to play a significant role with evidence in animals, but not human, studies. Here, we present a case of severe *Naja atra* (Chinese cobra) snakebite, identify the toxic components and highlight the possible role of toxins that remain in tissues around the bite site after a cobra snake bite.
Case report: A 68-year-old female was bitten by a *Naja atra* snake and presented to hospital 8 hours later. Her clinical course was complicated by severe tissue necrosis even after treatment with 10 vials of specific antivenom. We collected her blood and wound discharge to determine the concentration of whole venom or toxins, cytotoxin A3 and a short-chain neurotoxin using an enzyme-linked immunosorbent assay (ELISA). We found high concentrations of venom and cytotoxin A3 remained present in the wound discharge fluid until complete decontamination of the bite site by wide and advanced debridement to remove these toxins and promote wound healing.
Conclusion: The toxic compounds in the venom, especially cytotoxin A3, persisted in local tissue, and might play a key role in the pathology of dermonecrosis in cobra envenomation. Advanced debridement as early as possible may minimize the extent of tissue destruction in cobra envenomation.

108. Well bee-haved critters: a 21-year retrospective analysis of mass envenomations by honeybees, hornets and wasps in Sweden

Marc Stevens and Erik Lindeman
Swedish Poisons Information Centre, Stockholm, Sweden

Objective: The dangers of stings from honeybees, wasps and hornets in the order Hymenoptera are well-known, and are mainly related to IgE-mediated reactions to isolated stings. Conversely, mass-stinging events (MSEs, >50 stings in adults, >20 in children) by hymenopterans are capable of causing multiple organ dysfunction as a direct result of the venom load received. Elevated liver enzymes, rhabdomyolysis, kidney injury and even death have been reported. Herein, we present a 21-year retrospective analysis of MSEs reported to the Swedish Poisons Information Centre (PIC), a national resource with a catchment area of ~10 million individuals. Sweden is home to multiple hymenopteran species, including domesticated western honeybees (*Apis mellifera*), wasps (*Vespula germanica* and *Vespula vulgaris*) and hornets (*Vespa crabro)*.
Methods: All cases of consultations involving >5 stings by hymenopterans in our electronic database coded as posing *intermediate*, *clear* and *serious* risk between January 2000 and September 2021 were enrolled and charts were reviewed where applicable. Demographics, number of stings, species and clinical outcomes (where available) were collected.
Results: Of 4093 enrolled calls regarding hymenopteran stings to the PIC during a 21-year period, 373 involved >5 stings, of which 10 MSEs in adults and 17 in children and adolescents were identified. No cases with symptoms attributable to toxic effects of envenomation could be identified. Wasps (*V. germanica* and *V. vulgaris*) were clearly overrepresented, constituting 85% of all enrolled cases and 91% of paediatric MSEs, whereas bees were mainly implicated in MSEs involving beekeepers. Interestingly, not one single MSE with >100 stings was recorded.
Conclusion: Our data (further supported by paper records dating back 60 years) confirm that MSEs are a rare occurrence in Sweden. This could be explained by the lack of highly-aggressive or large apid subspecies such as the Africanised honey bee (*A. mellifera scutellata*), the giant honey bee (*Apis dorsata*) or vespids such as the Asian giant hornet (*V. mandarinia*). Moreover, the relatively short summer season due to Sweden's northerly location (55° to 69° N) likely precludes overwintering of large wild insect colonies, limiting colony sizes. Our dataset is limited by a lack of detailed information regarding clinical outcomes in the majority of cases, and it is possible that not all MSEs are reported to the PC. Although rare, medical professionals in Sweden nevertheless need to remain cognisant of the risks associated with mass hymentopteran envenomation.

109. Action of snake venoms on rabbit eyes in an *ex vivo* model: macroscopic examination, histological and EVEIT/OCT results

Denise Tambourgi[a], Norbert Schrage[b], Francois Burgher[c], Markus Glaudo[d], Alan H. Hall[e] and Laurence Mathieu[c]
[a]Immunochemistry Laboratory Butantan Institute, Sao Paulo, Brazil; [b]Acro e.V., Aachen, Germany; [c]Prevor Laboratory, Valmondois, France; [d]Acto e.V., Aachen, Germany; [e]Toxicology Consulting and Medical Translating Services, Azle, Texas, United States

Objective: Evaluation of corneal penetration and injury of seven snake venoms on whole rabbit eyes *ex vivo*.
Methods: Eyes from slaughterhouse New Zealand White rabbits were obtained. Lyophilized venoms from Latoxan (Portes-lès-Valence, France), were stored at -20 °C. Stock solutions were prepared in sterile 0.9% sodium chloride at 10 mg/mL, aliquoted, and stored at -80 °C. Aliquots diluted to 1 mg/mL with sterile 0.9% sodium chloride were used. Samples (500 µL) of each venom or sodium chloride control were pipetted into the wells of an untreated iced 24-well plate. After initial stain-free macroscopic inspection, the corneas were exposed. The well plate was incubated for 15 min at 32 °C and 99% humidity. Eyes were then placed cornea up into a fresh 24-well plate and capped for

Table 1. Details of the snake venoms tested on whole rabbit eyes *ex vivo*. Venoms were selected from Category 1 of the World Health Organization worldwide distribution of medically important venomous snakes.

Species (abbreviation)	Common name	Main venom components* (% w/v)	Venom delivery method
Naja naja (NN)	Indian cobra	3FT (65%); PLA (11%)	Biting
Naja atra (NA)	Chinese cobra	3FT (84%); PLA_2 (12%)	Biting and spitting
Naja mossambica (NM)	Mozambique spitting cobra	3FT (69%); PLA_2 (27%)	Biting and spitting
Naja nigricollis (NI)	Black-necked spitting cobra	3FT (73%); PLA_2 (22%)	Biting and spitting
Bothrops lanceolatus (LA)	Fer-de-lance, Martinican pit viper, Martinique lancehead	SVMP (74%); SVSP (14%)	Biting
Bothrops jararaca (JA)	Jararaca	PLA_2 (20%); SVSP (29%); SVMP (36%); NP (23%)	Biting
Hemachatus haemachatus (HH)	Ring-necked spitting cobra, rinkhals	3FT (63%); PLA_2 (13%)	Biting and spitting

*3FT three-finger toxin, PLA phospholipase, PLA_2 phospholipase A_2, SVMP snake venom metalloprotease, SVSP snake venom serine protease, NP natriuretic peptide

overnight incubation. The following day, stain-free macroscopic inspection and Optical Coherence Tomography (OCT) were performed. Eyes were submerged in 3.7% formaldehyde for at least 24 hours. Corneas were excised and divided into halves and stained for histological analysis.
Results: All eyes before venom exposure had normal macroscopic and OCT appearances. Control eyes remained normal throughout the study. Venoms-exposed eyes all had changes in corneal morphology, with venoms from NN, NA, NM, NI and HH (Table 1) causing more significant penetration and injury to the epithelial and stromal layers. These venoms produced increases in corneal thickness exceeding the OCT cut-off detection range. LA and JA venoms caused slightly increased corneal thickness. Controls had normal histology. Severe alterations of the whole corneal structures were observed with NN, NA, NM, NI and HH venoms.
Conclusion: Venoms from snakes exhibiting spitting behavior (NA, NN, NM, NI, HH) induced more significant corneal changes than non-spitting snakes (LA, JA). Envenomation and injury to the cornea can clearly be evaluated by this methodology, suggesting that prompt and efficacious decontamination might ameliorate or prevent such injuries.

110. Scorpion stings in Israel: Real-time species identification reduces emergency room referrals

Yael Lurie[a], Iris Levdov-Avital[b], Orit Granat[b], Boaz Shacham[c], Yoram Zvik[d] and Daniel Kurnik[e]

[a]Israel Poison Information Center, Clinical Pharmacology and Toxicology Section, Rambam Health Care Campus; Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel; [b]Israel Poison Information Center, Clinical Pharmacology and Toxicology Section, Rambam Health Care Campus, Haifa, Israel; [c]National Natural History Collections, The Hebrew University of Jerusalem, Jerusalem, Israel; [d]National Natural History Collections, The Hebrew University of Jerusalem; The Scorpion Research Lab, Hoopoe Ornithology & Ecology, Yeroham, Israel; [e]Clinical Pharmacology Institute, Clinical Pharmacology and Toxicology Section, Rambam Health Care Campus; Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel

Objective: Among 25 scorpion species in Israel, four are considered dangerous to humans (*Leiurus hebraeus, Androctonus crassicauda, Androctonus bicolor, Androctonus amoreuxi*). Until 2020, the Israel Poison Information Center (IPIC) recommended emergency department (ED) observation for most patients with scorpion sting victim, since reliable species identification was impossible. Since 2019, a zoology expert group has assisted the IPIC in scorpion species identification. Our aim was to evaluate the impact of real-time scorpion species identification on IPIC's recommendations for patient disposition and patient outcome after scorpion stings.
Methods: A retrospective evaluation of IPIC recommendations in cases with scorpion stings before (2015-2019) and after (2020) the start of collaboration with the zoology expert group. When available, a photograph of the scorpion was sent to a dedicated WhatsApp group, and species identification was reported to the IPIC.
Results: Between 2015 and 2020, the IPIC provided 1,004 consultations regarding scorpion stings (annual mean ± SD, 163 ± 18). Victims were aged 28 ± 18 years (range 0.4-83 years), and 53% were male. Most calls (67%) were from healthcare professionals and 33% from the public. Scorpion identification: Between 2015-2018, the culprit scorpion was identified in a single case. In 2019, the expert group was established, but photographs were sent and the scorpion identified in only 5 of 163 cases. During 2020, among 157 cases, 55 (35%) photographs were sent and identified. The median time from picture upload to identification was 0.5 minutes (range 0.25-12 minutes). Among identified species, *Hottentotta judaicus* was most common (30%), and 10 (18.2%) were known as dangerous to humans (5 cases each of *L. hebraeus* and *Androctonus* spp.). IPIC management site recommendations**:** Between 2015-2019, IPIC consultants recommended ED observation in most cases (91%-94%). In 2020, only 114/157 (73.5%) of cases were referred to the ED, while 29 callers (19%) and 12 callers (8%) were recommended home or clinic observation, respectively (Pearson's χ^2 for difference among the years, $P < 0.001$). Among 60 public callers, 18 (30%) were recommended home observation, and on follow-up calls, one subject had no valid phone number, and all others did well without the need for further healthcare referral.
Conclusion: Real-time expert identification of non-toxic scorpion species allows avoidance of unnecessary ED referrals for many patients and is likely to reduce patient anxiety.

111. Repeated palytoxin poisoning by inhalation after cleaning of aquarium stones and emptying of a palytoxin-contaminated water tank

Anja J. Huusom[a], Anne C. Curtz[b] and Lotte C.G. Hoegberg[c]

[a]Department of Occupational and Environmental Medicine, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark; [b]Allergy Clinic Department of Dermatology and Allergy, Gentofte Hospital, Copenhagen, Denmark; [c]Department of Anaesthesiology and Intensive Care, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark

Objective: The toxicity of palytoxin is surpassed only by few bacterial toxins. We evaluate the timeline of and quantify palytoxin exposure in relation to the onset of palytoxin poisoning symptoms among a family engaging in aquarium cleaning and emptying in their home.
Case report: A father bought ornamental stones with poisonous *Zoanthus* coral residues for his saltwater aquarium from an Internet sales forum. Whilst wearing nitrile gloves, he poured boiling water over the stones and scrubbed them with a scour sponge for 40 minutes. His elderly father stood a few meters behind him, the three children (aged 2, 6, and 10 years) were sitting 15 meters away in a sofa group with their grandmother and the family dog. The stones cooled for 5 minutes on the sofa table before they were submersed in the water-filled aquarium. Hours later, the mother entered the house and stayed for 15 minutes only. Five hours after cleaning the father developed a headache, tachycardia, chest pain, tachypnoea, paresthesia in his hands, confusion, fever, nausea and vomiting, and was rushed to the hospital where a cardiovascular event was ruled out. Within the next few hours, the three children and the grandparents consecutively developed fever, confusion, nausea and vomiting. The dog vomited and had seizures, whereas the mother was asymptomatic. The HAZMAT team did not measure any gasses and the natural gas boiler was without faults. All patients were treated for gastroenteritis after the diagnosis of carbon monoxide poisoning was rejected, and all were discharged within 48 hours. The dog developed rhabdomyolysis and acute kidney failure. Later, when the palytoxin contaminated stones were suspected as the cause of the family's illness, the father and his father emptied the aquarium over 2 hours by siphoning off the water to bottles and double bagging and discarding the stones whilst the

mother cleaned the house and the children were in their rooms. Eight to ten hours later the two males developed headache, muscle aches and fever, the mother and children had nausea and fever which fully subsided within 48 hours.
Conclusion: Although palytoxin is a large non-proteinaceous molecule it is inhalable during aerosol and droplet generating procedures with palytoxin-contaminated water. In this case re-exposure and recurrence of severe toxic symptoms occurred after emptying of a water tank with contaminated water over 48 hours after the initial exposure suggesting a long-lasting (> 48 hours) stability of palytoxin in water.

112. Utilization of 3-dimensional (3D) scanner technology to measure circumference and volume of limbs in patients bitten by venomous animals

Rittirak Othong and Warangkana Pongpat

Department of Emergency Medicine, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand

Objective: While three-dimensional (3D) scanners are widely utilized in modern medicine, there is yet to be reliable evidence of using a 3D scanner for measuring limb circumferences in patients bitten by venomous animals. The objective of this study was to compare the precision of limb circumference measurement between a 3D scanner and a measuring tape.
Methods: This was a cross-sectional analytic study. Patients over 18-year-old bitten by *Trimeresurus* spp. visiting the emergency department (ED) of Vajira Hospital between 1 October-20 December 2019 were included. Circumference of each bitten limb and the contralateral unbitten limb were measured by a measuring tape and a 3D scanner (Structure Sensor®). Each of two physicians measured limb circumferences twice using each of the two methods at the first ED visit, 24, 48, and 72 hours after the snake bite. Each limb had 3 reference points for measurement using both methods.
Results: Of the 17 patients who had complete follow-ups at the 4-time points included, there were 408 reference points (204 pairs of either lower or upper limbs) for measurement. It was found that the intra- and interrater reliabilities of measuring lower limb circumferences were excellent for both the measuring tape [intraclass correlation (ICC) = 0.922-0.999] and the 3D scanner (ICC =0.865-0.992). The ICCs of the measuring tape and the 3D scanner were between 0.590-0.990 and 0.220-0.976, respectively. Comparing the interrater reliabilities between these two methods, the ICCs of the lower limb circumference and the lower limb volume were greater than 0.9 in every site. Bland Altman plot also demonstrated the two methods were precise and could be used interchangeably.
Conclusion: The 3D scanner is comparable to the measuring tape in its ability to precisely measure limb circumferences, especially for the lower limbs, and it has an added ability to calculate the limb volume.

113. Human poisoning by neurotoxic phycotoxins related to the consumption of shellfish: cases registered by the French Poison Control Centres from 2012 to 2019

Sandra Sinno-Tellier[a], Eric Abadie[b], Luc de Haro[c], David Boels[d], Jérôme Langrand[e], Gaël Le Roux[f], Magali Labadie[g], Juliette Bloch[a], Nathalie Paret[h] and Nicolas Delcourt[i]

[a]French Agency for Food, environmental and Occupational Health & Safety, Maisons-Alfort, France; [b]French National Institute for Ocean Science, Sete, France; [c]Poison Control Centre, Marseille University hospital, Marseille, France; [d]Pharmacology and Toxicology Department, Nantes University hospital, Nantes, France; [e]Poison Control Centre, Paris University hospital, PARIS, France; [f]Poison Control Centre, Angers University hospital, Angers, France; [g]Poison Control Centre, Bordeaux University hospital, Bordeaux, France; [h]Poison Control Centre, Lyon University hospital, LYON, France; [i]Poison Control Centre, Toulouse University hospital, Toulouse, France

Objective: In June 2019, a paralytic shellfish poisoning (PSP) case related to the consumption of mussels contaminated by saxitoxins at a concentration below the regulatory threshold came to the attention of the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) [1]. This pointed to probable undetected human cases of poisoning by neurotoxic phycotoxins. We conducted a review of shellfish poisonings recorded by the French Poison Control Centres (PCCs), looking for a link with phycotoxin concentrations in production areas when possible, in order to identify those cases presenting neurological signs compatible with neurotoxic phycotoxins.
Methods: Retrospective study of poisoning cases by bivalve shellfish recorded by the PCCs from 2012 to 2019. All medical records were reviewed by a toxicologist. Cases that could be related to neurotoxic phycotoxins were selected and described. Diagnosis was based on symptoms compatible with ingestion of contaminated shellfish and on environmental data of shellfish production areas (analysed by the French National Institute for Ocean Science, Ifremer), or notifications to the European Rapid Alert System for Food and Feed for imported shellfish.
Results: Among the 619 shellfish poisoning cases recorded by the PCCs from 2012 to 2019, 22% (n = 134) had at least one neurological symptom (headache, dizziness or paraesthesia). Review of the medical records for the 134 patients led to the suspicion of 14 cases of PSP and one case of amnesic shellfish poisoning (ASP). Five patients experienced persistent neurological symptoms. High concentrations of saxitoxins were found in shellfish production area for six cases whereas the harvested origin remains unknown for six others; two more cases were linked to the June 2019 alert. Concentration of domoic acid were above the regulatory threshold for the ASP case. Saxitoxins or domoic acid were not tested in the blood or urine of these patients.
Conclusion: ANSES, PCCs and Ifremer developed a specific questionnaire and recommend actions to take (to keep any meal leftovers and go to the emergency department of a hospital to collect biological samples), when neurological symptoms related to shellfish consumption are reported to a PCC. Daily prospective monitoring of shellfish poisoning cases registered in the national PCCs database was also implemented. To date, no other cases of neurotoxic phycotoxins poisoning were suspected among new shellfish poisonings registered by the PCCs.

Reference

[1] Delcourt N, Arnich N, Sinno-Tellier S, et al. Mild paralytic shellfish poisoning (PSP) after ingestion of mussels contaminated below the European regulatory limit. Clin Toxicol (Phila). 2021;59:76–77.

114. The epidemiology and clinical features of spider bites in South Africa

Catharina E. Du Plessis, Carine J. Marks and Helmuth Reuter

Stellenbosch University, Parow, South Africa

Objective: Globally, few spiders are regarded as harmful to humans. Of the more than 2000 species found in South Africa, the following are regarded as medically important *Latrodectus*, *Cheiracanthium* and *Loxosceles*. Limited data is available on the medical consequences of these spiders; therefore, the aim of this study was to address some of the uncertainties surrounding the clinical features of these spider bites. A secondary objective was to compile an algorithm for the identification of spider bites to ensure more rapid and effective treatment.
Methods: Data from two datasets (consultation forms from Tygerberg Poisons Information Centre and electronic data from the Poison Information Helpline of the Western Cape) were retrospectively reviewed for suspected spider bites involving humans. Data was extracted for the period January 2005 to December 2017. Key variables included patient and caller demographics, geographical location, type of spider and clinical features.
Results: During the study period, 1917 suspected spider bite calls were recorded. Most of these calls originated from the Western Cape (n = 1085, 56.6%); predominantly received from the general public (n = 1139, 59.4%). Bites mostly occurred during the warmer months of the year, specifically in January and February (n = 208, 10.9%). The spider bites were recorded as: 284 (14.8%) neurotoxic bites, 241 (12.6%) cytotoxic bites, 91 (4.7%) other bites and 1301 (68%) unidentified bites. Only 11.3% of the bites met the criteria of definite bite. The administration of antivenom was advised in 80 of the 138 positively identified button spider bites. Generalised pain, muscle pain and cramps and sweating were the symptoms most often recorded. The largest concentration of "definite" *Latrodectus* bites were reported from the area where *L. indistinctus* is found. Only five (2.1%) cytotoxic spider bites were positively identified including two sac spiders, two violin spiders and one six eyed sand spider. The majority of suspected cytotoxic spider bites (n = 211, 86.8%) could not be confirmed. Swelling, redness and pain were common clinical features with cytotoxic spider bites. Clinical features recorded were used to compile an algorithm for the identification and rapid treatment of spider bites.
Conclusion: Although commonly found around houses, only a few spiders will cause severe effects. Besides button spiders where clinical features are well described, the identification and cause of necrotic wounds are difficult to establish. The proposed algorithm should be taken into consideration when making a diagnosis. South African spider antivenom is effective and should be administered if indicated.

115. A retrospective cohort study of antivenom for reduction in limb swelling from green pit viper envenomation

Supa Niruntarai, Pit Chansomboon and Rittirak Othong

Department of Emergency Medicine, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand

Objective: To evaluate the effect of antivenom for the reduction in limb swelling after green pit viper envenomation. Reduction in pain and rates of adverse events after antivenom administration are also studied.
Methods: This retrospective cohort study was conducted by collecting data of patients who were bitten by a green pit viper and presented at the emergency department (ED) at 2 public hospitals in Bangkok. Medical records of patients with the diagnosis of green pit viper envenomation were retrospectively reviewed from 1 January 2007 to 15 February 2021. Limb circumferential lengths of both the affected side and unaffected side were measured at ED admission, then at 24 ± 6, 48 ± 6, and 72 ± 6 hours after the bite. Data were statistically compared between the intervention (antivenom) and control (no antivenom) groups.
Results: In total 57 patients were included, 17 in the intervention group and 40 in the control group. The reduction in limb swelling in the intervention group was significantly better than that of the control group within the first 72 hours after the bite (ANOVA, P = 0.019). The reduction in circumferential length was 0.66 cm versus 0.18 cm at 24 ± 6 hours, 0.84 cm versus 0.62 cm at 48 ± 6 hours, and 1.37 cm versus 0.66 cm at 72 ± 6 hours. The percentage reduction in limb circumference was significantly better in the intervention group compared to the control group (3.40% versus 0.62% at 24 ± 6 hours, 3.96% versus 2.63% at 48 ± 6 hours, and 5.71% versus 2.73% at 72 ± 6 hours (ANOVA, P = 0.022). The reduction in pain score was similar. One case (5.9%) had anaphylaxis following antivenom administration.
Conclusion: The results of this study suggest that green pit viper antivenom might help decrease the size of limb edema following green pit viper envenomation throughout 72 hours after onset.

116. Circumstances of bites by non-native reptiles in France

Gaël Le Roux[a], Sébastien Larréché[b] and Alexis Descatha[a]

[a]Poison Control Center, Angers, France; [b]HIA Bégin, Saint Mandé, France

Objective: To describe cases of bites by exotic reptiles in France, in terms of the species involved and the circumstances.
Methods: A retrospective observational study was conducted in all reported cases of non-native reptile bites from 2000 to 2020 to French poison centres.
Results: A total of 218 cases of bites by non-native reptiles of the *Toxicofera* clade have been recorded in France between 1 January 2000 and 31 December 2020. A lizard (*Heloderma suspectum* (Gila monster), *Pogona vitticeps* (central bearded dragon) and *Varanus exanthematicus* (savannah monitor)) was involved in 7 cases (3.2%), a snake in all other cases (211 cases, 96.8%). Seven snake families were involved. Pythonidae (31.6%), Colubridae (22.5%) and Boidae (19.7%) were the most frequently represented. Among the snakes, 31 are considered venomous (elapids, viperids, dipsadids, lamprophiids, and among the colubrids, *Thrasops flavigularis*), biting 51 patients (23.4%). Bites occurred on the upper limb in 190 cases (87.2%) and on the head in 9 cases, almost exclusively by boids. There was one case of ocular projection of venom by *Naja mossambica*. The severity according to the PSS was distributed as follows: PSS0/1 187 cases (85.8%), PSS2 23 cases (10.6%), and PSS3 8 cases (3.7%). Two cases were left with sequelae (finger amputation after a *Naja naja* bite and arm amputation after a *Bothrops asper* bite). The sex ratio (M/F) was 1.79 (140/78). The mean age was 29.0 ± 15.8 years (4 months-67 years). The mean age of patients bitten by a

venomous species was higher than those bitten by a non-venomous species (37.7 ± 14.2 years versus 26.6 ± 15.5 years, $p < 0.001$). PSS 2/3 severity cases were more frequent in men than in women (17.9% versus 7.7%, $p = 0.039$). Sixty-seven cases (30.7%) occurred in the evening (18:30 to 23:00) and 22 cases (10.1%) occurred during the deep night (midnight to 07:00). In 186 cases (85.3%), the bite occurred at home and at the workplace in 19 cases (8.9%). Cases occurring in the workplace were significantly more severe than those occurring at home (35.0% PSS 2/3 cases versus 13.4%, respectively). Feeding/nursing activity accounted for 88.2% cases of venomous reptile bites.
Conclusion: Bites by exotic reptiles are rare events but needs specific skills in toxicology. Bites are potentially serious when they involve venomous animals, particularly in the workplace.

117. Viper bite: don't suck it off!

Marion Legeay, Stéphanie Rochet and Gaël Le Roux
Poison Control Center, Angers, France

Objective: In the case of a viper bite, it is not recommended to perform suctioning of the wound because its effectiveness has not been demonstrated. However, this procedure is rarely performed by the victims or their relatives. This case describes an unusual consequence of this practice.
Case report: A 60-year-old man with no previous medical history was bitten on his left index finger at the proximal phalanx while placing his hand on the ground near a bush. He quickly decided to try to extract the venom by making himself bleed and then sucking it out with his mouth. He did this several times in a row. He was admitted to the emergency room 30 minutes later with edema of the entire hand up to the wrist. He then developed vagal discomfort and lip edema with macroglossia. There was no dyspnea. He received 1 ampoule of 4 mL of specific antivenom, an antihistamine and steroids. One hour after the bite, he presented collapsed with blood pressure at 60/30 mmHg and vomiting. He received 0.5 mg of adrenaline IM, which corrected the pressure but not the oedema. The labial and hand edema decreased the next day with improvement of mobility. No abnormalities were found in the biological testing. A negative serum tryptase testing ruled out an anaphylactic cause, in addition to the lack of immediate effectiveness of antihistaminic drug and steroids. The snake was not formally identified but was probably *Vipera berus* or *Vipera aspis*.
Conclusion: This clinical case suggests that suctioning in a prehospital environment by the victim is ineffective and can be potentially dangerous, with a potential diffusion of the viper's venom through the oral mucous membranes.

118. Experimental studies to compare available antivenoms to treat *Bothrops* genus snakebite envenoming in the French Territories in the Americas

Dabor Resiere[a], Jonathan Florentin[b], Hossein Mehdaoui[c], Remi Neviere[d], José Gutiérrez[e] and Bruno Mégarbane[f]

[a]Critical Critical Care Unit, University Hospital of Martinique (French West Indies), Fort-de-France, France; [b]University Hospital of Martinique, Fort-de-France, France; [c]University Hospital of Martinique (French West Indies), Fort-de-France, France; [d]Department of Cardiology, University Hospital of Martinique (French West Indies), Fort-de-France, France; [e]Instituto Clodomiro Picado, Faculdad de microbiologia, Universidad de Costa Rica, San José, Costa Rica; [f]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, Paris University, INSERM UMRS 1144, Paris, France

Objective: In the French Territories in the Americas, *Bothrops* snakebite envenoming represents a public health issue. In Martinique, *Bothrops lanceolatus* is the only snake responsible for envenoming with thrombotic complications, whereas *Bothrops atrox* is responsible for most envenoming in French Guiana. The first antivenom specific to *Bothrops lanceolatus*, Bothrofav1®, produced in 1991, reduced complications. However, in 2004, an upsurge in cases of ischemic stroke despite early antivenom infusion, suggested a decline in effectiveness. A new antivenom, Bothrofav2® was produced in 2011 and manufactured in France; but its marketing will cease in 2022. Polival-ICP® (manufactured in Costa Rica) and Antivipmyn Tri® (manufactured in Mexico) are successfully used to treat *Bothrops atrox* envenoming in French Guiana. To address the risk of Bothrofav2® non-availability, we compared the effectiveness of all three antivenoms on *Bothrops lanceolatus* venom using an experimental approach.
Methods: We conducted third-generation antivenomics quantitative analyses, *in vivo* mouse and *in vitro* assays comparing Bothrofav2®, Polival-ICP® and Antivipmyn Tri® on *Bothrops lanceolatus* venom.
Results: Bothrofav2® immunocaptured all major *Bothrops lanceolatus* venom protein components, underscoring its high neutralizing efficacy (Table 1). Our *in vivo* and *in vitro* assays demonstrated its effectiveness in the neutralization of lethal, local and systemic hemorrhagic, oedema forming, myotoxic, thrombocytopenic, proteinase and phospholipase A2 activities, showing a higher preclinical efficacy as compared to a previous batch used in the past. Polival-ICP® had the higher neutralizing activity against lethal, haemorrhagic and *in vitro* coagulant activities of the *Bothrops lanceolatus* venom than Antivipmyn Tri®. Bothrofav2® and Polival-ICP® antivenoms similarly neutralize the venom-induced myotoxic effects while Antivipmyn Tri® did not neutralize the lethal activity at the highest antivenom level tested.
Conclusion: Based on preclinical investigations, the three available anti-Bothrops antivenoms are almost similarly effective. Our findings will allow optimizing antivenom use in *Bothrops* genus snakebite, especially in case of reduced availability of Bothrofav2®.

Table 1. Toxic and enzymatic activities of the venom of *B. lancoleatus* and its neutralization.

	Venom activity*	Neutralization by the antivenom Bothrofav2® (mg antivenom protein/mg venom)
Lethal (LD_{50}, µg/g)	6.0 (5.0-7.3)	12.0 (4.8-21.6)
Local hemorrhagic (MHD, µg)	3.7 ± 0.2	7.8 ± 1.1
Systemic hemorrhagic (MHD, µg)	10	103
Edema-forming	0.9 ± 0.2	34.8 ± 7.0
Thrombocytopenic (TD_{50}, µg)	32 ± 16	5.2
Proteinase (U/mg)	4.5	8.3 ± 0.9
Phospholipase A2 (µEq/mg/min)	2.4 ± 0.3	5.7 ± 1.1

LD_{50} medial lethal dose, MHD minimum hemorrhagic dose; TD_{50}, thrombocytopenic dose 50%; * expressed as median or mean ± SEM

119. Clinical features and management of snakebite envenoming in French Guiana

Dabor Resiere[a], Stéphanie Houcke[b], Jean Marc Pujo[c], Didier Hommel[b], Bruno Mégarbane[d] and Hatem Kallel[b]

[a]Intensive Care Unit, Cayenne General Hospital, French Guiana, Intensive Care Unit, University Hospital of Martinique(French West Indies), Fort-de-France, France; [b]Intensive Care unit, cayenne General Hospital, French Guiana, Cayenne, French Guiana; [c]Emergency department, Cayenne General Hospital, French Guiana, Fort-de-France, French Guiana; [d]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, Paris University, INSERM UMRS 1144, Paris, France

Objective: Management of snakebite envenoming in is based on symptomatic measures and antivenom (AV) administration (Antivipmyn Tri®, Instituto Bioclon, Mexico). Our study aimed to assess clinical manifestations, the efficacy, and safety of Antivipmyn Tri® (with two different dose regimens) in the management of snakebite.
Methods: Our study is a prospective observational investigation, conducted in the Intensive Care Unit (ICU) of Cayenne General Hospital between 1 January 2016 and 31 December 2019. We included all patients hospitalized for snakebite envenoming. Our study contained three treatment groups (without AV, 3 vials, and 6 vials Antivipmyn Tri®).
Results: During the study period, 133 patients were included. The main clinical symptoms were edema (98.5%), pain (97.7%), systemic hemorrhage (18%), blister (14.3%), and local hemorrhage (14.3%). AV was prescribed for 83 patients (62.3%), and 17 of them (20%) developed early adverse reactions. Biologic parameters at admission showed defibrination coagulopathy in 124 cases (93.2%), International Normalized Ratio (INR) >2 in 104 cases (78.2%), and partial thromboplastin time >1.5 seconds in 74 cases (55.6%). Median time from snakebite to AV was 9.0 hours (IQR, 5.2-20.4). Median time from snakebite to achieve a normal dosage of fibrinogen was 47.0 hours versus 25.3 hours, that of Factor II 24.6 hours versus 15.1 hours, that of Factor V 31.4 hours versus 19.4 hours, and that of Factor VIII 21.3 hours versus 10.2 hours in patients without and with AV, respectively ($p < 0.001$ for all factors).
Conclusion: Patients receiving Antivipmyn Tri® showed a reduction in the time to return to normal clotting tests, compared to those who did not. We suggest assessing other antivenoms available in the region to compare their efficacy and safety with Antivipmyn Tri® in French Guiana.

120. Comparison of the clinical effects of *Bothrops lanceolatus* and *Bothrops atrox* venoms and their reversal using Bothrofav® antivenom – a rat study

Sébastien Larréché[a], Simon Mathé[a], Lucie Chevillard[a], Patricia Risède[a], Dabor Résière[b], Virginie Siguret[a] and Bruno Mégarbane[a]

[a]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris University, Paris, France; [b]Intensive Care Unit, University Hospital of Martinique, Fort-de-France, Martinique

Objective: Snake envenoming is a major public health issue resulting in about 2.7 million cases worldwide yearly. The venom of *Bothrops lanceolatus*, a snake from Martinique Island, is characterized by the occurence of thrombotic events, unlike hemorrhagic syndromes with continental Bothrops such as *Bothrops atrox*. Bothrofav® (Microparm Ltd, UK) antivenom is effective to treat envenoming-related complications. We describe possible specificities in the envenoming manifestations between the two *Bothrops* species (*lanceolatus* and *atrox*) in a rat model focusing on organ dysfunction, coagulation impairment and prevention using the Bothrofav® antivenom.
Methods: Rats were randomized in three groups receiving a subcutaneous injection of saline (control), 220% of the lethal dose-50% of *B. lanceolatus* (Latoxan, France; determined at 12 mg/kg) and *B. atrox* venoms (Latoxan, France; determined at 6 mg/kg) ($n = 5$ rats/group). We studied the neurological (using a clinical scale of sedation), respiratory (using plethysmography and arterial blood gas analysis), liver (transaminases), renal (diuresis, creatinine) and coagulation functions (viscoelastometry, platelet count, serum fibrinogen, thrombin generation test) in the envenomed and control rats. Then, we tested the preventive effects of Bothrofav® pretreatment on coagulation test impairments ($n = 5$ rats/group). We determined the area under the curve for the studied parameter versus time, if required. Comparisons between the groups were performed using Student t-tests (2 groups) or ANOVA with Dunnett's post-tests (≥ 3 groups).
Results: No significant differences were observed between the two venoms regarding the time-course of the resulting neurological, respiratory, renal and hepatic toxicities. *B. atrox* venom was characterized by the rapid onset of significant thrombocytopenia ($p < 0.001$), corrected by Bothrofav®. *B. lanceolatus* venom was characterized by the delayed onset of significant functional hyperfibrinogenemia ($p < 0.01$), not corrected by Bothrofav®. Thrombin generation was significantly less important with *B. lanceolatus* than *B. atrox* venom ($p < 0.01$).
Conclusion: Hyperfibrinogenemia secondary to *B. lanceolatus* venom, potently due to a lower thrombin generation, may be one of the causes of the prothrombotic profile associated with *B. lanceolatus* envenomation. Further investigations may be relevant to study other factors such as the immune response or endothelial function that could also contribute to *B. lanceolatus* venom-attributed hypercoagulability.

121. Coronary artery thrombosis after a *Vipera aspis* bite: a case report

Lucia Bernasconi[a], Azzurra Schicchi[a], Davide Lonati[a], Benedetta Brolli[a], Cristina Grazioli[a], Valentina Negrini[a], Roberto Pirozzolo[b], Jessica Caprio[c], Giulia Scaravaggi[a] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]Intensive Care Unit, Santa Corona Hospital, Pietra Ligure, Italy; [c]Intensive Care Unit, Santa Corona Hospital, Pavia, Italy

Objective: In Italy, three viperids (*Vipera aspis, Vipera berus, Vipera ammodytes)* can cause severe toxicity. There are few reports about local thromboembolic complications, and systemic manifestations are uncommon after European snakebites. We report a case of viper envenomation with coronary artery thrombosis complicated by ventricular fibrillation.
Case report: A 62-year-old, with a history of cardiovascular disease (3 stents after abnormal exercise stress test), chronically treated with ticagrelor and aspirin, was admitted to the

Emergency Department (ED) after a snakebite on the right arm (herpetologist identification: *Vipera aspis*). On presentation, 2 hours after the bite, he had vomiting, hypotension (90/60 mmHg), and mild oedema at the bite site. The first electrocardiogram (ECG) was normal. Laboratory tests in the ER showed: activated partial thromboplastin time (APTT) ratio 0.71 (reference 0.83-1.27), troponin I 14.2 ng/mL (reference <19.8 ng/L), and D-dimer concentration 7151 ng/mL. Over the next 3 hours he had four episodes of ventricular fibrillation, with restoration of spontaneous circulation (ROSC) after defibrillation and cardiopulmonary resuscitation (CPR). Owing to hemodynamic instability, he was intubated and 1 vial of *Viper Venom Antitoxin↓ (Biomed)* was administered intravenously without adverse reaction. The post-ROSC ECG showed ST-elevation on anteroseptal and lateral leads, and percutaneous transluminal coronary angiography (PTCA) was performed with evidence of a thrombus on the bifurcation of the anterior descending coronary artery D1 without an underling atherosclerotic plaque. Intracoronary eptifibatide double bolus dose and IV infusion for 12 hours was administered. Thromboelastography (TEG) for coagulation assessment was used after PTCA to verify thrombus breakdown. Neurological clinical manifestations also occurred 14 hours after the bite with bilateral ptosis and facial paraesthesia. These symptoms were considered secondary to snake venom and not to a cerebral thrombotic event because of the symmetric manifestations and the neurotoxic characteristics of the *Vipera aspis* venom. The patient required 9 days of hospitalization; he had no neurologic, cardiac or local sequelae.

Conclusion: Snake venom is a mixture of proteins and peptides among which there are snake venom serine proteases (SVSPs) and metalloproteinases that can target coagulation factors, possibly causing pro-coagulative clinical complications. *Vipera aspis* has been known to cause primarily neurotoxic manifestations due to the presence in its venom of a neurotoxin with a A_2-phospholipase activity; pro-coagulant factors have also been isolated from its venom. In this case it is possible to speculate that coronary artery thrombosis was due to a systemic pro-coagulative status caused by direct venom toxic effect in a patient with underlined predisposing factors.

122. Accidental ingestion of alcoholic beverages in dogs

Nicola Bates, Zoe Tizzard and Nick Edwards

Veterinary Poisons Information Service, London, United Kingdom

Objective: Alcoholic beverages may be left unattended and readily accessible to pets. We examined the types of beverages, clinical signs and outcome in dogs that accidentally ingested an alcoholic beverage.

Methods: A retrospective study of cases involving ingestion of alcoholic beverages in dogs reported to the Veterinary Poisons Information Service (1993-2021). Only cases with follow up information were included. Severity of poisoning was scored using the Poison Severity Score modified for dogs.

Results: There were 93 cases. Of these the beverages involved were wine (n = 30, including two each of sparkling and fortified wines), liqueurs (n = 29), spirits (n = 28), beer or lager (n = 5) and one cocktail (White Russian containing coffee liqueur, vodka and cream). The most common drink overall was a single brand of Irish cream liqueur (n = 21, 23%). Common clinical signs were ataxia (48%), vomiting (15%), inebriation (14%), lethargy/depression (12%), hypothermia (12%) and drowsiness (11%). The dose was estimated in one asymptomatic case (7 g ethanol/kg). In 16 symptomatic dogs the mean amount of ethanol ingested was 3.5 g/kg (range 0.5-9 g/kg). In 10 cases the dogs ate fruits that had been used to flavour spirit and then discarded. These were damsons (n = 4) and sloes in gin (n = 3), raspberries (n = 1) and cherries in vodka (n = 1) and plums in brandy (n = 1). Overall, 16 dogs remained well and 75 recovered (minor n = 46, moderate n = 28, severe n = 1). The time to recovery ranged from 3-48 hours (mean 17.4 hours, n = 27). There were no deaths, but two dogs (2%) were euthanased. A 37 kg Labrador drank 750 mL of Irish cream liqueur (17% ethanol, 3.4 g ethanol/kg body weight) and developed disorientation, inebriation, vomiting, coma, urinary incontinence, stiffness and convulsions. A West Highland White terrier developed collapse, dehydration and hypothermia after an unknown amount of whisky and failed to respond to supportive care. Of the 10 dogs that ingested ethanol-soaked fruits severity of poisoning tended to be moderate to severe (n = 7 and n = 1, respectively), rather than minor (n = 2).

Conclusion: Dogs will drink wine, spirits and liqueurs but find cream liqueurs particularly attractive; the cream probably makes these beverages palatable to dogs. The few cases involving beer and lager may be because they contain less ethanol and are often drunk from a bottle or can and not a glass making them less accessible for pets. Discarded ethanol-soaked fruits used to flavour spirits tended to be associated with more pronounced poisoning and care should be taken to dispose of these safely where pets cannot access them.

123. Severe local tissue injury from accidental use of pressurised surgical spirit instead of water during dental descaling in cats and dogs

Nicola Bates, Zoe Tizzard and Nick Edwards

Veterinary Poisons Information Service, London, United Kingdom

Objective: Dental hygiene in cats and dogs, as in humans, is important to maintain oral health. Regular brushing of teeth in pets may be impractical and periodic descaling of teeth under general anaesthesia may be required. The VPIS received a number of enquiries where pressurised surgical spirit (ethanol 90%. methanol 5%) had been used in descaler machines instead of purified water. We examined the circumstances, clinical signs and outcome in these cases.

Methods: A retrospective review of cases involving the use of surgical spirit in veterinary dental machines instead of purified water in companion animals reported to the Veterinary Poisons Information Service (2015-2021).

Results: There were 16 cases overall, involving 13 dogs and 3 cats. The dogs had a mean age of 7 years 6 months (range 4 years 10 months to 12 years, n = 8) and mean weight 11.5 Kg (range 4-20 Kg, n = 9). Details were known for two cats (10 years, 5.2 Kg and 15 years, 4.8 Kg). The most common clinical signs were oral and/or tongue ulceration (n = 8), lip, sublingual, oral, tongue and/or pharyngeal oedema (n = 7), salivation (n = 4) and sloughing of oral and/or tongue mucosa (n = 2). The tongue in some cases was described as wooden, protruding and/or immobile. The outcome was known in 7 canine cases. Three dogs remained asymptomatic and two recovered, but a 5 kg Jack Russell Terrier was still recovering at the time of follow up. She developed oral inflammation within 30 minutes, glossitis, lip oedema and sloughing of the tongue. An oesophagostomy tube was required for feeding and she was discharged home after 4 days hospitalisation with the tube still in place. There was one fatal case where a dog "crashed whilst having the dental and couldn't be saved" and was euthanased. All 3 cats recovered (taking 11 days in one case). Investigation revealed that the surgical spirit and purified water products from the same suppliers were available in identical containers. This was the case with two suppliers.

Conclusion: Accidental application of pressurised surgical spirit to the oral and tongue mucosa can cause severe local injury with swelling, inflammation and ulceration. Both dogs and cats use their tongue to manipulate food, and to eat and drink, therefore a significant injury to the tongue has serious acute and potentially long-term health consequences. Poisons centres have a role to identify and report preventable errors such as this and engage with manufacturers and suppliers to raise awareness and help reduce the incidence of these events.

124. Severe nephrotoxicity after fosfomycin overdose in a cat

Michela Pierro[a], Valeria M. Petrolini[b], Davide Lonati[b], Lucia Bernasconi[b], Benedetta Brolli[b], Valentina Negrini[b], Cristina Grazioli[b], Azzurra Schicchi[b] and Carlo A. Locatelli[b]

[a]Postgraduate School in Emergency Medicine, University of Pavia, Pavia, Italy; [b]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy

Objective: Fosfomycin is a broad-spectrum bactericidal agent that interferes with the synthesis of peptidoglycan by inhibiting the enolpyruvate-transferase enzyme. In veterinary medicine, fosfomycin is used to treat infectious diseases of broilers and pigs, and has sometimes also been used to treat bacterial infections in rabbits, cattle, dogs and horses [1]. The nephrotoxic effect of fosfomycin was demonstrated in cats in 2008. Three days after treatments at 20 mg/kg/bid, a significant increase in creatinine concentrations (without signs of uremia, such as vomiting, lethargy and anorexia) was observed in young cats, but not in adults. However, light microscopy showed tubular necrosis in both young and adult cats [2]. Moreover, acute renal injury was demonstrated in an adult cat, already on therapy for 2 months with prazosin for arterial hypertension, after oral administration of fosfomycin calcium at a dose of 20 mg/kg bid for 4 days [3]. We describe a case of poisoning with a high dose of fosfomycin in an adult cat that resulted in acute renal failure.
Case report: A 10-year-old female cat was mistakenly given a single dose of about 1 g fosfomycin (250 mg/kg). In the following days the cat manifested vomiting, anorexia, weakness, and increasing lethargy and was presented for attention by a veterinarian. Blood chemistry tests carried out on the third day revealed a significant increase in urea (699 mg/dL, reference range 30-65), creatinine (18 mg/dL, reference range 0.5-1.8), phosphorus (27.7 mg/dL, reference range 3-8 mg/dL), potassium (6.7 mmol/L, reference range 3.2-5.5 mmol/L) and a mild decrease of calcium concentrations (6.9 mg/dL, reference range 7.2-12 mg/dL). Supportive therapy was started, but the following day the clinical condition worsened further, as did the renal function (urea 764 mg/dL, creatinine 25.3 mg/dL). Therefore, in agreement with the owner, the cat was euthanized.
Conclusion: In our case, the cat was given a single dose, but ten times higher than the one used for the previously reported cases. This case further confirms the fosfomycin nephrotoxicity in cats.

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126. Breastfeeding during venlafaxine therapy: a case report of neonatal toxicity

Georgios Eleftheriou, Raffaella Butera, Mariapina Gallo, Andrea Giampreti, Lorella Faraoni, Maria Gioia Contessa and Giuseppe Bacis

Poison Control Center, Bergamo, Italy

Objective: Infants breastfed by mothers under venlafaxine therapy receive venlafaxine and its active metabolite through breastmilk, but concurrent side effects have been reported rarely. We present a case of excessive sedation and poor weight gain resolved after breastfeeding interruption in a breast fed baby whose mother was taking venlafaxine.
Case report: A 7-day-old female neonate was admitted in a neonatal intensive care department for excessive sedation and poor weight gain. She was born at 39 weeks' gestation to a 26-year-old gravida, treated with venlafaxine, 150 mg/day. Birth weight was 3190 g; Apgar Score was 9 at 1 minute and 10 at 5 minutes. On day 2, the weight was 3020 g. At day 3 of life, while at home, the infant became difficult to rouse and nursed for only 2-3 minutes at a time. The mother reported that breastfeeding was frequently interrupted by apparent distress and easy fatigability. The mother sought medical attention at 7 days of age because of progressive worsening. On admission the infant was somnolent, difficult to rouse and hypotonic, with normal rectal temperature. Infant's weight was 3080 g, with an average weight gain of 12 g/day, instead of the physiological 25 g/day. Clinical and laboratory investigations ruled out sepsis, respiratory distress syndrome, aspiration pneumonia, and metabolic disorders. Urine toxicology screening for substances of abuse was negative. Using high-performance liquid chromatography the infants' blood venlafaxine and desvenlafaxine concentrations were 1.5 ng/mL and 9.2 ng/mL, respectively (normal therapeutic concentration in adults 100-400 ng/mL with detection limit of 1 ng/mL). The infant was switched from breastfeeding to formula feeding on day 8 postpartum. Exclusion of breastmilk from the patient's diet was associated with an improvement in alertness and weight gain (125 g over the next 5 days). The improvement of the symptoms after breastmilk interruption ruled out the hypothesis of late neonatal abstinence syndrome.
Conclusion: The prompt clinical improvement after switching from breastfeeding to formula feeding, clearly demonstrates that the infant's symptoms were related to venlafaxine toxicity, in spite of the low venlafaxine and desvenlafaxine concentrations detected. Many authors report similar venlafaxine blood concentrations but no acute adverse effects or abnormal weight gain. This case illustrates the need to monitor for excessive sedation and reduced weight gain in breastfed babies whose mothers are taking venlafaxine. At present, laboratory data remains difficult to interpret as adult therapeutic ranges do not correspond to non-toxic concentrations in infants. Further large-scale studies on the safety of venlafaxine in breastfed infants are needed.

127. Exposures to psycholeptics and cardiovascular drugs during heat waves

Michael Deters, Friederike Rau and Dagmar Prasa
Poisons Information Centre, Erfurt, Germany

Objective: Similar to the UK National Health Service, the German Climate and Health Alliance published a list of drugs problematic during heat waves containing many psycholeptics and cardiovascular drugs [1,2]. We investigated whether temperature elevation affects exposure to these drugs.
Methods: In a retrospective study we compared cases of exposure to psycholeptics (PSL-EC) and cardiovascular drugs (CVD-EC) in therapeutic dose and in overdose reported to the Poisons Information Centre (PIC) Erfurt in the heat months June to September of the heat wave years 2003, 2006, and 2015-2019 (HY) with mean air temperature of 17.6 °C and the non-heat wave years 2004-2005, and 2007-2014 (NHY) with mean air temperature of 16.2 °C. Data collected included frequency of cases of exposure, symptom severity, circumstances of exposure, age, and sex of involved persons.
Results: In the heat months of 2003 to 2019 we observed a discontinuous increase of PSL-EC (2003: 556, 2019: 1007) and CVD-EC (2003: 153, 2019: 210). During HY, similar rates of asymptomatic or mild PSL-EC (64.4% versus 64.0%) but higher rates of asymptomatic or mild CVD-EC (72.3% versus 67.9%) and lower rates of moderate PSL-EL (13.6% versus 12.5%) and CVD-EC (9.3% versus 7.8%), as well as severe PSL-EC (5.7% versus 4.3%) and CVD-EC (4.9% versus 3.4%) were observed than during NHY. Accidental PSL-EC (11.5% versus 9.7%) and CVD-EC (41.6% versus 36.8%) were higher, and PSL-EC (66.9% versus 68.5%) and CVD-EC (48.0% versus 51.0%) in suicidal intention were less frequent. During HY, the proportion of adolescents (5.6% versus 4.3%), middle-aged adults (60.1% versus 50.0%), and seniors (14.7% versus 10.1%) was higher in PSL-EC and that of babies (2.3% versus 1.0%), and seniors (19.1% versus 15.9%) was higher in CVD-EC than in NHY. The proportion of genders in PSL-EC (male: 36.2% versus 35.2%, female: 61.0% versus 61.7%) and CVD-EC (male: 43.5% versus 43.0%, female: 50.6% versus 50.2%) remained unchanged during HY and NHY.
Conclusion: Although in comparison to non-heat wave years no higher rates of moderate or severe exposure to psycholeptics or cardiovascular drugs were detected in heat wave years, medication of patients on psycholeptics or cardiovascular drugs should be observed critically during heat waves because they affect the body's usual cooling mechanisms.

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128. A user-friendly model to simulate the kinetics of lead with or without succimer (DMSA) chelation in patients poisoned with lead

Jan C. van Eijkeren[a], Irma de Vries[a], Robbert B.T. Verkooijen[a], Dylan W. de Lange[b] and Claudine C. Hunault[a]
[a]Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht, Netherlands; [b]Dutch Poisons Information Center; Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, Netherlands

Objective: We previously developed a chelation lead therapy (CLT) model that predicts blood lead concentrations after succimer (dimercaptosuccinic acid, DMSA) therapy in patients poisoned with lead [1]. This model has been validated, but remains complex. We aimed to simplify our CLT model to facilitate its utilisation by clinical toxicologists.
Methods: We simplified the code of the original CLT model and compared the parameter values and output of the simplified CLT model with the output of the original one using data of previous patients [2]. The Log Likelihood value was used as a measure of goodness of fit of the models. We further illustrated possible applications of the simplified model by simulating three classical situations of lead poisoning using previously published data: acute ingestion of a traditional remedy by an adult patient, chronic exposure of a worker by inhalation during his professional life, and young children exposed to lead after a fire in Paris.
Results: The output of the simplified CLT model did not differ significantly with that of the original model (Table 1). To obtain predictions of blood lead concentrations over time, clinicians only have to answer simple questions on the patient's age, date of presentation at hospital and route and duration of exposure. Predictions are possible for adults and children, exposure by either ingestion or inhalation, and with or without succimer chelation.
Conclusion: The simplified CLT model performed well and is easier to use than the original model. Its validity should be confirmed based on a prospective multicenter study before extensive routine use.

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Table 1. Comparison of the parameter values in the original and the simplified models based on data from seven patients treated with succimer in [2].

	P 1[a]	P 2[a]	P3[b]	P 4[b]	P 5[a]	P 6[a]	P 7[a]
Succimer-lead association constant	400	460	805	725	290	550	890
	390	530	880	795	310	555	870
Log likelihood							
Original CLT model	−77.2	−109.0	−69.8	−88.3	−99.1	−93.7	−51.9
simplified CLT model	−73.2	−111.9	−71.2	−87.7	−100.7	−94.8	−46.9

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130. Unsuccessful attempt at self-medicating alcohol withdrawal using phenibut: a case report

Haris Jakavicius, Gabija Mikuleviciene, Gabija Laubner and Robertas Badaras

Toxicology center, Republic Vilnius University Hospital, Vilnius, Lithuania

Objective: In Eastern Europe, phenibut is used to self-medicate alcohol withdrawal, anxiety, and insomnia. After several patients were hospitalized some with life-threatening conditions, supplements with phenibut were made legal in Lithuania. We report a case of phenibut usage in alcohol withdrawal condition ending with delirium, which was the main trigger to completely ban supplements with phenibut and its legal use in Lithuania [1].
Case report: A 41-year-old male was admitted to the emergency department (ED) after he became aggressive and disoriented. Agitation and psychosis made it impossible to collect the patient's medical history. Upon admission, his blood pressure was 180/100 mmHg, heart rate 155 bpm and respiratory rate 23 bpm. Blood samples, pH, and psychoactive substances test (PST) in urine were collected. PST was negative. The serum ethanol concentration was 2.7 g/L (58.6 mmol/L). He was sedated with intravenous diazepam infusions. The effect, though, was short, and he remained aggressive with hallucinations. Delirium tremens was rejected as a diagnosis because of heavy alcohol intoxication. He was transferred to an intensive care unit due to the vague medical history and severe somatic state. The patient was intubated and sedated using morphine and diazepam. On the second day, he developed status epilepticus. Diazepam was ineffective and thiopental was used to control the seizures and was continued for sedation until day 4. On day 6, he was extubated. When he recovered fully he explained that for 3 weeks he has been drinking heavily. He wanted to stop alcohol consumption and had bought a supplement with phenibut to reduce the symptoms of alcohol withdrawal. He legally bought the supplement from an online fitness store. On day 10, after full recovery, he was discharged.
Conclusion: Even though phenibut is described as a medication to treat alcohol withdrawal and anxiety, this case clearly showed that when phenibut is used with alcohol it can provoke delirium or aggravate agitation. It is clearly not a good medication to treat alcohol withdrawal. After this case, we notified the State Medicines Control Agency. We aimed to forbid usage and supply of any products with phenibut in Lithuania. In 2020, Phenibut was recognized as a dangerous drug and completely banned in Lithuania's market.

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131. The use of antidotes in the management of methotrexate poisoning: UK Experience

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

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

Objective: Methotrexate (MTX) is an anti-proliferative agent that inhibits dihydrofolate reductase. Two antidotes are available to treat patients with MTX toxicity. Folinic acid is administered as a rescue therapy to bypass the effects of MTX on dihydrofolate reductase, by directly providing a source of reduced folate. Glucarpidase (Voraxaze®) is a recombinant enzyme which rapidly metabolises extracellular MTX to non-toxic metabolites. The objective of this study was to evaluate the use of antidotes in the treatment of MTX toxicity reported to the UK National Poisons Information Service (NPIS) via telephone enquiries.
Methods: A retrospective search of the UK NPIS Poisons Information Database (UKPID) was performed (2015–31 October 2020) to identify cases relating to MTX exposure where treatment with antidotes was discussed.
Results: During the study period 261 enquiries relating to MTX were received, involving 223 individual patients (168 cases MTX alone; in 55 cases other agents were involved). Of these cases instances where the use of an antidote to treat MTX toxicity were identified. Folinic acid rescue was discussed in 90 patients with MTX-related toxicity (40.3% of all cases; 68 cases following ingestion; 22 parenteral). Folinic acid had already been administered to 36 patients prior to telephoning and NPIS recommended administration in a further 54 patients. Glucarpidase was discussed in 23 patients (10.3% of all cases). Of these, glucarpidase was advised in 4 patients who had received high-dose-MTX treatment in the context of deteriorating renal function and/or persistently high MTX concentrations and had already been administered prior to contact with NPIS in one patient. Glucarpidase was discussed as a possible option in 5 of the 23 patients: one case following high-dose-MTX treatment; 3 cases of therapeutic error (weekly doses on a daily basis); and one of suspected chronic accumulation. In the remaining 13 patients, treatment with glucarpidase was not indicated for the following reasons: time since exposure (5 patients; 1-8 days); lack of severe features of toxicity (6 patients); low methotrexate concentration (1 patient); patient on haemodialysis (1 patient).
Conclusion: Approximately 4 cases of MTX toxicity a month were discussed with NPIS. In around 40% of all patients folinic acid had been administered or was recommended. Treatment with glucarpidase was discussed in around 10% of patients, and was recommended or administered in 5 patients (following high-dose-MTX treatment). It is likely that not all patients treated with glucarpidase are discussed with NPIS with many managed according to local oncology guidelines.

132. Setting up a pilot nutrivigilance service in a National Poisons Information Centre

Nicola Cassidy, Patricia Casey, Niamh English, John X. Herbert, Feargal O'Connor, Conor Hurley, Sinead Doyle and Edel Duggan

National Poisons Information Centre, Dublin, Republic of Ireland

Objective: A nutrivigilance system detects adverse events associated with food or food supplements. The aim of this study was to set up a pilot nutrivigilance service in a National Poisons Information Centre (NPIC).
Methods: A nutrivigilance pilot project was carried out by NPIC from November 2020 to February 2021. The project was registered with Quality and Safety as per hospital protocol. All symptomatic enquiries reported to NPIC concerning potential poisonings due to ingestion of multivitamins were included in the study. Exclusion criteria included prescribed vitamins and co-ingestions. Having obtained consent, a follow-up call was undertaken. Information collected included age, sex, name of products, place of purchase, source of enquiry, symptoms, severity, investigations and treatment. A causality score based on ANSES methodology [1] was calculated for each symptom. A nutrivigilance expert group validated the score and made recommendations to the Food Safety Authority of Ireland.
Results: Overall, 29 enquiries to the NPIC involving multivitamin ingestions were followed up. Of these 22 cases were excluded as no symptoms developed. One case was excluded as it was a prescribed vitamin. A causality score was determined for 6 cases assessing 10 symptoms. The most frequent adverse effect reported was gastrointestinal (50%) followed by dermatological effects (20%). All 6 cases involved accidental ingestion in children (age $<$10 years) and the majority were boys (80%). The severity score was minor (PSS1) in all cases. The duration of effects ranged from hours to 3 days. Symptoms resolved on stopping the product. The product was reintroduced at lower doses in 2 cases with no reoccurrence of symptoms. Causality was excluded in one case as symptoms were present before product consumption. Symptoms were likely associated to product consumption in 30% of cases and possibly linked in 60%. An extrinsic score was determined for 18 vitamins; 6 symptoms had well documented evidence to support a link, 2 had little evidence and 2 had no evidence. The Nutrivigilance Working Expert group recommended increasing consumer awareness of the side effects of vitamin A, vitamin D and iron. Prolonged use of multivitamins is not recommended without the advice of a healthcare professional.
Conclusion: Current resources were used to set up a pilot nutrivigilance service in Ireland. Further human and IT resources are required to develop the service.

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133. Establishment of a novel electronic consult medical toxicology service

Avery Michienzi[a], Samuel Collins[b], Kimberly Dowdell[c] and Christopher Holstege[a]

[a]Department of Emergency Medicine, University of Virginia, Charlottesville, United States; [b]University of Virginia, Charlottesville, United States; [c]Department of Internal Medicine, University of Virginia, Charlottesville, United States

Objective: Electronic consults (eConsults) are a billable clinical exchange between care providers facilitated within the electronic medical record (EMR) [1]. The goal of eConsults is to increase timely access to specialists and improve provider education [1]. eConsults are meant as a platform for primary care providers to ask focused questions to specialists and receive written responses documented in the EMR, thus avoiding unnecessary referrals to specialty clinics. When eConsults are placed by a provider, the specialist is to respond within a week in the EMR. The objective of this project was to establish a novel eConsult clinical toxicology service to assist in answering non-emergent focused outpatient questions that required Medical Toxicologist expertise.
Methods: The Medical Toxicology eConsult service was developed by a public university's Medical Toxicology Division in collaboration with primary care and telehealth services. The team created templates to facilitate outpatient eConsults to ensure the service was used for non-emergent care. Our study is a descriptive cross-sectional review of the eConsult Medical Toxicology service over three years.
Results: From 2018 to 2021, there were 53 Medical Toxicology eConsults. Consult topics included: urine drug screen interpretation (33); heavy metal lab interpretation (9); follow-up snake bite care (2); herbal supplements (2); benzene (1); epoxy (1); pesticide (1); nitrous oxide (1); baclofen taper (1); nonspecific occupational exposure (1); concern for intentional poisoning (1). Of these consults, 43 were completed with electronic eConsult notes, 6 were determined to be too complex and referred to the Medical Toxicology clinic, 1 was referred to dermatology clinic, 1 was referred to pain management, 1 was declined due to acuity, and 1 was declined due to lack of appropriate information.
Conclusion: This is the first known eConsult service established for the specialty of Medical Toxicology. The most frequently asked questions involved interpretation of urine drug screens and heavy metal testing. Misinterpretation of these tests can lead to inappropriate management by primary care and further unnecessary testing [2]. Access to a Medical Toxicologist's expertise rapidly via brief eConsults can significantly impact patient care and provide formal documentation directly into the electronic medical record.

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135. Watch out for the "fluortasty" beef!

Paula E C. Hammer[a], Janne J. Møller[a], Ann C. Lyngberg[a], Jonas C W. Holm[a], Morten Lindhardt[b] and Ole S. Mortensen[a]

[a]Department of Occupational Medicine Holbæk University Hospital, Holbæk, Denmark; [b]Department of Intern Medicine Holbæk University Hospital, Holbæk, Denmark

Objective: Until the early 2000s perfluorooctane sulfonate (PFOS) was extensively used in firefighting foams, but its use has since then been gradually prohibited in many European countries due to its hazardous environmental and health effects [1]. PFOS is extremely persistent in the environment and bioaccumulates throughout ecosystems [1]. We present a case series of human hazardous exposure to PFOS through contaminated beef cattle in Denmark.
Case series: In August 2021 187 people including 40 children and 2 pregnant women were confirmed to be exposed to high levels of PFOS through blood tests after consuming beef cattle, that had grazed near a firefighting school in Korsoer. The source of contamination was wastewater containing residual PFOS from firefighting foam from the firefighting school, which flowed through the pastures. The geometric mean concentration of PFOS in the serum of the exposed individuals was 43 ng/mL, with minimum and maximum concentrations of 1.1 and 553 ng/mL, respectively. In comparison, a study from 2020 found a 97.5% percentile among Danish adults of 21 ng/mL [2]. To our knowledge, the concentrations of PFOS found in the present case series are among the highest ever reported from food contamination [3].
Conclusion: Despite regulative legislation, there are still large amounts of PFOS in the environment leading to potential hazardous human exposure. Following the present case series, Danish authorities have initiated a systematic investigation of possible similar sources of contamination near firefighting schools, military bases and airports throughout the country.

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136. The effect of a nationwide ransomware cyberattack on the Irish health service on the provision of poisons information in Ireland

John X. Herbert[a], Ronan Conroy[b] and Edel Duggan[a]

[a]National Poisons information Centre, Ireland, Dublin, Republic of Ireland; [b]Department of Epidemiology and Public Health Medicine, Royal College of Surgeons in Ireland, Dublin, Republic of Ireland

Objective: The Health Service Executive (HSE) is the publicly funded healthcare system in the Republic of Ireland. The HSE suffered a major ransomware cyberattack on 14 May 2021 which caused all of its IT systems nationwide to be shut down. Internet access in all Irish hospitals was suspended immediately. TOXBASE® is the primary clinical toxicology database of the National Poisons Information Service (NPIS) in the UK. Access to this online database is available to all hospital Emergency Departments in Ireland via a centralised contract with NPIC. Some hospitals saw a return of Internet access after six weeks. The National Poisons Information Centre (NPIC) retained un-interrupted Internet access through various means. We examine the effect of this cyberattack on the enquiries to the NPIC and the sources of poisons information in Ireland.
Methods: We performed a retrospective review of the enquiries received by the NPIC in the 6 weeks before and six weeks after the cyberattack in 2021. We also reviewed the enquiries of the corresponding periods in 2020 and 2019. We looked at the number of hits received by the TOXBASE® website and TOXBASE® app accesses during these periods [1]. Data were analysed with StataSE release 17 using regression models with robust standard errors. The effect of month of call was modelled using a two way ANOVA with month and year as predictors.
Results: Daily enquiry numbers to the NPIC were approximately normally distributed. Enquiry frequencies were marginally higher in 2020 than in other years ($p = 0.029$). Enquiry frequency was significantly higher in the period following the cyberattack in 2021, with an adjusted mean increase of 3.8 enquiries per day ($P = 0.021$). TOXBASE® hits from the NPIC were significantly higher in 2021 than in previous years ($P < 0.001$) but there was no significant difference in the period following the cyberattack ($P = 0.471$). There was a sharp decline in TOXBASE® hits from Irish hospitals after the cyberattack. The baseline rate for 2021 was significantly higher than previous years ($P < 0.001$) and the decline produced contact levels significantly lower than previous years ($P < 0.001$). TOXBASE® app usage is low in Ireland and there was no significant change in the period after the cyberattack ($P = 0.079$).
Conclusion: The six week period following the cyberattack resulted in a significantly higher number of enquiries received by the NPIC and a significant decrease in TOXBASE® hits from Irish hospitals.

Reference

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138. Barium and strontium overdose with fluctuating plasma concentrations and cardiac arrest managed with potassium, endoscopy and dialysis

Nazila Jamshidi[a], Nina Dhaliwal[a], Dean Hearn[b], Craig McCalman[b], Ross Wenzel[c], Zeff Koutsogiannis[a] and Darren M. Roberts[a]

[a]New South Wales Poisons Information Centre, The Children's Hospital Westmead, Sydney, Australia; [b]Department of Intensive Care, Lismore Base Hospital, Lismore, Australia; [c]NSW Health Pathology, Trace Elements Laboratory, Royal North Shore Hospital, Sydney, Australia

Objective: To describe a case of acute barium carbonate and strontium carbonate poisoning complicated by cardiac arrest, managed with potassium replacement, dialysis and endoscopic removal of retained metals.
Case report: A 38-year-old woman presented with vomiting 90 minutes after intentional self-poisoning by ingesting 3 cups of barium carbonate and strontium carbonate (unknown proportions) obtained for ceramic glazing. Her initial venous blood gas was significant for pH 7.56, pCO_2 21 mmHg, bicarbonate 19 mmol/L, potassium 2.8 mmol/L, lactate 2.0 mmol/L, white cell count 15.9 x 10^9/L, and creatinine 53 μmol/L. Electrocardiogram (ECG) was significant for prolonged QT interval of 520 msec. She was initially managed with intravenous potassium and magnesium replacement. Four hours post-ingestion she developed proximal muscle weakness (power 3/5) in both upper limbs and a serum potassium 2.2 mmol/L despite continuous intravenous replacement (30 mmol/h). Aggressive potassium replacement via a central venous catheter was instituted. At 12 hours post-ingestion, serum potassium improved (3.0 mmol/L), but with persistent weakness, QT prolongation and frequent ventricular ectopics. At 15 hours post-ingestion, she became agitated and developed abdominal pain, deteriorating clinically with profound muscle weakness and then developed polymorphic ventricular tachycardia and cardiac arrest. She was treated with defibrillation, intravenous magnesium, and endotracheal intubation. Bloods 15.5 hours post-ingestion demonstrated acute kidney injury (creatinine 118 μmol/L), potassium 6.4 mmol/L and metabolic acidaemia (nadir pH 7.14, pCO_2 51 mmHg, bicarbonate 16 mmol/L, base excess -11.0 mmol/L). Continuous veno-venous haemodialysis (CVVHD) was initiated for metabolic derangement and barium enhanced elimination. Chest X-ray 17 hours post-ingestion demonstrated a large radio-opaque mass, thought to be the barium and strontium in the stomach. Gastroscopy was performed and the foreign material was removed from the gastric body and duodenum 41 hours post-ingestion. Hyperkalaemia and QT prolongation resolved over the following 4 hours. She was extubated 58 hours post-ingestion and CVVHD was ceased on day 3. Creatinine peaked at 348 μmol/L on day 7 but returned to normal by discharge. Double peaks in barium concentrations were noted subsequently, increasing from 94 μmol/L on admission to 195 μmol/L at 16 hours post-ingestion, then 95 μmol/L at 20 hours post-ingestion, increasing to 193 μmol/L at 30 hours post-ingestion.
Conclusion: Early intervention with aggressive potassium replacement is required in severe barium poisoning but rebound hyperkalaemia can occur. Gastrointestinal decontamination including endoscopy and oral magnesium sulphate may still be useful 12 hours post-ingestion, and consider enhanced elimination in patients with severe and progressive barium toxicity despite standard supportive treatment.

139. Good outcome in severe ethylene glycol poisoning: never give up treatment too early

Knut Erik Hovda[a], Henning Wimmer[b], Sten Froyshov[c], Pjotr Sowa[d] and Dag Jacobsen[e]

[a]The Norwegian CBRNE Centre of Medicine, Department of Acute Medicine, Oslo University Hospital, Oslo, Norway; [b]Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [c]Department of Acute Medicine, Oslo University Hospital, Oslo, Norway; [d]Department of Neuroradiology, Oslo University Hospital, Oslo, Norway; [e]The National Poisons Information Centre, National Institute of Health, Oslo, Norway

Objective: Ethylene glycol poisoning may have a good prognosis despite a seemingly hopeless initial situation: Weeks of coma without sedation may lead to discharge with little or no sequelae. We present a severe ethylene glycol case who survived despite massive changes in cerebral imaging, to illustrate the importance of not giving up active treatment too early in this patient group.
Case report: A 48-year-old male was found unconscious at home with respiratory failure and rapidly deteriorated to cardiac arrest. Cardiopulmonary resuscitation (CPR) was performed for approximately two hours. On arrival, he was still in cardiac arrest, with arterial blood gas (ABG) analysis revealing pH 6.52, pCO_2 7.15 kPa, base excess -35 mmol/L, lactate 1.3 mmol/L. Since toxic alcohol poisoning was one differential diagnosis, fomepizole was administered. The osmolal gap was 87 mOsm/kgH_2O, anion gap 46 mmol/L, serum ethanol $<$5 mmol/L, serum ethylene glycol 50 mmol/L, and serum glycolate 30 mmol/L. He received massive amounts of buffer before being established on extracorporeal membrane oxygenation (ECMO) and continuous veno-venous haemodialysis (CVVHD). One day later no circulatory support was needed and he was weaned off ECMO. He was still comatose (Glasgow Coma Score (GCS) 3) without any sedation and had extension spasm in his upper limbs. Brain computerised tomography (CT) scan showed massive cerebral edema and signs of hydrocephalus. Magnetic resonance imaging (MRI) revealed severe pathology of central structures (basal ganglia, mesencephalon, and medulla oblongata). The front of his neck became swollen (not present on arrival), and was found to be an enlarged thyroid gland after ultrasound and CT imaging. His free thyroxine concentration increased from 11 to $>$100 pmol/L. He received extensive intensive care treatment for approximately 5 weeks, including ventilator support and CVVHD. Steroids were given to treat an anticipated massive toxic thyroiditis. Gradually, the edema in both his neck and brain normalized, as did his thyroxine concentration, he regained consciousness, started to move his limbs, opened his eyes, and eventually started to talk. Weekly MRI scans showed a gradual improvement, but with edema in central structures lasting for weeks. He was discharged from a rehabilitation center with relatively minor physical and mental sequelae five months after the incident.
Conclusion: The present case supports critical evaluation before weaning intensive care unit (ICU) treatment in massive ethylene glycol poisoning - even in cases with a seemingly poor prognosis. The perivascular deposition of calcium oxalate crystals in almost all organs (brain, kidneys, heart) with subsequent reversible edema may be a pathophysiological explanation for this.

140. Life-threatening hypokalaemia caused by chronic liquorice ingestion: a case report

Roberto Zoppellari[a], Chiara Lazzari[a], Milo Vason[a], Daria Osti[a], Giuseppe Santoro[a], Giulia Dallocchio[a] and Davide Lonati[b]

[a]Department of Anaesthesia and Intensive Care, S. Anna Hospital, Ferrara, Italy; [b]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS and University of Pavia, Pavia, Italy

Objective: Chronic use of liquorice can lead to an alteration of renin-angiotensin-aldosterone axis [1]. The major bioactive principle of this natural root is glycyrrhizic acid, hydrolized to glycyrretic acid in the intestine, which inhibits the enzyme 11-β-hydroxysteroid dehydrogenase. That can induce hypokalaemia,

hypertension and metabolic alkalosis. Other complications include dysrhythmias and acute rhabdomyolysis. We report a case of chronic liquorice ingestion.
Case report: A 38-year-old women weighing 52 kg, presented via ambulance to the Emergency Department with a reported state of agitation, fasciculations and spasms. Upon arrival at hospital she was lethargic, barely responsive to pain, with blood pressure 144/96 mmHg. The electrocardiogram (ECG) showed sinus rhythm 95/min and increased QTc (750 ms). Arterial blood gas analysis showed metabolic alkalosis and hypokalaemia with increase of lactic acid: pH 7.6, pCO_2 38 mmHg, pO_2 75 mmHg, potassium 1.6 mEq/L, and lactate 12.2 mmol/L. Cerebral tomography was normal. At admission to the intensive care unit (ICU) two episodes of torsade de pointes occurred and hypertension (200/100 mmHg) was observed. She was treated with intravenous potassium supplementation (15 mEq/h for 24 hours, 10 mEq/h on the 2nd day and 5 mEq/h on the 3th day). Dysrhythmia and hypertension had a spontaneous resolution. An electroencephalogram showed slow but not epileptiform abnormalities. Her parents reported the customary use of liquorice and also that she had hypertension, treated with nebivolol. Toxicological investigations showed the presence of glycyrrhizic acid (151 μg/L at admission and 111 μg/L after 24 hours). Blood chemistry tests showed a great increase of creatine kinase, up to 8134 U/L (normal <145 U/L), and myoglobin, up to 3087 ng/mL (normal 14-66 ng/ml), without kidney injury. On the 4th day she was discharged from the ICU to a medical department, with normalized blood gases, potassium, ECG and blood pressure. The patient had a good recovery.
Conclusion: We emphasize the role of prompt treatment with potassium infusion and early clinical suspicion of this rare case of hypokalaemia, in which it has been possible to confirm the presence of a very high concentration of glycyrrhizic acid in the patient's serum.

Reference

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141. A curious method to commit suicide

Juan Ortega Pérez, Antonio Caballero Bermejo, Alexandra Maria Guiu Martí, Catalina Homar Amengual, Bernardino Barceló Martín and Jordi Puiguriguer Ferrando

Hospital Universitario Son Espases, Palma de Mallorca, Spain

Objective: The COVID-19 pandemic has generated an increase in anxiety-depressive disorders throughout society, with an evident impact on children and adolescents, further precipitated by limitations in social activities during confinement. The increase in home isolation with abuse of new technologies, often far from parental control, involves risky situations such as the case we present.
Case report: A 19-year-old man diagnosed with major depressive disorder, with psychiatric admissions since July 2019 for overdose with suicidal intent was home treated with methylphenidate 40 mg, mirtazapine 15 mg and vortioxetine 10 mg. In August, the patient was searching for information on the Internet about euthanasia and suicide without pain in different pages and Internet forums. He bought two products online (by Amazon) that seemed effective for this purpose: a kilogram packet of sodium nitrate and a bottle of antifreeze. Finally, he decided on the first option due to the risk of suffering after ingesting antifreeze. On August 26 (4:00 pm), he ate a tablespoon (80 mg) of sodium nitrate. He developed dyspnea and feeling overwhelmed so he decided to informed his family of what he had done and an ambulance was called. He was transferred to hospital and given oxygen. At 7:00 pm in the emergency department he was noted to have a greyish coloration ("hot dead" appearance) with poor respiratory mechanics, tachycardic, tachypneic, with signs of peri-arrest: blood pressure 96/50 mmHg, heart rate 145 bpm, respiratory rate 30/min, oxygen saturations 70%. He also had uncoordinated movements, and could not obey orders. The patient was sedated for intubation and mechanical ventilation. An arterial blood gas analysis performed after intubation showed: pH 7.35, pO_2 165 mmHg, pCO_2 24 mmHg, base excess -10.4, bicarbonate 14.5 mEq/L, potassium 3.1 mmol/L, methemoglobin 83%, carboxyhemoglobin 1.4%, lactate 13.3 mmol/L. Methylene blue 1% (75 mg intravenously) and activated charcoal by nasogastric tube were administered (after intubation). Later, he was admitted to the intensive care unit (9:20 pm). Physicians from this unit decided to administrate hydroxocobalamin (5 g intravenously at 00.39 am). The patient was extubated and discharged from the intensive care unit 36 hours after his admission to the department of Internal Medicine, without clinical complications; later he was transferred to Psychiatry Department.
Conclusion: The toxic mechanism of sodium nitrate is related to the generation of methemoglobin. This patient survived a potentially lethal methemoglobin level following intentional ingestion of sodium nitrate with prompt administration of an antidote.

142. Severe bencyclane poisoning without haemodynamic consequences

Ágnes Bakos and Andrea Érsek

Péterfy Hospital and Jenő Manninger National Institute of Traumatology, Budapest, Hungary

Objective: Bencyclane is an old, smooth-muscle relaxing drug. It has been used in peripheral, cerebral circulation disorders, gastrointestinal and urologic diseases. Due to direct calcium channel blocker effect, in case of overdose it can cause negative inotropic and vasodilating effects, and pass through the blood-brain barrier to provoke psychosis, coma and convulsion. We present a case of bencyclane poisoning with confusion, myoclonic jerks and recurrent seizures.
Case report: A 34-year-old woman arrived at our hospital by ambulance. Her past medical history included alcohol abuse and caesarean section. She ingested 2000 mg bencyclane with suicidal intention 2.5 hours before her admission. She had a seizure at the scene. On presentation the patient was alert (Glasgow Coma Score 13), but was confused with normal vital signs, nystagmus, ataxic movement, dilated pupils and involuntary myoclonic jerks of her hands. An electrocardiogram (ECG) showed sinus rhythm (78/min) with QRS 80 ms and QT 380 ms. During the examination she had a generalised tonic-clonic convulsion. Administration of midazolam resulted in cessation of her convulsion, but she had to be intubated due to respiratory failure. Arterial blood gas analysis showed pH 7.00, $PaCO_2$ 74 mmHg, PaO_2 75.5 mmHg, bicarbonate 17.9 mmol/L, base excess -13.8 mmol/L, oxygen saturation 83.9%, lactate 18.8 mmol/L and glucose 6.5 mmol/L. She was ventilated in the intensive care unit (ICU). Gastric lavage was performed via nasogastric tube, but no fragments were recovered. Laboratory test showed leucocytosis, but other parameters were unremarkable. Her acid-base parameters and condition improved rapidly with supportive care. She was extubated the day after admission. Computer tomography (CT) of the brain showed no pathology. She recovered without

any complications, and was discharged from our hospital on the third day.
Conclusion: Calcium channel blocker poisoning is mainly associated with cardiovascular symptoms and patient usually require hemodynamic support [1]. In our case, bencyclane poisoning caused confusion, myoclonic jerks and epileptic seizures, but no hemodynamic disturbance was observed. Severe bencyclane poisoning is rare in clinical practice, so the frequency and cause of hemodynamic and neurological complications is difficult to assess. Further case studies would be needed to investigate this.

Reference

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143. Hidden baclofen poisoning

Ágnes Bakos[a], Mária Mátyus[b], Veronika Wolf[b] and István Elek[a]

[a]Péterfy Hospital and Jenő Manninger National Institute of Traumatology, Budapest, Hungary; [b]Hungarian Defence Forces Medical Centre, Budapest, Hungary

Objective: Baclofen poisoning causes non-specific neuropsychiatric and cardiological symptoms and may result in differential diagnostic problems. We present a patient with mixed poisoning who developed acute agitated confusion, tonic muscle cramps and finally the toxicology examination confirmed baclofen poisoning.
Case report: A 66-year-old female was found by her family in an unresponsive state with empty medicinal containers of alprazolam, bisoprolol and a few baclofen pills of her son. Her past medical history included hypertension, ischaemic heart disease, stroke, hypothyroidism, breast ablation due to cancer and psychiatric treatment. On admission, she was soporous, with a Glasgow Coma Score (GCS) of 9. Her vital signs were blood pressure 140/100 mmHg, pulse 80/min, temperature 36.5 °C and respiratory rate 18/min. Upon arrival she received 0.25 mg flumazenil intravenously and her vigilance improved. Blood gas and laboratory results were unremarkable. An electrocardiogram (ECG) showed sinus rhythm with left bundle branch block without increase in cardiac enzyme. The toxicology study supported benzodiazepine poisoning. The patient's vital signs remained stable with supportive treatment, but the next morning her behaviour changed [1]. Sometimes she was agitated, at other times she was somnolent, and tonic muscle cramps were observed in the left upper limb. The rest of her neurological examination was normal. Computerized tomography of the brain showed no new pathology. The neurologist suggested phenytoin then valproate treatment and after detoxification an electroencephalogram (EEG) due to suspicion of complex partial epilepsy. Based on the symptoms and pills at the scene the patient's initial blood sample was reanalysed for baclofen by gas chromatography-mass spectrometry (GC-MS) and a serum baclofen concentration 2300 ng/mL (therapeutic range 80-400 ng/mL) was detected. To avoid baclofen-induced seizure the flumazenil was not repeated; she was given diuretic and supportive therapy. On the next two days the serum baclofen concentrations were 160 and 140 ng/mL. In parallel with the decrease in serum concentration, the patient's clinical symptoms improved rapidly, and anticonvulsant therapy was not required. She was discharged from the hospital on the 4th day after psychiatric examination.
Conclusion: Agitated confusion and tonic muscle cramp may draw attention to baclofen poisoning [1]. Routine toxicology screening does not include the measurement of serum baclofen, but it may be useful for differential diagnostic purposes, because it may affect treatment, and further diagnostic tests can be avoided.

Reference

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144. Vaginal burns due to application of an alum crystal

Uwe Stedtler[a], Xenia Petry[a], Patrick Molnar[b] and Maren Hermanns-Clausen[a]

[a]Poisons Centre, University Medical Centre Freiburg, Freiburg, Germany; [b]Department of Gynecology, Obstetrics and Reproductive Medicine, University Medical Centre Freiburg, Freiburg, Germany

Objective: Alum is corrosive and alum solutions are corrosive or irritant depending on the concentration. Despite these potentially dangerous qualities, it is used in mainstream medicine, as well as a traditional remedy. We report a patient who suffered significant vaginal burns from an alum crystal.
Case report: A 42-year-old patient presented to the gynaecological hospital because of pain in her vagina. One or two days previously she had put an approximately 1 x 2 cm alum crystal into her vagina. Six weeks earlier she had suffered an abortus incompletus and the application of a crystal of alum is a common traditional remedy in her home country to improve the restitution of vagina after childbirth. However the crystal is supposed to be applied for a short time but was forgotten and left in place for one or two days. Physical examination showed an unremarkable vulva but the vaginal mucosa was indurated and covered with white exudate. The introitus was constricted and on inserting the speculum white exudate was discharged. Transvaginal sonography could not be performed successfully. Therapy was daily irrigation with saline, analgesia and local application of tampons with estriol ointment. This treatment markedly relieved the pain, and the patient was discharged with ambulatory care on day two.
Conclusion: Traditional remedies may have significant adverse effects especially when aggravated by application errors. Here prolonged application of an alum crystal to mucosa caused moderate severe burns.

145. Severe carbamazepine overdose associated with shock, repeated seizures and extreme high serum concentrations treated by extended intermittent hemodiafiltration

Csaba Pap[a], Gyöngyi Kiss[b], Gyöngyi Zana[b], Ágnes Szombath[b] and István Elek[b]

[a]Department of Emergency Medicine and Clinical Toxicology, Péterfy Hospital, Budapest, Hungary; [b]Intensive Care Unit, Péterfy Hospital, Budapest, Hungary

Objective: Massive overdose of carbamazepine may result in deep coma and organ dysfunction and it can mimic brain death.

According to recent recommendations intermittent hemodialysis is the preferred extracorporeal treatment. We present a case of a patient who developed shock, repetitive seizures, cerebral oedema, and long-lasting toxic encephalopathy with an extreme serum carbamazepine concentration exceeding 80 mg/L and had a full recovery.

Case report: A 49-year-old male was found unresponsive in a public place. He was last witnessed to be awake about 3 hours earlier. Based on his last sms sent to one of his friend he ingested 44 g (585 mg/kg) of carbamazepine retard. On admission to our department his vital signs and parameters were as follows: Glasgow Coma Score (GCS) 3, blood pressure 116/84 mmHg, heart rate 92 bpm, oxygen saturation 100% on oxygen therapy with a face mask, body temperature 36.3 ^{0}C, pH 7.32, lactate 3.4 mmol/L, potassium 3.00 mmol/L, and sodium 135.9 mmol/L. The patient's initial serum carbamazepine concentration was 45.9 mg/L. He was intubated with mechanical ventilation. He was treated with repeated gastric decontamination followed by whole bowel irrigation along with multiple dose activated charcoal. A substantial amount of pill fragments were retrieved on gastric lavage. At 4.5 hours after admission his serum carbamazepine concentration was 56.24 mg/L. According to the Extracorporeal Treatments in Poisoning (EXTRIP) Workgroup 2D suggestion, extracorporeal elimination with intermittent hemodiafiltration (HDF, Qb 400 mL/min) was initiated 8 hours after admission. Four hours later he developed repeated seizures and severe hypotension requiring administration of noradrenaline. The peak serum carbamazepine concentration was 84.73 mg/L 16 hours after admission. Taking the EXTRIP 1D recommendation into consideration intermittent HDF (Qb 400 mL/min) was continued for a further 12 hours. The total amount of filtrate was 145 liters. His serum carbamazepine concentration dropped to 38.12 mg/L 30 hours after admission. He was comatose for 2 days, and required the administration of noradrenaline for 44 hours. He developed anemia, pneumonia and delirium tremens. After treating him with two bags of red blood cell concentrate, antibiotics, clonidine, tiapride and lorazepam his state gradually stabilized and the patient could be discharged from the intensive care unit (ICU) 9 days after admission and from the hospital 16 days after admission.

Conclusion: In severe carbamazepine overdose repeated gastric and intestinal decontamination and "off-label", long-lasting intermittent HDF can be effective even several hours after ingestion to prevent a fatal outcome.

146. Cobalt, chromium and copper after antidotal treatment of a patient with a damaged cobalt-chromium hip implant *in situ*

Daniela Pelclova[a], Karel Lach[b], Jan Hach[c], Milos Kubanek[d], Katerina Kotikova[a] and Michal Grünwald[f]

[a]Toxicological Information Centre, Department of Occupational Medicine, Charles University and General University Hospital, Prague, Czech Republic; [b]Institute of Public Health Institute, Ostrava, Czech Republic; [c]Department of Orthopedics and Traumatology Mělník Hospital, Mělník, Czech Republic; [d]Department of Cardiology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [f]General Practitioner, Blansko, Czech Republic

Objective: We treated a female patient with toxic concentrations of cobalt due to a damaged metal-on-metal hip prosthesis, the removal of which had to be postponed twice for

Table 1. Concentrations of cobalt, chromium and copper in serum and urine (±30%) in a patient with a damaged cobalt-chromium hip implant.

			Cobalt	Chromium	Copper	Cobalt	Chromium	Copper
Date	Treatment	Sample collection	Blood (µg/L)	Blood (µg/L)	Blood (µg/L)	Urine	Urine	Urine
Normal concentrations			< 0.9	< 0.5	650-1650	0.1-0.6 µg/L 0.0-4.2 µg/g creatinine	0.3-1.2 µg/L 0.4-1.4 µg/g creatinine	5-40 µg/L <50 µg/g creatinine
February 2018	no		181*	80*				
November 2019	no		53	67				
January 2020	DMPS 10 days 400 mg/day p.o.	Pre-treatment	96	81		375 µg/L	157 µg/L	
	yes	During treatment				250 µg/L	138 µg/L	
	no	1 week post-treatment	95	101				
September 2020	NAC 10 days 20 g/day p.o.							
	no	2 weeks post-treatment	71	86				
February 2021	no		67	145				
April 2021	DMPS 20 days 400 mg/day, p.o.	Pre-treatment	93	157		490 µg/g creatinine	280 µg/g creatinine	
	yes	During treatment (mean)				571 µg/g creatinine	309 µg/g creatinine	
May 2021	no	1 week post-treatment	81	158				
September 2021	no		118	166				
October 2021	DMPS 20 days 400 mg/day, p.o.	Pre-treatment	103	149	933	530 µg/g creatinine	330 µg/g creatinine	12 µg/g creatinine
	yes	During treatment (mean)	117	157	1070	creatinine	278 µg/g creatinine	87 µg/g creatinine

*plasma, NAC N-acetylcysteine, DMPS 2,3-dimercapto-1-propane sulfonate (unithiol)

technical and epidemiological reasons. The efficiency of antidotal treatment under such circumstances is unknown.
Case report: A 41-year-old woman (1980, BMI 20.7) with right-sided developmental hip dysplasia underwent metal-on-metal hip replacement in 2007. In 2018, dysfunction of the endoprosthesis was found and in November 2019 acetabular osteolysis and component loosening was identified. Investigations did not show systemic cobalt toxicity: electromyography (EMG), electrocardiogram (ECG), echocardiography, audiometry, and thyroid stimulating hormone were normal. However, plasma cobalt and chromium were highly elevated to concentrations at which toxic cardiomyopathy occurs (Table 1). In January 2020 2,3-dimercapropropane-1-sulfonate (DMPS, unithiol) was given. Although a significant effect on cobalt and chromium concentrations was not seen, the patient described improvement of her anorexia, weakness, headache, confusion, and blurred vision. In September 2020 she took acetylcysteine (NAC) orally for 10 days but did not feel improvement and a second DMPS course was performed in April 2021 as serum concentrations were high; she felt better for 6 months. In October 2021 she asked for a third DMPS course that was started due to high serum concentrations and second postponing of hip surgery. Serum and urine arsenic and copper were also measured. There was a 10-fold increase in copper urine elimination, but serum copper was only slightly increased.
Conclusion: Cobalt and chromium serum concentrations were steadily elevated but no significant effect of DMPS in lowering serum concentrations was seen, even though cobalt (but not chromium) output slightly increased and the patient described improvement of her symptoms. This, however, could not be verified objectively. The effect of NAC did not last long-term and although recent literature demonstrates a stronger effect, removing an impaired prosthesis in such conditions is inevitable.

147. Methemoglobinemia due to sodium nitrite ingestion: not always a result of an intentional overdose during 2021

Valentina Negrini[a], Azzurra Schicchi[a], Lucia Bernasconi[a], Valeria M. Petrolini[a], Eleonora Buscaglia[a], Cristina Grazioli[a], Benedetta Brolli[a], Franco Tagliaro[b] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]Department of Diagnostics and Public Health - Unit of Forensic Medicine, University of Verona, Verona, Italy

Objective: Sodium nitrite is an inorganic salt used as a food preserving agent. Nitrates/nitrites are potent oxidizing agents that in a toxic dose may result in profound life-threatening methemoglobinemia. Sodium nitrite is generally present in food in a minimum amount and the acceptable daily intake is up to 0.06 mg/kg body weight. In a period in which there has been an increase in cases of methemoglobinemia due to intentional ingestion of sodium nitrite our Poison Control Centre (PCC) managed an outbreak of methemoglobinemia due to food contamination.
Case series: Between 1-4 June 2021, 8-patients in 3 different towns in Italy, presented to the Emergency Department (ED) with peripheral cyanosis and methemoglobinemia after history of eating a tuna-based meal. Details of the clinical manifestations at ED admission, methemoglobin level (MetHb), treatment, second level analysis and outcome are described in Table 1. Food contamination was suspected because of the case distribution in different towns. Sample collection at ED admission was performed and the PCC coordinated a national alert spread through the Ministry of Health, and second level analysis on available patient samples and the potential involved food. Nitrates were present in both patient samples and in a production lot of fresh tuna.
Conclusion: Sodium nitrite intoxication can be fatal if not recognized. Methylene blue (MB) should be available in the ED; in our cases a single dose of 1 mg/kg was sufficient to resolve methemoglobinemia with no rise in MetHb after administration. Sample collection to perform second level analysis is fundamental to confirm diagnosis and identify the source. PCCs have a crucial role in syndromic surveillance; in this case cooperation between local physicians, the Ministry of Health and the laboratory ensured optimal management of a potential national threat.

148. 1, 2-Dichloroethane intoxication in Estonia: a case series

Vladislav Mihnovitš[a] and Raido Paasma[b]

[a]Tartu University Hospital, Tartu, Estonia; [b]Pärnu Hospital, Pärnu, Estonia

Objective: 1,2-Dichloroethane (DCE) is commonly used as an industrial organic solvent. It is a volatile, clear, liquid with a pleasant smell and sweet taste. The general population is exposed to DCE primarily from inhalation of ambient air. Limited information is available regarding effects on humans, mostly from case reports [1]. We report 4 cases of acute DCE toxicity in Estonia in September 2020.
Case series: Four patients were hospitalized after heavy drinking during a get-together the previous night (Table 1). They were drinking an unknown substance, later identified as DCE, thinking it was a cheap substitute for alcohol. A fifth member of the group had passed away in the morning and the others presented with severe weakness, vomiting and diarrhea. All of the patients were initially thought to have surrogate alcohol poisoning, but blood tests were negative. The first patient (Case 1) presented in an unstable condition with lowered level of consciousness,

Table 1. Details of patients with methemoglobinemia (MetHb) after ingestion of sodium nitrite-contaminated tuna. All the patients recovered.

Case	Town	Sex	Age	Symptoms	Methemoglobin (%) on admission	Methylene blue dosage	Methemoglobin (%) 3 hours after methylene blue	**Plasma nitrate* concentration (mmol/L)**
1	Lavagna	F	66	Syncope, cyanosis	54.2	1 mg/kg once	2.8	245
2	Brindisi	M	45	Syncope, headache	43.4	1 mg/kg once	3.9	356
3	Brindisi	F	43	Syncope, vomiting	7.8	1 mg/kg once	0.9	96
4	Brindisi	M	11	Vomiting, acrocyanosis	26	1 mg/kg once	1.9	179
5	Brindisi	M	10	Syncope, vomiting, cyanosis	49	1 mg/kg once	2.6	210
6	Benevento	M	61	Abdominal pain, vomiting	0.7	Not administered	–	Not performed
7	Benevento	F	87	Abdominal pain, vomiting	2.1	Not administered	–	Not performed
8	Benevento	F	63	Cyanosis, abdominal pain, vomiting	6.1	1 mg/kg once	0.3	Not performed

*Only the nitrate ion could be measured in exposed patients, as nitrite was rapidly converted to nitrate.

Table 1. Characteristics of four male patients hospitalised with oral 1,2-dichloroethane intoxication.

Case number	Age (years)	Admission GCS	Admission pH and base excess (mmol/L)	Admission lactate (mmol/L)	Highest ALT (U/L) AST (U/L)	Highest CK (U/L) myoglobin (μg/L)	Highest INR	Initial SOFA score
1	33	11	pH 7.121 BE -19.5	11.3	ALT 2359 AST 4333	CK 535, myoglobin 1253	3.2	14
2	44	10	pH 7.422 BE -5.6	4.4	ALT 3495 AST 7884	CK 11986, myoglobin 17531	5.96	14
3	62	15	pH 7.362 BE -6.8	1.4	ALT 3995 AST 10640	CK 27590, myoglobin 68461	4.09	14
4	41	15	pH 7.692 BE 0.2	6.9	ALT 78 AST 190	CK 211, myoglobin N/A	1.01	1

Abbreviations: M male; GCS Glasgow Coma Score; BE base excess; ALT alanine transaminase; AST aspartate transaminase; CK creatine kinase; SOFA Sequential Organ Failure Assessment Score; N/A not available.

severe metabolic acidosis, vasoplegic shock and coagulopathy. The second and the third patients (Cases 2 and 3) were more alert and hemodynamically stable at admission, but their condition quickly followed the path of the first patient. All three developed cardiovascular, renal, liver failure and had signs of disseminated intravascular coagulation. Treatment with blood products, multiple high doses of vasopressors, renal replacement therapy with hemoadsorption and mechanical ventilation was initiated. Management also included bicarbonate, N-acetylcysteine and glucocorticosteroid infusions. All three patients developed signs of brain death and treatment was stopped. Patients 1, 2 and 3 died 13, 54 and 70 hours after admission, respectively. The fourth patient, a 41-year-old male who only drank a few sips of the substance remained stable during hospitalization. Although, his initial lactate was elevated it quickly normalized with fluid therapy. He was discharged to a local hospital the next day.

Conclusion: DCE is a highly toxic substance and exposure can cause multiorgan failure and death.

Reference

[1] Agency for Toxic Substances and Disease Registry. 2001. Toxicological profile for 1,2-Dichloroethane. Update. US Department of Health and Human Services, Public Health Service [cited 1 November 2021]. Available from https://www.atsdr.cdc.gov/toxprofiles/tp38.pdf

149. Factors contributing to the severity of rhabdomyolysis in acute poisoning

Gordana Vukovic Ercegovic[a], Jasmina Jovic Stosic[a], Natasa Perkovic Vukcevic[a], Olivera Potrebic[a], Nemanja Rancic[b], Snezana R. Jankovic[c] and Slavica Vucinic[a]

[a]National Poison Control Center, Military Medical Academy, Belgrade, Serbia; [b]Center for Clinical Pharmacology, Military Medical Academy, Belgrade, Serbia; [c]Institute of Scientific Information, Military Medical Academy, Belgrade, Serbia

Objective: To identify contributing factors for the onset and severity of rhabdomyolysis in acute poisonings.

Methods: Data were collected from medical records of acutely poisoned patients with creatine kinase (CK) > 1500 U/L (moderate and severe rhabdomyolysis according to Poisoning Severity Score) treated from January 2016 to December 2020. Case records were reviewed for age, gender, agents, level of consciousness, blood pressure and oxygen saturation (SaO_2) on admission, the time elapsed since exposure, maximal CK, renal function parameters, need for hemodialysis and outcome. According to CK level, patients were divided in two groups, group 1 (G1) with CK 1500-10000 U/L and group 2 (G2) with CK >10000 U/L.

Results: Overall 269 patients were included (male 58%, female 42%, median age 42), 213 with moderate (G1) and 56 with severe rhabdomyolysis (G2). The average value of CK in G1 and G2 were 3974.81 ± 2177.26 U/L and 50598.09 ± 49744.78 U/L, respectively. Male gender frequency in G2 was significantly higher compared to G1 (73% versus 54%, $p = 0.016$). Toxic agents in G1 were neuroleptics (31%), benzodiazepines (21%), drugs of abuse including ethanol (17%), antiepileptics (14%) and other substances (17%). Dominant agents in G2 were drugs of abuse including ethanol (50%; mostly opioids), followed by neuroleptics (16%), antiepileptics (9%), and benzodiazepines (7%). Drugs of abuse were significantly more frequently identified as the cause of rhabdomyolysis in G2 ($p < 0.001$), while neuroleptics were significantly more frequent in G1 ($p < 0.001$). The time from exposure to admission was >12 hours in 68% of G2 patients, while in 67% of G1 patients it was <6 hours. Patients with CK >10000 U/L had significantly lower SaO_2 (83% versus 91%, $p < 0.001$), systolic (103 versus 120 mmHg, $p < 0.001$) and diastolic blood pressure (58 versus 69 mmHg, $p < 0.001$) on admission compared to patients in G1. Correlation between impairment of consciousness on admission and the level of rhabdomyolysis was not found. Renal function parameters (urea, creatinine) were significantly higher in G2 ($p < 0.001$). Hemodialysis (HD) was indicated in 10 patients in G2. Neurological sequelae (postanoxic encephalopathy, peripheral nerve injury) were noted in 15 patients in G2. Fatal outcomes were registered in 16 patients (6%), 10 in G2 (18%) and 6 in G1 (3%).

Conclusion: Male gender, type of agent (mostly opioids), hypotension, low SaO_2 and prolonged time elapsed since exposure, were the main factors contributing to rhabdomyolysis in acute poisonings. Given the high lethality, severe rhabdomyolysis can be considered a significant risk factor of fatal outcome in acute poisoning.

150. Annex VIII (Article 45; Regulation 1272/2008) – Life After "Brexit": A UK perspective

Pardeep S. Jagpal, Ted Cheung, Bornnali Das, Hayley A. Williams and Sally M. Bradberry

National Poisons Information Service (Birmingham Unit), Birmingham, United Kingdom

Objective: Obligations under Annex VIII of EU Regulation 1272/2008 (Classification, Labelling and Packaging) came into force on 1 January 1 2021. This presented a significant technical challenge to European Appointed Bodies who access harmonised chemical safety data submitted to the European Chemicals Agency Poison Centre Notification Portal (ECHA PCN). The UK Appointed Body was unable to access the ECHA PCN and was required to upgrade its national submission system to accept poison centre notifications for Northern Ireland [1].
Methods: We reviewed the impact of the introduction of Annex VIII on the UK Appointed Body, the National Poisons Information Service (NPIS) (Birmingham Unit).
Results: Between 1 January 1 2021 and 30 September 2021, the NPIS successfully registered 6,324 harmonised Annex VIII compliant dossiers from industry. Three areas of impact were identified that required specific intervention from NPIS. 1. Clarity for stakeholders: Since Annex VIII came into force the need to engage with industry to support them to better understand their obligations for submitting safety information in the UK (Great Britain and Northern Ireland) remains essential. The NPIS frequently communicates to stakeholders that following the end of the UK Transition Period, the submission of safety data sheets (SDS) are only suitable for Great Britain (England, Wales and Scotland). Submission of safety information for consumer/professional products to be placed on the market in Northern Ireland requires compliance with EU legislation that stipulates the use of a harmonised format. 2. Unsuccessful dossier submission: For incomplete/incorrect harmonised files that are unable to register to the new UK system, NPIS works closely with stakeholders providing support to ensure future successful dossier submission. The main cause of submission failure is the production of dossiers in third party software rather than IUCLID 6, which is developed by the European Chemicals Agency. The NPIS has updated its website to provide more detailed guidance including a link to the IUCLID 6 YouTube channel for video tutorials. 3. Information security and infrastructure: For stakeholders using direct system-to-system submissions to the ECHA PCN, the process of submitting dossiers directly to the Appointed Body for Northern Ireland has raised some data security concerns. At the present time submission of dossiers is undertaken by email which utilises multi-factor authentication. NPIS is also capable of accessing dossiers through secure cloud storage filesharing systems.
Conclusion: Stakeholders need to continue to collaborate and disseminate information to industry about the requirements of Annex VIII and how to meet these obligations.

Reference

[1] Jagpal PS, Bradberry SM. Challenges facing the UK National Poisons Information Service (NPIS) ahead of EU exit and commencement of Annex VIII of Article 45 (Classification, Labelling and Packaging). Clin Toxicol (Phila). 2021;59:573–574.

151. Comprehensive product data for poisons centres: contributions of EAPCCT and its members

Herbert Desel[a], Pieter Brekelmans[b] and Ronald de Groot[b]

[a]German Federal Institute for Risk Assessment (BfR), Berlin, Germany; [b]Dutch Poison Center - University Medical Center Utrecht, Utrecht, Netherlands

Objective: The majority of exposures resulting in poisoning or concern are caused by mixtures, while poisons centres' (PC) advice is based on knowledge of toxic hazards of substances in almost all cases. The link is provided by product information provided by industry. In 2021, mandatory notification following the European Poison Centres Notification (PCN) Format came into force after more than 13 years of discussion and development. The contributions of the EAPCCT and its members to this process were analysed.
Methods: Regulation (EC) No 1272/2008 (Classification, Labelling and Packaging (CLP)) and documents of several working groups on the harmonisation process were screened and analysed for EAPCCT contributions.
Results: CLP, article 45 states "on emergency health response" that poisons centres "shall have at their disposal all the information required. … The [European] Commission shall carry out a review to assess the possibility of harmonising the information … following consultation with relevant stakeholders such as the … EAPCCT." Thus, the EAPCCT was consulted in 2009 and – after several meetings – invited to present their views with six presentations at a high-level stakeholder workshop in 2010. Reviewing this meeting the European Commission decided in favour of a harmonisation of information. Subsequently, the EAPCCT was invited to propose a format. The document "EAPPCT Guidelines" for product notification was developed, presented to the Commission and used as starting point for the development of the new Annex VIII of CLP. This Annex forms the legal basis of the format, finally implemented after many rounds of discussion involving EAPCCT and several other stakeholders in 2017. According to the legal text, the European Chemicals Agency (ECHA) as a powerful player developed the technical PCN Format embedded in and expanding the technical standard International Uniform ChemicaL Information Database, version 6 (IUCLID 6) in 2019. Since 2017, the EAPCCT was no longer involved as official stakeholder, but many individual EAPCCT members representing poisons centres provided important contributions focusing on PC needs. In 2020, two legal amendments of Annex VIII format were requested by industry to improve workability for companies handling highly valuable compositions of their products. This led to updates of the PCN Format increasing its complexity. Substantial training of PC staff is needed to ensure understanding and correct use of the dataset for the PC services.
Conclusion: Product data submitted in the PCN Format has become an important dataset. EAPCCT has been recognized officially as a valuable European partner when poisons centres' services are involved.

152. Prognostic factors in calcium-channel blocker poisoning managed medically or with veno-arterial extracorporeal membrane oxygenation: an observational cohort study

Sebastian Voicu, Isabelle Malissin, Nicolas Deye and Bruno Mégarbane

Department of Medical and Toxicological Critical Care, Lariboisière Hospital, INSERM UMRS-1144, Paris University, Paris, France

Objective: Calcium-channel blocker (CCB) poisoning is the main cause of cardiotoxicant-attributed death. However, prognostic factors have been poorly studied while essential to the decision of veno-arterial extracorporeal membrane oxygenation (ECMO)

implementation. We aimed to evaluate mortality in CCB-poisoned patients and determine predictors of death due to CCB-attributed cardiovascular failure (CVF).
Methods: We performed a single-center observational study including all successive CCB-poisoned patients admitted to the intensive care unit (ICU) from January 2000 to December 2020. Catecholamine dose was expressed as the sum of epinephrine + norepinephrine + isoprenaline infusion rate. CCB-attributed CVF death was defined as mortality resulting from persistent CVF due to CCB despite adequate fluid, catecholamine and antidotal treatment.
Results: In total 263 patients were included (age 51 years [40-64] (median [IQR]); presumed ingested doses, 11-fold [5-23] the recommended daily doses; cardiotoxicant co-ingestions, 43%). During the first 24 hours, blood lactate concentration was 3.6 mmol/L [1.9-6.6], QRS duration 0.08 s [0.08-0.11] and left ventricular ejection fraction (LVEF) 60% [55-65]. We observed no death in the 53 patients who did not require catecholamine during ICU stay; 11 deaths [7%, from CCB-induced CVF (N = 5) and septic shock (N = 6)] in the 169 patients treated with catecholamines but not ECMO; and 21 deaths (51%) in the 41 ECMO-treated patients. All nine patients admitted with refractory cardiac arrest died. In ECMO-free CVF patients, survivors had lower peak catecholamine doses (7 mg/h [3-15] versus 32 mg/h [30-60], p = 0.0007), higher LVEF (60% [60-70] versus 50% [50-50], p = 0.0016) and less frequently cardiac arrest (3/158 (1.9%) versus 2/5 (40%), p < 0.0001) than non-survivors from CCB-attributed CVF. In multivariable analysis, only the peak catecholamine dose (Odds ratio, 1.06; 95%-confidence interval, 1.01-1.11) and LVEF (0.81; 95%CI, 0.68-1.07) were significantly associated with death (area under the curve of the model, 0.97; 95%CI, 0.91-0.99, p = 0.0001). According to this model, patients with 40% LVEF and 15 mg/h catecholamines and patients with 50% LVEF and 45 mg/h catecholamines have a 50%-risk of death due to CCB-attributed CVF.
Conclusion: Overall mortality in CCB-poisoned patients managed in the ICU is 7% in patients not requiring ECMO and 51% in patients treated with ECMO. Predictive factors of death are LVEF alteration and peak catecholamine dose in the first 24 hours, and these should be taken into consideration when deciding about ECMO implementation.

153. Use of extracorporeal cardiopulmonary resuscitation for cardiac arrest from acute pediatric poisoning: a US cohort from 2003 to 2019

Matteo Di Nardo[a], Danilo Alunnifegatelli[b], Marco Marano[c] and Hong K. Kim[d]

[a]Pediatric Intensive Care Unit, Bambino Gesù Children's Hospital, Rome, Italy; [b]Department of Public Health and Infectious Disease, Sapienza University of Rome, Rome, Italy; [c]Pediatric Intensive Care Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy; [d]University of Maryland School of Medicine, Baltimore, United States

Objective: Acute pediatric poisoning may present with in-hospital cardiac arrest and require extracorporeal cardiopulmonary resuscitation (ECPR). There is limited evidence regarding the use and outcome of ECPR support in acute drug-induced cardiac arrest. Thus, we sought to describe the clinical characteristics and outcome of ECPR support in pediatric poisoning with in-hospital cardiac arrest.

Table 1. Pre-ECMO versus 24-hour post-ECMO clinical parameters among survivors versus non-survivors in pediatric poisoned patients.

	Non-Survivors	Survivors	P-value
Pre-ECMO			
Hypotension*, n (%)	6 (100)	5 (100)	0.297
pH	7.2 (7.2, 7.3)	7.3 (7.3, 7.4)	0.065
PCO_2 (mmHg)	39 (32, 79)	39 (37.2, 55.2)	0.806
PO_2 (mmHg)	68 (53, 83)	70.5 (64.2, 75.5)	0.806
HCO_3 (mmHg)	22.1 (14, 29)	26.5 (19.2, 37.8)	0.327
SaO_2 (%)	84 (72, 92)	85 (76, 95)	0.459
Lactic acid (mmol/L)	7.5 (6.3, 8.3)	6.3 (3.8, 8.2)	0.564
24-hours post-ECMO			
Hypotension*, n (%)	4 (66.7)	2 (40)	0.055
pH	7.4 (7.2, 7.5)	7.4 (7.3, 7.5)	1.000
PCO_2 (mmHg)	37 (34.6, 43.2)	38 (37, 41.5)	0.376
PO_2 (mmHg)	183 (103.8, 290)	154 (120.5, 235.0)	0.827
HCO_3 (mmHg)	23.3 (19, 28.9)	22 (20, 27)	0.827
SaO_2 (%)	96 (93.1, 98.5)	98 (93.2, 99)	0.247
Lactic acid (mmol/L)	4.1 (3.4, 10.6)	2.7 (2.5, 2.8)	0.221

*Hypotension defined according to age as described in American Heart Association Guidelines 2020
Data are presented as median values, and interquartile ranges.

Methods: We performed a secondary analysis of a prior retrospective study of pediatric patients (0-18 years) in the US who received extracorporeal membrane oxygenation (ECMO) for acute poisoning using Extracorporeal Life Support Organization's ECMO registry. Eligible cases were systematically identified using the International Classification of Disease (ICD) code for poisoning from 1 January 2003 to 31 December 2019. Study investigators reviewed all ICD codes to identify acute poisoning cases. Cases with ECPR support due to drug-induced cardiac arrest were included. Descriptive analysis and chi-squared/Wilcoxon rank-sum test were performed.
Results: During the study period, 86 cases of acute poisoning with known exposures were identified; 28 cases (33.3%) experienced cardiac arrest prior to ECMO cannulation. Of these 71.4% (n = 20) experienced cardiac arrest after a single substance exposure and 28.6% (n = 8) after multiple substances exposure. Eleven cases (12.8%) received ECRP. Opioids and antidepressants (27.3%, n = 3 each) were two most commonly reported exposure among ECPR patients. Six cases (54.5%) were intentional exposures. The overall survival rate was 45.4%. Hemodynamic and metabolic (acid/base) parameters for pre-ECMO and 24-hour post-ECMO are summarized in Table 1. These clinical parameters were similar between survivors and non-survivors. Persistent systemic hypotension was more frequent in non-survivors 24 hours after ECMO deployment.
Conclusion: ECPR reported a survival of 45.5% which is similar to the one of the general PICU population requiring ECMO for cardiac failure. Based on these data, we believe that where available ECPR should be offered in case of pediatric cardiac arrest due to poisoning.

154. Echocardiography in hypotensive poisoned patients: the potential role of measurement of mitral annular plane systolic excursion (MAPSE) in differential diagnosis and management

Csaba Pap

Department of Emergency Medicine and Clinical Toxicology, Budapest, Hungary

Table 1. Echocardiographic parameters in poisoned patients with hypoperfusion and/or hypotension.

	H n = 12	C n = 17	V n = 22	O n = 2	H + C n = 4	H + V n = 8	C + V n = 4
mean MAPSE, mm	15.3	7.2	21.7	18.1	7.4	22.9	8.3
MAPSE <8 mm*	0/12	14/17	0/22	0/2	3/4	0/8	1/4
MAPSE >18 mm*	3/12	0/17	20/22	1/2	0/4	8/8	0/4
mean SVi, mL/m^2	41.6	24.7	53.6	47.2	26.3	55.1	31.4
IVC max diameter, mm	10.4	16.1	13.2	14.1	10.1	9.9	12.7
IVC collapsibility index, %	38.3	28.1	26.3	32.5	34.7	ND	ND
Clinical improvement after echo-guided therapy	10/12	13/17	19/22	2/2	2/4	7/8	2/4

*Note patients with MAPSE 8-18 mm are not shown.

MAPSE: mitral annular plane systolic excursion; SVi: stroke volume index; IVC: inferior vena cava; n: number of patients; H: hypovolemic shock; C: cardiogenic shock; V: vasoplegic shock; O: obstructive shock; H + C hypovolemic and cardiogenic origin of shock; H + V: hypovolemic and vasoplegic origin of shock; C + V: cardiogenic and vasoplegic origin of shock; ND: no correct data

Objective: Acute poisoning can result in hypotension by various mechanisms: hypovolaemia, vasoplegia, reduced ventricular systolic function and inflow/outflow obstruction. Each of them requires different therapeutic measures. The four core types and main mechanisms of shock can readily be identified by echocardiography allowing even modification of initial therapy. Focused point-of-care echocardiography performed by non-cardiologists has become an accepted component of the practice of emergency and critical care medicine. Mitral annular plane systolic excursion (MAPSE) is an M-mode derived echocardiographic marker of left ventricular (LV) longitudinal function. It correlates well with other markers of LV function, is simple, reliable and easily obtainable even for untrained observers. Its normal range is considered 11-17 mm. We evaluate the usefulness of MAPSE for differential diagnosis and treatment guiding in poisoned patients presenting with hypotension to our department.
Methods: In a one-year retrospective study we collected the demographic, clinical and echo data of patients presenting to our department with a blood pressure less than 90/60 mmHg and signs of hypoperfusion or less than 80/50 mmHg even after fluid loading along with the suspicion of acute overdose. Cases where the diagnosis of poisoning could not be confirmed or those with severe structural heart disease or known ventricular dysfunction were excluded. The echo parameters were determined by a cardiologist. Lateral M-mode MAPSE was obtained on all echocardiograms and each measurement was compared to patient characteristics, their hemodynamic profiles and certain echo parameters.
Results: See Table 1.
Conclusion: In combination with IVC + IVC collapsibility index, MAPSE as part of a focused, point-of-care echocardiography seemed to be a useful method to determine the main mechanism of shock and guide adequate therapy in poisoned patients. It can reflect LV hyperkinesis in vasoplegic shock, LV normokinesis or mild hyperkinesis in hypovolemic shock and LV hypokinesis in cardiogenic shock.

155. INTOXICATE study. Comparison of patients with/without ECG-changes and with/without abnormal values: a pilot study

Sam M. Zwaag, Claudine C. Hunault and Dylan W. de Lange

Dutch National Poisons Information Centre (NPIC), University Medical Center Utrecht, Utrecht, Netherlands

Objective: An intensive care unit (ICU) requirement score (IRS) has been developed to identify poisoned patients who need ICU admission [1]. A large prospective observational study, the INTOXICATE study (www.toxicstudy.org) is currently conducted to evaluate its usefulness and to investigate if electrocardiogram (ECG) abnormalities and abnormal laboratory values (present before ICU admission) add to the predictive value of the IRS.
Methods: The primary and secondary outcomes were an IRS >6 and in-hospital death, respectively. ECG and laboratory data were collected before ICU admission. Patients with incomplete data were excluded. The statistical relationships between the different parameters were investigated using Wilcoxon tests for quantitative parameters and Fisher exact tests for qualitative parameters.
Results: Overall, 226 patients from 49 units in 17 different countries were included between 2 November 2020 and 25 October 2021. ECG results seem to be independent of the outcome (Table 1). Laboratory values such as arterial pH, sodium, chloride and lactate show a statistically significant association with the outcome.
Conclusion: In this pilot study, we found that an abnormal ECG has limited association with the IRS. More patients have to be included (>2000) to be able to distinguish between outcomes of patients with different cardiac abnormalities and show the influence of ECG- and laboratory changes in specific subgroups of intoxicated patients.

Reference

[1] Brandenburg R, Brinkman S, de Keizer NF, et al. In-hospital mortality and long-term survival of patients with acute intoxication admitted to the ICU. Crit Care Med. 2014;42:1471–9.

156. Extracorporeal membrane oxygenation (ECMO) use in adults for acute poisoning in the US: a retrospective study from 2003 to 2019

Zachary J. Rogers[a], Kent M. Mok[a], Matteo Di Nardo[b], Danilo Alunnifegatelli[c], Kevin M. Jones[d] and Hong K. Kim[a]

[a]University of Maryland Medical Center, Baltimore, United States; [b]Pediatric Intensive Care Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy; [c]Department of Public Health and Infectious Disease, Sapienza University of Rome, Rome, Italy; [d]Shock Trauma Center, University of Maryland Medical Center, Baltimore, United States

Table 1. Comparison of patients with and without ECG changes, and patients with and without abnormal lab values in the INTOXICATE study.

	Total population (N = 226)	*Patients with endpoint (N = 60)*	*Patients without endpoint (N = 166)*	*p-value*	*Patients with a normal ECG (N = 130)*	*Patients with an abnormal ECG (N = 48)*	*P-value*
IRS score >6, N (%)	179 (79)	57 (95)	122 (73)	<0.001	104 (80)	42 (88)	0.3
In hospital death, N (%)	21 (9)	21 (35)	0 (0)	<0.001	5 (4)	4 (8)	0.3
ECG available, N (%)	178 (79)						
Abnormal ECG	48 (27)	11 (26)	37 (27)	1			
QRS	94 (84-104)	100 (87-115)	94 (85-102)	0.1	93 (84-101)	94 (85-102)	0.02
QT	401 (356-446)	400 (350-450)	404 (360-444)	0.5	399 (350-422)	404 (360-444)	<0.001
Laboratory parameters							
Arterial pH	7.35 (7.26-7.4)	7.35 (7.19-7.4)	7.37 (7.31-7.42)	0.003	7.36 (7.29-7.42)	7.36 (7.3-7.4)	0.2
Sodium (mmol/L)	139 (136-141)	137 (135-140)	139 (137-141)	0.04	139 (137-141)	139 (137-141)	0.1
Potassium (mmol/L)	3.8 (3.5-4.2)	3.9 (3.6-4.6)	3.8 (3.5-4.2)	0.1	3.8 (3.5-4.2)	3.8 (3.5-4.2)	0.9
Chloride (mmol/L)	104 (101-108)	103 (99-105)	105 (102-108)	0.03	104 (101-107)	104 (101-107)	0.4
Lactate (mmol/L)	2 (1.1-3.2)	2.6 (1.4-4.8)	1.6 (1-2.5)	0.001	1.7 (1-10.2)	1.7 (1-2.6)	0.01

* data are presented as median (percentiles 25th-75th)

Objective: ECMO is increasingly utilized in acutely poisoned patients, however, there is no clinical guideline to help determine the optimal time or clinical indication for EMCO. We aim to determine the clinical characteristic of ECMO use in poisoning and factors associated with mortality.
Methods: A retrospective study was conducted using the Extracorporeal Life Support Organization's (ELSO) ECMO registry. Adult patients (>18 years old) who received ECMO for acute poisoning in the US were identified using the International Classification of Disease (ICD) code for poisoning (ICD-9: 960-989 and ICD-10: T36-T65) from 1 January 2003 to 30 November 2019. Two study investigators reviewed all ICD codes for each case to determine case inclusion. Descriptive analysis and chi-squared/Wilcoxon rank-sum test were performed to assess the demographic and clinical characteristics of survivors and non-survivors.
Results: Systematic search of ELSO registry identified 506 cases; 216 were excluded, leaving 290 in the final study cohort. The median age was 34 years and 114 (39.3%) were female. The most common toxin exposure was opioid (n = 74; 25.5%) followed by cardiovascular agents (n = 41; 14.1%). The intention of exposure was unknown in the majority of cases (n = 84; 29%); 23.8% reported suicide/self-harm (n = 69) and 22.4% were unintentional exposures (n = 65). Overall 58.3% (n = 169) of the cases required pulmonary support and 160 received venovenous ECMO (VV-ECMO). The survival rate was 63.8% (n = 185). Demographic and exposure characteristics were similar between survivors versus non-survivors. A larger proportion of cases with opioid exposure survived compared to other agents. Significantly higher survivor rate (71.3% versus 54.5%; p = 0.013) was observed among those who received VV-ECMO compared to VA-ECMO. Clinical parameters for pre-ECMO and 24-hour post-ECMO are summarized in Table 1. Persistent metabolic acidosis and lactic acidosis was associated with mortality.
Conclusion: ECMO support can improve hemodynamic, metabolic and ventilatory parameters. Persistent metabolic acidosis and lactic acidosis were associated with death.

157. Pediatric suicide attempts by self-poisoning: a multicentre Spanish register

Lidia Martínez-Sánchez[a], Lorena Algarrada[b], Irene Baena[c], Paula Vázquez[d], Consuelo Benito[e], Ingrid Guillén[e], Ana Rodríguez[f], Victoria López[g], Ana Peñalba[h], Liliana Mangione[i], Francisco J. Humayor[j], Nuria Clerigué[k], Beatriz Azkunaga[l], Neus Pociello[m],

Table 1. Pre-ECMO versus 24-hour post-ECMO clinical parameters among survivors versus non-survivors in poisoned patients.

	Non-Survivors	Survivors	P-value
Pre-ECMO			
Hypotension*, n (%)	26 (44.8)	46 (33.8)	0.197
pH	7.2 (7, 7.3)	7.2 (7.1, 7.3)	0.358
PCO_2 (mmHg)	53.5 (39.8, 74.2)	53 (46, 69)	0.547
PO_2 (mmHg)	61 (44.7, 84.5)	60 (48.2, 83)	0.903
HCO_3 (mmHg)	20 (14.8, 29)	22.8 (19, 27)	0.159
SaO_2 (%)	85 (75, 92)	86 (76, 94)	0.459
Lactic acid (mmol/L)	6 (3, 12)	4.6 (2.5, 7.7)	0.092
24-hours post-ECMO			
Hypotension*, n (%)	13 (22.4)	19 (14)	0.215
pH	7.4 (7.3, 7.4)	7.4 (7.4, 7.4)	0.149
PCO_2 (mmHg)	40 (36, 43)	40 (36, 45)	0.637
PO_2 (mmHg)	84.5 (66.2, 165.8)	96.5 (70, 134.8)	0.653
HCO_3 (mmHg)	24 (21, 27)	25.2 (23, 28)	0.027
SaO_2 (%)	96 (92.8, 98.2)	97 (93.2, 99)	0.247
Lactic acid (mmol/L)	4.8 (1.9, 9.6)	2 (1.3, 3.3)	0.001

*Systolic blood pressure: < 90 mmHg or MAP <65 mmHg
Data are presented as median values, and interquartile ranges.

Jose A. Muñoz[n], María D. Rodríguez[o], Begoña de Miguel[p], Paula García[p], Carlos García-Vao[q], Pablo Gómez[q], Jara Gaitero[r], Juan C. Molina[r], Teresa Núñez[s], Anna Pizà[t], Helvia Benito[u], Carmen Campos[v], Laura Herrero[w], Ana G. Andrés[x], Zelidety Espinel[i], Rebeca Lanuza[y] and Ramon Fernández[z]

[a]Pediatric Emergency Department, SJD Barcelona Children's Hospital, Intoxications Working Group of the Spanish Society of Pediatric Emergencies, Esplugues de Llobregat, Spain; [b]Pediatric Emergency Department, SJD Barcelona Children's Hospital, Esplugues de Llobregat, Spain; [c]Pediatric Emergency Department, Parc Taulí Health Corporation, Sabadell, Spain; [d]Pediatric Emergency Department, University Hospital Gregorio Marañón, Madrid, Spain; [e]Pediatric Emergency Department, University Hospital Puerta del Hierro, Majadahonda, Spain; [f]Pediatric Emergency Department, University Hospital Dr Peset, Valencia, Spain; [g]Pediatric Emergency Department, University Hospital Son Espases, Palma de Mallorca, Spain; [h]Pediatric Emergency Department, University Hospital Marqués de Valdecilla, Santander, Spain; [i]Pediatric Emergency Department, University Hospital Insular Materno-Infantil, Las Palmas de Gran Canarias, Spain; [j]Pediatric Emergency Department, Basurto University Hospital, Bilbao, Spain; [k]Pediatric Emergency Department, University Complex of Navarre, Pamplona, Spain; [l]Pediatric Emergency Department, Cruces University Hospital, Barakaldo, Spain; [m]Pediatric Emergency Department, University Hospital Arnau de Vilanova, LLeida, Spain; [n]Pediatric Emergency Department, Donosti University Hospital, San Sebastián, Spain; [o]Pediatric Emergency Department, Infanta Cristina University Hospital, Parla, Spain; [p]Pediatric Emergency Department, La Paz University Hospital, Madrid, Spain; [q]Pediatric Emergency Department, Del Tajo University Hospital, Madrid, Spain; [r]Pediatric Emergency Department, Niño Jesús University Children's Hospital, Madrid, Spain; [s]Pediatric Emergency Department, Infanta Elena University Hospital, Valdemoro, Spain; [t]Pediatric Emergency Department, Mútua Terrassa University Hospital, Terrassa, Spain; [u]Pediatric Emergency Department, Rio Hortega University Hospital, Valladolid, Spain; [v]Pediatric Emergency Department, Miguel Servet University Hospital, Zaragoza, Spain; [w]Pediatric Emergency Department, Mendaro Hospital, Mendaro, Spain; [x]Pediatric Emergency Department, Complejo Asistencial Universitario León, León, Spain; [y]Pediatric Emergency Department, Zaragoza University Hospital, Zaragoza, Spain; [z]Pediatric Emergency Department, Cabueñes University Hospital, Cabueñes, Spain

Objective: Suicidal ideation and attempts in children have increased over the last few years. This study aims to evaluate the social, epidemiological, and clinical characteristics of patients who attended a Spanish pediatric emergency department (PED) after a self-poisoning suicide attempt.
Methods: A prospective cohort study based on a multicentre register. Patients under 18 years who attended after a self-poisoning suicide attempt from January 2021 to September 2021 were included. Informed consent was obtained from patients and parents. Twenty-five PEDs participated. The poisoning severity was classified using the Poisoning Severity Score.
Results: There were 281 cases registered, of which 255 (90.1%) were females. In 183 (65.1%) there was at least one mental health disorder previously diagnosed (affective disorders in 102; 36.3%), 162 (57.7%) reported previous attempts and 232 (82.6%) notified self-harm. A first-degree familiar psychiatric disorder was present in 108 (38.4%). The main reason reported for the self-poisoning was a familiar conflict (80; 28.5%) but 90 patients (32.0%) considered there was no trigger. The most commonly implicated substances were benzodiazepines (101; 35.9%), paracetamol (93;33.1%) and selective serotonin re-uptake inhibitor (SSRI) antidepressants (55; 19.6%). In 40.9% more than one agent was used. The median number of pills ingested was 15 (p25-75 = 10-24). At hospital arrival, 47 (16.7%) presented an altered pediatric assessment triangle. The most frequent symptoms were neurological (130; 63.4% among 205 cases with symptomatology) and gastrointestinal (99; 48.3%). There was mild toxicity in 186 (66.2%), moderate in 19 (7.8%), and severe in 4 (1.4%). There were no fatal cases or permanent sequelae. Gastrointestinal decontamination was performed in 147 cases (52.3%), of which 143 (97.3%) included activated charcoal and 6 (4.1%) gastric lavage. There were 66 cases (23.5%) where an antidote was administered, with N-acetylcysteine being the most common (50; 75.8%). Among the cases, 148 (52.7%) were admitted, 12 (4.3%) to a pediatric critical care unit. Almost all the patients (277; 98.6%) were assessed by a mental health professional during the hospital stay.
Conclusion: Self-poisoning suicide attempt is an important health problem in the Spanish PED. Personal and familial psychiatric history, previous attempts, or self-harm are common. The presence of toxicity was frequent, although it was mild in the majority of patients. These children need a multidisciplinary approach, which was done in almost all the cases registered.

158. A pilot program of training in early childhood home poisoning and injury prevention using a remote video game: VirtualSafeHome©

Alan Woolf, Peter Weinstock and Jeffrey Jacobsen

Boston Children's Hospital; Harvard Medical School, Boston, Massachusetts, United States

Objective: Poisoning and other household injuries are frequent events among toddlers. Over 900,000 poisonings among US children ≤5 years old are reported annually [1]. Results from a 2011-2016 survey found >385,000 US preschoolers had blood lead concentration ≥5 μg/dL [2]. Children are twice as likely to die in a house fire. Counseling families on poisoning prevention and home safety is an important function of healthcare workers. We developed a novel teaching module: VirtualSafeHome© (VSH), a self-contained, Internet-based home-safety learning tool with gaming characteristics, to improve awareness of household hazards. The aims of this pilot study were to determine the functionality of VSH and investigate usage characteristics.
Methods: The prototype VSH kitchen was built in Unity [3] and delivered (as a website) using 3DVista [4] and Wix [5]. Twenty-one childhood kitchen hazards were embedded in the game. A player points-and-clicks when spotting a hazard; a bulleted factoid describing the hazard pops up with an audio victory announcement. We recruited a convenience sample of volunteer adults between February-October 2021. Participants completed a brief demographics questionnaire and 5-item pre/post-test hazards knowledge surveys. Gaming outcomes included number and types of hazards discovered, duration of the session, and a comparison of pre/post-test scores.
Results: Fifteen adults (9 female) aged 21-57 years (median: 30 years) completed the module and surveys. All participants were able to navigate the game. The average playing time was 7.7 minutes (median 6.12 minutes); 80% elected to spend at least 5 minutes playing the module. 80% of players reported that they were somewhat or extremely satisfied with the game. Childhood hazards knowledge (5 items) pre/post scores rose for 6 players (40%). Players identified a median 13 hazards (range: 3-21); a majority found at least 14 out of 21 hazards. Two players identified all 21 hazards.
Conclusion: A remote gaming tool can be a useful modality in educating adults on the recognition of home hazards that threaten the safety of young children.

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159. Association of hyperthermia with adverse outcomes in the anticholinergic toxidrome

Grant Comstock, Sasha K. Kaiser and Sam Wang

Rocky Mountain Poison and Drug Safety, Denver, United States

Objective: Anticholinergic toxicity is associated with hyperthermia, largely through diminished heat dissipation. Because of the association between drug-induced hyperthermia and adverse outcomes in sympathomimetic or serotonin toxicity, anticholinergic-induced hyperthermia is frequently treated with aggressive sedation and monitoring in critical care settings. However, the clinical significance of anticholinergic-induced hyperthermia is unknown. The objective of this study was to determine if patients with severe outcomes and critical illness from anticholinergic toxicity had a higher temperature than those without significant clinical sequelae.
Methods: This was a retrospective, case-control analysis comparing peak emergency department (ED) temperature amongst anticholinergic patients who experienced severe outcomes with those who did not. Severe outcome was defined as seizure, ventricular dysrhythmia, hypotension, or intubation. We enrolled consecutive hospitalized patients of all ages who received a bedside diagnosis of anticholinergic toxicity by a medical toxicologist and had a clear causative agent. Cases were excluded if exposed to coingestants known to cause temperature dysregulation or seizure, had alternate etiology of fever, or if medical records were incomplete. The analysis was powered to detect a temperature difference of 2° C between groups.
Results: From 1 January 2016 through 21 September 2021, 259 charts were reviewed; 48 met inclusion criteria for analysis. Nineteen (39.6%) patients had severe outcomes: 13 seizures, 8 cases with hypotension, 4 intubations, and 1 ventricular dysrhythmia. There were no fatalities. Mean peak ED temperature amongst patients with severe outcome was 37.2 °C (SD 0.70) versus 37.3 °C (SD 0.75) without severe outcome, with a temperature difference of -0.08 °C (95% CI -0.51 – 0.3). Receiver operating characteristic (ROC) curve analyzing the testing characteristics of temperature for severe outcomes yielded an area under the curve (AUC) of 0.52. Secondary analysis found no statistically significant difference in temperature when evaluating individual severe outcomes.
Conclusion: We found no difference in peak ED temperature between patients who had severe outcomes due to anticholinergic toxicity as compared to those who did not. Additionally, peak ED temperature does not appear to be predictive of more severe outcomes in patients with anticholinergic toxicity. No cases of severe hyperthermia (> 40 °C) were captured in this study, and these findings may therefore not apply to extreme hyperthermic states. We posit that unlike temperature dysregulation in patients with sympathomimetic or serotonin toxicity, temperature is not predictive of critical illness in anticholinergic poisoned patients.

160. Prognostic factors of severity and need for antidote administration in acute digoxin and *Nerium oleander* poisoning

Luca Ratibondi[a], Azzurra Schicchi[a], Davide Lonati[a], Valeria M. Petrolini[a], Lucia Bernasconi[a], Valentina Negrini[a], Benedetta Brolli[a], Alberto Malovini[b], Cristina Grazioli[a] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]Laboratory of Informatics and Systems Engineering for Clinical Research, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy

Objective: Acute poisoning with cardioactive steroids (CAS) can be due to ingestion of digoxin (drug) or CAS-containing plants (i.e. oleander, *Nerium oleander)*. Establishing reliable admission prognosticators is crucial for early identification of patients at risk of severe poisoning who should benefit from specific antidote treatment (Digoxin-Fab). The most recent study on prognosticators of digoxin intoxication dates to 1982, while no study has been published on *N. oleander*. Since 1982, the commercialization of a safe and effective antidote (DigiFab®) in 1986 and advances in supportive care has changed mortality of this poisoning. We assess severity prognosticators at hospital admission.
Methods: A retrospective study including all digoxin/oleander poisoned patients referred to our Poison Control Centre, 2004-2021. Inclusion criteria were: self-ingestion of digoxin/oleander, digoxin plasma concentration and potassium concentration at hospital admission. Patients were stratified in 3 groups (mild, moderate, severe) according to peak potassium concentration and severity of cardiac impairment. We determined the predictive factors of severity based on univariate comparisons (using chi-squared and Mann-Whitney tests) followed by multivariate logistic regression analyses. The method of plasma digoxin determination was not recorded due to the nature of the study.
Results: There were 230 patients: 138 (mean age 44 years; M/F 65/73) in the plant and 92 (mean age 61 years; M/F 38/53) in the drug group. Most (82%) were symptomatic. Two died (digoxin group). Digoxin-specific Fab was administered in 25% of oleander-poisoned patients, and 50% of digoxin patients (Table 1). It was immediately available in only 48% of cases. There was significant correlation between the initial potassium concentration and clinical severity, in the oleander ($p < 0.0001$) and digoxin group ($p = 0.0113$); the digoxin concentration in oleander poisoning appears to relate to clinical severity ($p = 0.0121$). A strong correlation between the initial value of potassium, digoxin and heart rate was found with the need of antidote administration in both poisonings ($p < 0.0120$).
Conclusion: Updated prognosticators are fundamental to early identification of patients needing prompt antidote. Our study determined reliable and useful bedside prognostic factors of severity and the need for antidote administration using admission potassium and digoxin concentration.

Table 1. Values of potassium concentration, digoxin concentration and heart rate at admission, and correlation with poisoning severity (mild, moderate, severe) and antidote administration (yes/no). Data are presented as median (interquartile difference) of numeric continuous or discrete explanatory variables.

Nerium oleander

		Poisoning severity			
Variable	*n*	*Mild*	*Moderate*	*Severe*	*P-value*
Potassium concentration (mEq/L)	87	3.95 (0.75)	4.4 (0.85)	4.8 (1.11)	**<0.0001**
Digoxin concentration (ng/mL)	87	0.3 (0.66)	0.6 (0.55)	0.84 (1.11)	**0.0121**
Heart rate (bpm)	87	87 (15)	54 (5.5)	44 (25)	**<0.0001**

Digoxin

		Poisoning severity			
Variable	*n*	*Mild*	*Moderate*	*Severe*	*P-value*
Potassium concentration (mEq/L)	61	4 (0.6)	4.6 (1.02)	4.5 (1.23)	**0.0113**
Digoxin concentration (ng/mL)	61	4.7 (3.8)	8.02 (7.45)	7 (4.7)	0.0671
Heart rate (bpm)	61	76 (14)	60 (24)	40 (25.75)	**<0.0001**

Nerium oleander

		Antidote administration		
Variable	*n*	*No*	*Yes*	*P-value*
Potassium concentration (mEq/L)	82	4 (0.7)	4.8 (0.7)	**<0.0001**
Digoxin concentration (ng/mL)	82	0.32 (0.57)	0.98 (0.75)	**<0.0001**
Heart rate (bpm)	82	56 (37)	51 (22.5)	**0.0120**

Digoxin

		Antidote administration		
Variable	*n*	*No*	*Yes*	*P-value*
Potassium concentration (mEq/L)	55	3.9 (0.5)	4.5 (0.69)	**0.0010**
Digoxin concentration (ng/mL)	55	4.54 (3.45)	8 (4.12)	**0.0005**
Heart rate (bpm)	55	70 (9.5)	50 (29.5)	**0.0011**

161. Non-traumatic rhabdomyolysis: the Lithuania experience

Karolina Janonyte[a], Migle Kalinauskaite[a] and Gabija Laubner[b]

[a]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; [b]Centre of Toxicology Republican Vilnius University Hospital; Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Objective: Non-traumatic rhabdomyolysis is a rare but potentially fatal condition which results from myocyte damage and the release of intracellular contents [1,2]. Data on the prevalence of this syndrome in patients with acute toxic psychoactive substance and ethanol poisoning are limited [3,4]. The aim of this retrospective study was to assess the characteristics of patients diagnosed with non-traumatic rhabdomyolysis and to add to the knowledge on the etiology, pathogenesis, diagnosis, and treatment of the syndrome, as well as to investigate the complications associated with non-traumatic rhabdomyolysis, and their incidence.

Methods: Overall 35 people were included in the retrospective study. The patients' medical history and laboratory data from medical records were assessed. A literature search was performed using PubMed and Google Scholar databases. Data processing and statistical analysis were performed using R Commander, MS Excel and Statsmodels.

Results: Non-traumatic rhabdomyolysis was most commonly observed in males (80%) using psychoactive substances, including ethanol. Severe non-traumatic rhabdomyolysis was the most common in the study population and significantly more common than reported in the literature. Patients with creatine kinase activity above 40,000 U/L have a 7-fold increased risk of kidney damage. In the study population, 58% of the subjects had stage 3 acute kidney injury, which is many times higher than the frequency reported in the literature. The need for renal replacement therapy was determined by the creatine kinase activity on day 1. The total length of hospital stay was influenced by the creatinine concentration on day 1.

Conclusion: Non-traumatic rhabdomyolysis is a pathological process that poses an immediate threat to life. The most common cause of this syndrome is the use of ethanol and (or) psychotropic substances combined with prolonged immobilization. Early recognition and aggressive treatment of rhabdomyolysis can prevent the development of acute kidney injury.

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162. Incidence of rhabdomyolysis in single agent antimuscarinic exposures

Sasha K. Kaiser[a], Sabrina Kaplan[b], Hoanvu Nguyen[a], Robert Hendrickson[c] and Benjamin Hatten[d]

[a]Rocky Mountain Poison and Drug Safety, Denver, United States; [b]Denver Health Medical Center, Denver, United States; [c]Oregon Health and Sciences, Portland, United States; [d]University of

Colorado Department of Emergency Medicine, Denver, United States

Objective: The association between antimuscarinics and rhabdomyolysis is poorly understood. Many xenobiotics are thought to cause rhabdomyolysis either from direct muscle toxicity or due to secondary causes such as agitation, hyperthermia, and/or seizures. Data documenting the differing prevalence of rhabdomyolysis following exposure to individual antimuscarinic agents is lacking. We determine whether rhabdomyolysis is primarily associated with a specific agent or is a class effect that occurs after exposure to any antimuscarinic agent.
Methods: Retrospective analysis utilizing the Toxic Investigators Consortium (ToxIC) registry to evaluate proportions of single agent exposures resulting in rhabdomyolysis, as well as associated complications. Inclusion criteria incorporated all single agent "anticholinergic" exposures from 2010-2020 who were evaluated at the beside by a medical toxicologist. Clinical features related to rhabdomyolysis and the antimuscarinic toxidrome were collected. The primary outcome was the frequency of rhabdomyolysis. Secondary outcomes included frequency of acute kidney injury (AKI), hepatic injury, vital sign derangement, and antimuscarinic manifestations.
Results: In total, 2034 cases of anticholinergic single exposure were identified. Rhabdomyolysis, defined as a creatine phosphokinase (CPK) greater than 1000 U/L, occurred in 76 (3.7%) cases (Table 1). Rhabdomyolysis occurred in 4% (95%CI 3-5%) of diphenhydramine exposures, 8% (95%CI 3-16%) doxylamine, 3% (95%CI 1-8%) hydroxyzine, 10% (95%CI 3-24%) unspecified anticholinergic, and 4% (95%CI 1-15%) benztropine cases. Single cases of rhabdomyolysis occurred following exposure to dicyclomine, chlorphenamine, and promethazine. Patients presented with both antimuscarinic toxicity and rhabdomyolysis in 60 cases, the majority of these cases (75%) followed diphenhydramine exposure. Rhabdomyolysis and concurrent AKI occurred in three cases (diphenhydramine, doxylamine, and chlorphenamine). Rhabdomyolysis and elevated aminotransaminases occurred following exposure to diphenhydramine (n = 3), hydroxyzine (n = 2), chlorphenamine (n = 1), and one unspecified agent.
Conclusion: Following single agent antimuscarinic exposures, rhabdomyolysis occurred with similar frequency between reported agents. Associated AKI was rarely observed. Future studies should prospectively verify rates of rhabdomyolysis and examine independent risk factors predictive of rhabdomyolysis following antimuscarinic exposures.

Table 1. Antimuscarinic substances in cases with rhabdomyolysis from the Toxic Investigators Consortium (ToxIC) registry, 2010-2020.

Substance	Number exposed	Rhabdomyolysis cases	Prevalence
Diphenhydramine	1485	56 (74%*)	4%
Doxylamine	87	7 (9.2%)	8%
Hydroxyzine	134	4 (5.3%)	3%
Anticholinergic, not otherwise specified	40	4 (5.3%)	10%
Benztropine	47	2 (2.6%)	4%
Dicyclomine	18	1 (1.3%)	6%
Chlorphenamine	27	1 (1.3%)	4%
Promethazine	51	1 (1.3%)	2%

*Percent of total rhabdomyolysis cases

163. High-sensitivity troponin I in patients with rhabdomyolysis acutely intoxicated with psychotropic and chemical substances

Aleksandra Babulovska, Daniela Chaparoska, Zanina Perevska, Natasha Simonovska, Irena Jurukov, Kristin Kostadinovski and Kiril Naumovski

Clinical Centre, University Clinic of Toxicology, Medical Faculty, Ss Cyril and Methodius University in Skopje, North Macedonia

Objective: We determine high-sensitivity troponin I (hs-TnI) activity in patients with rhabdomyolysis following acute intoxication with psychotropic and chemical substances.
Methods: This is a clinically controlled prospective study conducted in 2019 at the University Clinic of Toxicology in Skopje. In this study, 140 patients with rhabdomyolysis were divided into two groups depending on the intoxicating substance i.e. psychotropic or chemical. Rhabdomyolysis was defined according to the Poisoning Severity Score. High-sensitivity troponin (hs-TnI) was measured in all patients with rhabdomyolysis three times, on the first, third, and fifth days of hospitalization. Data were statistically analyzed in SPSS software, version 22.0 for Windows (SPSS, Chicago, IL, USA).
Results: In all patients with rhabdomyolysis, the mean hs-TnI value on the first, third, and fifth days was 27.7 ± 78.3 μg/L, 43.7 ± 135.9 μg/L, and 28.73 ± 57.01 g/L, respectively. The comparison of hs-TnI in the three measurement times showed a significant difference (p = 0.001). On the third day of hospitalization in all patients the hs-TnI was significantly higher compared to the fifth day (p = 0.0001) as well as marginally insignificantly higher compared to the first day (p = 0.057). The value of hs-TnI on the fifth day was insignificantly higher compared to the first day (p = 0.021). We determined the highest values of hs-TnI in methadone intoxications (N = 5, 279.7 ± 190.7 μg/L, other drugs (N = 1, 138.4 μg/L); and benzodiazepines (N = 3, 213.9 ± 232.5 μg/L). Analysis by type of intoxication on the first, third, and fifth days showed that hs-TnI values were insignificantly higher in the psychotropic group compared with the chemical intoxication group.
Conclusion: The value of hs-TnI was slightly higher in patients with rhabdomyolysis after acute psychotropic intoxication. Elevated levels of hs-TnI in psychotropic intoxications were likely related to the specific etiologies such as illicit substance use, while chemical intoxication was associated with the clinical outcome of intoxication.

164. Experience with product notifications using the novel European Poison Centre Notification (PCN) format in Germany

Kathrin Begemann and Herbert Desel

German Federal Institute for Risk Assessment (BfR), Berlin, Germany

Objective: Companies importing or preparing mixtures classified as hazardous for physical or health hazards in the European Economic Area (EEA) have to submit product information to nationally appointed bodies (AB) according to Article 45 of the Regulation (EC) No 1272/2008 (CLP). Submissions for most

mixtures have to be provided in structured data dossiers as described by the Poison Centre Notification Format (PCN-F) since 1 January 2021. Key elements of PCN-F are product names, full formula data, a unique formula identifier (UFI, to be printed on the product label), hazard classification and labelling. An AB's early experience with PCN-F is reported.
Methods: All PCN-F-type submissions have been registered by the AB and imported into an in-house product database between May 2019 and October 2021. Analysis of the full dataset was performed with custom-made tools within this database.
Results: PCN-F dossiers have a complex structure consisting of more than 40 files each containing more than 1000 lines of eXtended Markup Language (XML) code for a typical product with simple formula. About 490,000 PCN-F dossiers containing data on 1.3 million products were registered; 59% of the dossiers were initial notifications, 35% notifications indicating dataset updates and 6% indicating new notification due to formula changes. There were 764,811 embedded mixture-in-mixture-type component datasets (MIM) included in the dossiers; 83.8% of these MIM contain information about their own composition (mainly according to the MIM supplier's safety data sheet) while 16.2% do not. Also, 3.0% of the MIM without compositional information contain a UFI and by this UFI are usually linked to another submission; 13.2% do not contain an UFI or a formula: almost all of these (12.9%) are linked to MIMs not classified for any hazard. All PCN-F dossiers contain at least one intended use category chosen from the European Product Categorisation System (EuPCS), important for bulk reporting on products or poisonings. The most frequently notified categories notifications were "Products for chemical or technical processes" (PC-TEC, n = 375,000), "Paints, coatings and related auxiliaries" (PC-PNT, n = 370,000), "Mixtures for further formulation" (F, n = 252,000) and "Construction products" (PC-CON, n = 80,000).
Conclusion: Managing PCN-F datasets is a challenge for ABs. A well-directed continuous quality assessment for completeness and correctness of submissions is an important prerequisite for acceptance of datasets by poisons centres and for undertaking statistical analysis to identify where improved risk management measures may be needed.

165. Implementation of a new poisons centres notification data submission procedure according to Annex VIII of the CLP Regulation in Germany

Herbert Desel, Frank Buchert, Mareike Budelmann, Esther Feistkorn, Marita Gessner, Ronald Keipert, Sebastian Pfeifer and Kathrin Begemann

German Federal Institute for Risk Assessment (BfR), Berlin, Germany

Objective: Germany started collecting product data for poisons centres (PCs) based on national legislation in 1990. Since 2002, the German Federal Institute for Risk Assessment (BfR) has been in charge of handling and making available all product datasets to the seven German PCs. The European Chemicals Agency (ECHA) developed the European Poison Centres Notification (PCN) format and procedures to transmit all product datasets to the appointed bodies based on the new Annex VIII of the Regulation (EC) No 1272/2008 (CLP) since April 2019. As a member of ECHA working groups BfR contributed to the development of the PCN format and procedures. The national product database was adapted to include PCN dossiers.
Methods: BfR runs a national product information database called GIFAS2. PCN Format was analysed and GIFAS2 was adapted to import, store, monitor and validate all PCN notifications.
Results: The technical structure of PCN data required a substantial upgrade of the database to enable combined retrieval and reporting on traditional and new product datasets. New data objects were created to store data elements (e.g. unique formula identifier (UFI), Reference Substance). Complex PCN data structures as mixtures embedded in other mixtures (MIMs), Interchangeable Component Groups, and standard formulas were converted to recursively interlinked existing data objects. The import procedure was changed to a semi-automatic registration of PCN dossiers submitted via the ECHA Submission Portal (ECHA-SP) or BfR's national Web portal enabling detailed reporting on daily data flows. Owing to the increased frequency of incoming submissions the BfR can only validate a random sample of submissions. The PCN notifications (most of them having passed an automatic technical validation procedure at ECHA-SP) are of higher quality compared to traditional product datasets. However, a few typical notification errors were identified, e.g. meaningless additional product names or incorrect use of languages or of the standard formula notification concept.
Conclusion: PCN data have been fully integrated into the national product database, with substantial IT workload. PCN data have been submitted to all German PCs and used in PC services since November 2019. Furthermore, PCN data have frequently been used by the BfR to undertake statistical analysis to identify where improved risk management measures may be needed, requested by the Competent Ministry. More comprehensive expert validation procedures are still under development, and considered important for improvement of data quality by PCs and BfR.

166. A retrospective study of poisons centre data of therapeutic agent exposures described by Anatomical Therapeutic Chemical (ATC) classifications

Eeva-Katri Kumpula[a] and Adam C. Pomerleau[b]

[a]National Poisons Centre, Dunedin, New Zealand; [b]National Poisons Centre, University of Otago, Dunedin, New Zealand

Objective: Poison centre surveillance data can be used to assess population risks of potentially harmful exposure to various medicines. Many centres like the New Zealand National Poisons Centre (NZNPC) use their own in-house classifications for medications which may be of historical origin and not specific enough to summarise medicine groups of interest. Lack of standardisation complicates international comparisons as the content of each class may not be self-explanatory. This study converted NZNPC exposure data into World Health Organization Anatomical Therapeutic Chemical (ATC) codes with the specific aim to standardise the substance classes presented, and to assist in interpretation of the findings [1].
Methods: Contacts to the NZNPC in 2018-2020 were analysed. Records of human patients exposed to at least one therapeutic agent were characterised by age (groups: 0-12 + unknown child, 13-19, 20-64, 65 years and over, unknown adult, unknown age), and substance data were converted into main Level 1 and subgroup Level 2 ATC codes and summarised. The online ATC Index 2021 search engine was used in assigning the codes [2].
Results: There were 29,677 records identified. Median patient age was 4.0 years (inter-quartile range 2.0-27.0), with 55% aged 0-12 or children of unknown age. Drugs acting on the nervous system (N) were the most frequently reported Level 1 ATC class

across all age groups, with an overall rate of 41% of all therapeutic substance exposures in the study. N02 analgesics were the biggest N subgroup across all age groups (20%), followed by N05 psycholeptics (9%) and N06 psychoanaleptics (8%). While cardiac medicines (C) comprised only 3-10% of therapeutic substance exposures in all other age groups, they comprised 32% for those aged 65 and over, with C07 beta blockers and C09 agents acting on the renin-angiotensin system most common.
Conclusion: N class drugs were commonly involved in exposures across all age groups, while C drugs were involved in exposures of those aged 65 years and over. ATC Level 2 subgroup codes provided further detail of which groups of medicines were most prevalent within Level 1 codes. A substance classification system which allows collapsing codes into their parent codes offers flexibility for analysis.

References

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167. Evaluation of the Spanish Toxic Surveillance System (STSS) to assess acute poisoning by chemicals in Spain as seen at the Emergency Department

Ana Ferrer-Dufol[a], Santiago Nogué-Xarau[b], Francisco Ruiz-Ruiz[c], Agustin Urdangarin[d] and Clara Serrano-Ferrer[e]

[a]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza, Spain; [b]FETOC, Barcelona, Spain; [c]Emergency Department, Clinic University Hospital, Zaragoza, Spain; [d]Documentation Service, Zaragoza University, Zaragoza, Spain; [e]Intensive Care Unit, Principe de Asturias Hospital, Alcalá de Henares, Spain

Objective: STSS, designed in 1999 between the Spanish Ministry of Health and a group of Clinical Toxicologists working in emergency departments (ED) of public hospitals, aims to report cases of acute poisoning by chemical products in their ED to evaluate the risks of exposure to these substances under the current EU regulations. We assessed the evolution and consistency of data over the 22 years of the Program.
Methods: The participating hospitals report cases of intoxication due to household, agricultural or industrial chemicals treated in their ED. The system started as a written postal communication with open fields and was developed into an online questionnaire in 2008 with drop-down fields, accessible around the clock by means of an encrypted system. The files are downloaded on a regular basis to a database (File Maker 9.0®) allowing compilation of final yearly report to be presented to the Health Ministry.
Results: The program has collected 17,702 cases from 32 hospitals covering a population of about 10 million people. Median age is 38.5 years. The distribution by sex is even: 8999 men and 8521 women. Domestic accidents are significantly prevalent (72%) followed by occupational accidents (14%) and suicide gestures (10%). Most chemicals involved are toxic gases (36%), caustics (23%), irritant gases (12%), solvents (8%), detergents (7%), and pesticides (7%). Main routes of exposure are respiratory (52%) and oral (34%). Ocular (11%) and cutaneous contact (4%) are much less frequent. Overall 68% of the patients were symptomatic at admission with digestive (28%), neurological (26%), respiratory (24%), and ocular (12%) symptoms, most of them mild. Most patients (80%) received some treatment, mainly symptomatic (53%). In 32% of the cases, an antidote or specific treatment was used, mainly oxygen in cases involving carbon monoxide exposure. Only 18% required hospital admission, 0.5-3% at the intensive care unit (ICU). The mortality rate is 1%: 67% cases due to suicide gestures, 23% to domestic accidents, and 4% to occupational accidents. Reported cases have increased, doubling the numbers in the second decade of the program reflecting the usefulness of the online submission tool. The population characteristics are quite homogeneous in terms of age, sex, type of poisoning, and evolution. A clear variation in agents exists with a rise of toxic gases from 13 to 36% and a decrease of pesticides from 11 to 2%.
Conclusion: STSS is a useful program to assess the profile of chemical poisoning at a continuous pace.

168. Role of a poison control center in toxicovigilance related to antidote treatment

Željka Babić

Institute for Medical Research and Occupational Health, Croatian Poison Control Center, Zagreb, Croatia

Objective: To test the potential for toxicovigilance of a newly implemented electronic system for poison centre data management, in the field of antidote use.
Methods: Data on the characteristics of cases involving pharmaceutical antidote treatment was extracted from the electronic system established in August 2021 for storing data from telephone consultations with the Croatian Poison Control Centre. All available records included (August-October 2021, 693 cases in total). In cases presenting with significant central nervous system (CNS) depression or respiratory depression caused by benzodiazepines or opioid overdose, flumazenil and naloxone, respectively, were considered indicated. N-acetylcysteine (NAC) was considered indicated in cases of paracetamol overdose with serum concentration above the possible toxicity line on the Rumack-Matthew Nomogram, or history of acute ingestion of more than 200 mg/kg or 10 g (whichever is less), and in repeated supratherapeutic overdose resulting in a cumulative dose >4 g paracetamol per 24 hours.
Results: In the study period, there were 59 cases of benzodiazepine ingestion (flumazenil was indicated in 11 of them, 19%), 12 cases of opioid misuse (naloxone was indicated in 7, 58%), and 16 cases of paracetamol ingestion (NAC, was indicated in 3 cases, 19%). Flumazenil and naloxone were readily available for treatment. At the time of the call, flumazenil was already administered in 8 of 11 indicated cases (73%), and naloxone in 5 of 7 indicated cases (71%). In four of 11 cases (36%) in which flumazenil was indicated, patients ingested additional psychoactive medications with potential for inducing seizures in overdose. Regarding naloxone, in one case of intravenous heroin overdose recurring toxicity was observed despite initial boluses of naloxone followed by continuous infusion. In another three cases involving long-acting opioids (buprenorphine and methadone), repeated or continuous dosing of naloxone in a case of symptom reoccurrence was recommended. Regarding NAC, in all three cases in which it was indicated based on reported paracetamol dose (which was planned to be confirmed by serum paracetamol determination in two cases), NAC treatment was not initiated by the time of the call. Poor availability of concentrated NAC solutions was sporadically mentioned.

Conclusion: The results support necessity of continued education of healthcare professionals involved in management of poisoning patients, promotion of poison control centre availability for consultations on antidote treatment, and establishment of a national contact point for antidote supply monitoring.

169. Alkylated creatine kinase: a dermal biomarker and enzymatic test principle for sulfur mustard

Dirk Steinritz[a], Harald John[b] and Horst Thiermann[b]

[a]Bundeswehr Medical Service Academy, Munich, Germany; [b]Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany

Objective: The chemical warfare agent sulfur mustard (SM) is banned under international law but has been used recently in Northern Iraq and Syria by the so-called Islamic State. When reaching the circulation, SM induces the alkylation of endogenous plasma proteins like albumin and hemoglobin which can be used as targets for the verification of systemic poisoning. The systemic biomarker generation depends on sufficient SM doses that must be absorbed by inhalation or by penetration of the skin. However, only a small fraction of dermally applied SM seems to penetrate the skin thus bearing the risk of insufficient formation of systemic biomarkers. We herein present creatine kinase (CK) B-type as a local biomarker for SM exposure on the skin. Moreover, we present a SM detector based on the inhibition of CK activity by SM.
Methods: Human and rat skin were proven to contain CK B-type by Western blot analysis. Following exposure to SM *ex vivo*, the CK-adduct was extracted from homogenates by immunomagnetic separation and proteolyzed afterwards. The cysteine residue Cys282 was found to be alkylated by the SM-specific hydroxyethylthioethyl (HETE)-moiety detected as the biomarker tetrapeptide TC(-HETE)PS. A selective and sensitive micro liquid chromatography-electrospray ionization high-resolution tandem-mass spectrometry (μLC-ESI MS/HRMS) method was developed to monitor local CK-adducts in an *in vivo* study with rats percutaneously exposed to SM. Moreover, *in vitro* CK activity in the presence of SM was assessed.
Results: CK B-type was found as highly abundant isoenzyme in rat and human skin. After *ex vivo* exposure to SM, the alkylated CK-derived biomarker tetrapeptide was detected and identified in both species. In an *in vivo* study, different SM doses resulted in the local formation of the HETE-CK adduct that served as a reliable qualitative local biomarker of the skin in all animals independent of the SM dose applied [1]. *In vitro* CK activity was significantly diminished after SM treatment [2]. Based on these results, we designed a CK-activity-based detector that can detect alkylating chemical warfare agents without cross-reaction to e.g. nerve agents.
Conclusion: CK or rather Cys282 in CK B-type was identified as a dermal target of local SM exposures. Inhibition of CK activity by SM was used to construct the SM-deteCKt assay.

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170. Sensitivity and specificity of the enzyme formate oxidase for diagnosing methanol poisoning

Yvonne Lao[a], Dag Jacobsen[b], Fridtjof Heyerdahl[c] and Knut Erik Hovda[d]

[a]Norwegian National Unit for CBRNE Medicine, Oslo University Hospital; Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [b]Institute of Clinical Medicine, University of Oslo; Norwegian Poison Information Centre, Norwegian Institute of Public Health, Oslo, Norway; [c]Air Ambulance Department, Oslo University Hospital; Institute of Clinical Medicine, University of Oslo; Norwegian Poison Information Centre, Norwegian Institute of Public Health, Oslo, Norway; [d]Norwegian National Unit for CBRNE Medicine, Oslo University Hospital; Norwegian Poison Information Centre, Norwegian Institute of Public Health, Oslo, Norway

Objective: The current gold standard for diagnosing methanol poisoning is detection of methanol by gas chromatographic methods or radioimmunoassay. These methods are often not available and they are time- and resource consuming. By detecting the toxic metabolite formate rather than the parent alcohol, simple enzymatic methods can be utilized, enabling a bedside approach. The first prototype using the enzyme formate oxidase has already been developed, and the first clinical testing in a methanol poisoned patient was recently published. The test was clearly positive bedside after four minutes, later confirmed by gas chromatography-mass spectrometry (GC-MS) [1]. A second, improved prototype of the bedside test is at present under development. The test principle is a colour change in the presence of formate. The aim of the present study was to evaluate the sensitivity and specificity for the enzyme formate oxidase used in the test, by visual and as well as a spectrophotometric read-out.
Methods: Spectrophotometric analyses were performed with a spectrophotometric setup, reading at 653 nm wavelength. Sensitivity was tested with the following formate concentrations: 1, 2, 4, 5, 6, 8, 10, 15 and 20 mmol/L. Specificity testing was performed against 18 different substances, including glycolic acid, lactic acid (D- and L-isomer) and beta-hydroxybutyric acid. Sensitivity was tested after five minutes for the various concentrations, while specificity was tested after 10 minutes to allow for any false positive results to appear.
Results: All concentrations of formate gave a visually identifiable colour change after five minutes, consistent with the spectrophotometric readings. Similarly, none of the 18 substances gave visual colour change or false positive readings on the spectrophotometer.
Conclusion: The sensitivity and specificity testing of the enzyme formate oxidase were good. All formate concentrations ($n = 9$) between 1 -20 mmol/L were detected both visually and by the spectrophotometer. No false positives were detected with any of the evaluation methods.

Reference

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171. Clinical evaluation of urine qualitative immunochromatographic techniques (ICT) for diagnosis and treatment of acute poisoned patients in the emergency department

Francisco Ruiz-Ruiz[a], Isabel Pérez-Panart[a], Elvira Tari-Ferrer[a], Ana Serrano-Ferrer[b] and Ana Ferrer-Dufol[c]

[a]Emergency Department, Clinic University Hospital, Zaragoza, Spain; [b]Psychiatric Service, Clinic University Hospital, Zaragoza, Spain; [c]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza, Spain

Objective: The use of immunochromatographic techniques (ICT) as point of care devices in the emergency department (ED) is generalized at our hospital for the diagnosis of the poisoned patient. The aim of this study is to verify the usefulness of these tools from the clinical point of view.
Methods: We reviewed the clinical files of 164 patients in which this procedure was used between October 2019 and November 2020. Reviewers were 4 members of the medical staff of our ED: 1 senior and 3 juniors, one of which is a psychiatrist.
Results: The mean age of patients was 37.3 ± 17.7 years; 64% were men. No age differences were observed based on sex. The most frequent reasons for requesting ICT were decreased level of consciousness (27% of cases), behavioral disturbances (18%), and self-harm attempts (16%). In 29% of the cases, there was a history of drug use and 35% had a psychiatric history. In 16% of the cases, a toxidrome was identified, the most frequent being the hypnotic-sedative. Neurological symptoms were observed in 44% of the patients, 9% had respiratory symptoms, 6% had cardiological symptoms, and 26% behavioral alterations. Blood tests were performed in 85% of the cases. From the clinical perspective, in 40% of the responses, the request for analysis was not adequate according to the reason for the consultation. In 30% of the responses, it was considered that had they been the patient's attendants, it would not have been requested. Considering the profile of the evaluator, significant differences were observed ($p < 0.001$), since the younger doctors were more critical of the usefulness of the ITC request in these cases. In 68% of cases, it was stated that it was not important to know the test result immediately. Regarding whether the test result was of interest in the final diagnosis of the case, 37% of the answers were affirmative, observing a statistically significant difference ($p < 0.001$): for the senior doctor, the percentage rose to 44% of the cases, whereas for the psychiatrist it was only 4%.
Conclusion: The results show a disparity of criteria in the evaluation of these tools among members of the same team. Nevertheless, the reviewers reach a certain degree of agreement on their scarce utility.

172. Analytical evaluation of the urine qualitative immunochromatographic techniques (ICT) for diagnostic and treatment of acute poisoned patients at the emergency department

Belen Founaud-Placer[a], Sebastian Menao-Guillén[b] and Ana Ferrer-Dufol[a]

[a]Unit of Clinical Toxicology, Clinic University Hospital, Zaragoza, Spain; [b]Biochemistry Service, Clinic University Hospital, Zaragoza, Spain

Objective: The use of immunochromatographic techniques (ICT) as point of care devices in the emergency department (ED) is generalized at our hospital for the diagnosis of the poisoned patient. The aim of this study is to verify the analytical reliability of these tools.
Methods: We reviewed the analytical results of 200 patients in whom this procedure was used between October 2019 and November 2020. The analytical results were checked with immunoenzymatic and gas chromatography-mass spectrometry (GC-MS) techniques performed at the Unit of Clinical Toxicology. The ICT panel includes opiates, cocaine, amphetamine, cannabis, phencyclidine (PCP), benzodiazepines, barbiturates, and tricyclic antidepressants.
Results: The lowest sensitivities were found for opiates (60.0%), cannabis (80.3%), benzodiazepines (81.4%), and amphetamines (83.3%). The lowest specificities were found by benzodiazepines (93.9%), tricyclic antidepressants (96.4%), and amphetamines (97.9%). The substances with the lowest Positive Predictive Value were methamphetamine (33.3%), tricyclic antidepressants (46.2%), morphine (71.4%), and amphetamines (79.0%). The substances with the lowest Negative Predictive Value were benzodiazepines (87.1%) and cannabis (94.4%). PCP and barbiturates did not test positive in any case. False positives were 11.4% of total positives and false negatives 1.4% of the total negatives.
Conclusion: The concordance of results reached 76.7%. Screening techniques seek to achieve high analytical sensitivity, which was obtained for all substances, except cannabis and benzodiazepines. This attempt to reduce false negatives often causes increased false positives and decreased specificity, as occurs most notably with benzodiazepines, tricyclic antidepressants, and amphetamines. In the case of benzodiazepines and amphetamines, there was poor sensitivity and poor specificity. The analytes for which the results matched best, both positive and negative, were 3,4-methylenedioxymethamphetamine (MDMA), methadone, and cocaine. The analytes whose results match worst were benzodiazepines, cannabis, tricyclic antidepressants, and amphetamines. To facilitate the interpretation for the clinician, it would be advisable for emergency laboratories to include information about the cut-off for each substance, as well as a list of interfering substances whenever a positive result is reported. All positive results should be confirmed by means of a reference technique.

173. Cardiac dysrhythmias provoked by intrathecal fluorescein and treated with intravenous lipid emulsion infusion

Jonas Moens[a], Stephanie Poels[b], Heleen Van Melckebeke[a], Karolien De Leener[a], Jonas Van Baelen[a], Dominique Vandijck[a] and Anne-Marie Descamps[a]

[a]Antigifcentrum, Neder-Over-Heembeek, Belgium; [b]Academic Hospital AZ Turnhout, Turnhout, Belgium

Objective: Intrathecal injection of fluorescein can be used to localise the exact site of cerebrospinal fluid leaks. Nevertheless, complications due to neurological and/or cardiovascular toxicity are described. We present a case of a patient with cardiac dysrhythmias responding to intravenous lipid emulsion infusion after

an adverse drug event with an intrathecal injection of fluorescein.
Case report: A localisation procedure with slow intrathecal injection of fluorescein was started in a woman with a cerebrospinal fluid leak. Due to a sudden panic reflex of the patient during the procedure, a dose of 50 mg fluorescein was instantaneously injected followed by an extravasation. Immediately afterwards, she presented two episodes of convulsions which were successfully treated with lorazepam. Then, she became more and more hypotensive and experienced sudden cardiac dysrhythmias together with worsening of airway function not responding to standard treatment. As fluorescein has lipophilic characteristics, treatment with intravenous lipid emulsion infusion was started. Within ten minutes after the infusion, the dysrhythmias faded out and the blood pressure stabilized. Once the patient was sufficiently stable, a cerebrospinal fluid drain was placed by a surgical procedure to flush out as much remaining fluorescein as possible. After two days of intensive care admission, the patient recovered without sequelae.
Conclusion: The aetiology of the neurological and cardiovascular toxicity of fluorescein remains unclear. To the best of our knowledge, we are unaware of any other reports supporting the use of intravenous lipid emulsion infusion for fluorescein toxicity. In the present case, the cardiac dysrhythmias provoked by fluorescein, were refractory to standard treatment but rapidly responded to intravenous lipid emulsion infusion. Our findings suggest that intravenous lipid emulsion infusion should be rapidly available as a safety measure for accidental overdose of intrathecal injection of fluorescein.

174. Bupropion and metabolite drug concentrations informing management in a patient with undifferentiated status epilepticus

Joshua Bloom and Samara Soghoian
New York City Poison Control Center, New York, United States

Objective: Drug concentrations of epileptogenic substances are often not immediately available in the acute setting, and many question whether confirming ingestion with drug concentrations is useful in clinical care. We report a case of an undifferentiated patient with status epilepticus and hemodynamic instability where drug concentrations established bupropion ingestion during the course of clinical care.
Case report: A 41-year-old female with a history of HIV, vasculitis, psychiatric disease, resolved hepatitis C, and pulmonary embolism was found unconscious at a private residence. Naloxone was administered by emergency medical personnel without effect. She was not found with drug paraphernalia or empty pill bottles; however, collateral information obtained by providers suggested that she had been feeling depressed in recent weeks. En route to the hospital she had a generalized tonic-clonic seizure and was endotracheally intubated. In the hospital she had persistent clonic movements with epileptic activity on her electroencephalogram; levetiracetam and lacosamide were added and she was placed on an infusion of midazolam, which resolved her seizures. She was weaned from oxygen and able to be extubated and transitioned to general medicine after about two weeks. A bupropion concentration had been sent early in her care, and resulted with toxic concentrations at >1000n g/mL bupropion and >3000 ng/mL hydroxybupropion. After this test result she admitted that she had taken bupropion in overdose. Her antiepileptics were discontinued, and she was treated for sequelae of critical illness over subsequent weeks. She was discharged to a rehabilitation facility almost six weeks after she presented.
Conclusion: Patients with intentional overdoses can lack motivation or ability to offer information on their ingestions, and providers are often left with diagnostic dilemmas. Although drug concentrations in our case were delayed, they did provide a diagnosis that allowed providers to discontinue antiepileptic therapies, sparing the patient from unnecessary therapies. Bupropion is a commonly prescribed antidepressant with potentially grave clinical effects in overdose, and its parent compound and active metabolites can be measured in the acute setting [1]. We would argue that drug concentrations can guide subacute and post-acute management in the undifferentiated critically ill patient, especially when patients are unable or unwilling to offer history to assist in their care.

Reference

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175. A retrospective study of medical toxicologist consultations provided by the New Zealand National Poisons Centre

Eeva-Katri Kumpula[a] and Adam C. Pomerleau[b]
[a]National Poisons Centre, Dunedin, New Zealand; [b]National Poisons Centre, University of Otago, Dunedin, New Zealand

Objective: The New Zealand National Poisons Centre (NZNPC) provides a free 24/7 telehealth service advising on poisonings for use by the public and healthcare professionals. The centre has been developing its medical toxicologist services further since 2017, with focused efforts on enhancing integrations with the broader clinical community in NZ through various outreach activities intended to increase awareness of medical toxicology services. This study aimed to characterise recent trends in medical toxicologist consultations and further describe selected characteristics of substances involved and reasons behind exposures.
Methods: NZNPC medical toxicologist consultations in 2018-2020 were analysed. Time trends in the numbers of consults, health professional types assisted, reason for exposure incident, and substances advised about were summarised. Therapeutic substance data were converted into Anatomical Therapeutic Chemical (ATC) codes using the online ATC Index 2021 search engine [1], while non-therapeutics were characterised by an in-house system of classification.
Results: Medical toxicologist consultation numbers increased by 26-70% annually. A total of 2,400 consultations were provided to healthcare professionals during the study period. A total of 40% of these 2,400 consultations were relating to intentional exposures, with 27% unintentional and 11% child exploratory exposures, 11% therapeutic errors, 4% substance abuse, and 8% exposures due to other and unknown reasons. A total of 1,517 of 2,400 consultations (63%) involved at least one therapeutic agent, and 883 had only non-therapeutics. There were 2,603 therapeutic substance exposures, and N02 (analgesics; 662), N05 (psycholeptics; 361), N06 (psychoanaleptics; 309), N03 (antiepileptics; 122) were the most common ATC groups involved. Of the 1,244 non-therapeutic substance exposures, industrial (299) and miscellaneous chemicals (177), and household spirits (119) were most common.

Conclusion: NZNPC medical toxicologist consultations increased during the study period, and commonly involved consultations about intentional exposures, and about ATC class N drugs (affecting the nervous system). The significant increases in consultations suggest a need for this specialist service among the medical community in New Zealand, and future research is needed to investigate equitable utilisation of this free consultation service.

Reference

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176. Benzodiazepine use during pregnancy: the Bergamo Teratology Information Service cohort study

Sara Zanisi, Anna Sangiovanni, Mariapina Gallo, Andrea Giampreti, Georgios Eleftheriou, Lorella Faraoni, Maria Gioia Contessa, Maria Giovanna Falchi, Raffaella Butera and Giuseppe Bacis

Poison Control Center and Teratology Information Service, ASST Papa Giovanni XXIII Hospital, Bergamo, Italy

Objective: In pregnancy, 10-15% of women experience emotional changes that increase the risk of anxiety and depression, which can lead to insomnia. During pregnancy, anxiety and depression can increase the risk of miscarriage, premature birth, low birth weight and fetal death. Benzodiazepine medications are commonly used to treat anxiety and insomnia. Many studies have shown conflicting results for the association between benzodiazepines use during pregnancy and birth defects, spontaneous abortion, preterm delivery and low birth weight. Exposure to these drugs in the last months of pregnancy can lead to neonatal withdrawal syndrome. In the present study, we determine whether benzodiazepine therapy in pregnancy is associated with adverse neonatal outcomes.
Methods: Pregnant women who contacted the Bergamo Teratology Information Service (TIS) between 1 January 2018 and 31 December 2020 were included in the study. We compared the data of a group of 99 pregnant women exposed to benzodiazepines alone, with data of a control group of 158 pregnant women exposed to acetaminophen/amoxicillin.
Results: Two cases of malformations were reported in children born to mothers exposed to benzodiazepines during pregnancy, while three cases of malformations were recorded in the control group (OR 1.04; 95%CI 0.17-6.33). Two patients exposed to benzodiazepines had therapeutic interruption of pregnancy due to chromosomal abnormalities. The difference between the two cohorts in terms of premature birth and low birth weight was not statistically significant (OR 2.24; 95%CI 0.85-5.90 and OR 3.11; 95%CI 0.88-10.93, respectively), but spontaneous abortion (OR 5.78; 95%CI 1.17-28.42) and neonatal withdrawal syndrome (OR 12.69; 95%CI 1.53-104.95) were increased with maternal benzodiazepine use.
Conclusion: According to our results, prenatal benzodiazepine use was not associated with an increased risk of congenital malformations, but it is associated with an increased risk of spontaneous abortion and neonatal withdrawal syndrome; however, it should be considered that anxiety and depression could also be associated with an increased risk of spontaneous abortion. The number of patients evaluated in this study is small, and large scale multicenter studies are needed to elucidate the safety profile of benzodiazepine use in pregnancy, since it is essential that pregnant women suffering from anxiety, depression and insomnia are adequately treated.

177. Misunderstanding a medical prescription resulting in severe haematological toxicity: a case report

Anna Celentano[a], Guido Gubertini[b], Marcello Ferruzzi[a], Fabrizio Sesana[a], Paolo Andrea Schenardi[c], Tommaso Conti[c], Matteo Maggi[c] and Francesco Scaglione[a]

[a]Milan Poison Control Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [b]First Division of Infectious Diseases, ASST FBF Sacco, Milan, Italy; [c]Postgraduate School of Clinical Pharmacology and Toxicology, University of Milan, Italy

Objective: Azathioprine is an imidazolyl derivative of 6-mercaptopurine and acts as an immunosuppressive antimetabolite. The most common and potentially severe adverse effects are hematologic (leukopenia, anemia, thrombocytopenia) and gastrointestinal effects (nausea, vomiting, diarrhea, abdominal pain). Filgrastim is a human granulocyte colony-stimulating factor (G-CSF) which acts on hematopoietic cells by binding to specific cell surface receptors and regulating neutrophil production, progenitor proliferation, and differentiation. It also affects some end-cell functional activation including phagocytic activity, cellular metabolism and antibody-dependent killing. We present a severe case of therapeutic error with azathioprine due to a misunderstanding of the medical prescription.
Case report: A 59-year-old male, weighing 68 Kg, was prescribed azathioprine 50 mg one tablet three times daily as a therapy for myasthenia gravis. Due to a misunderstanding of the medical prescription, the patient took three tablets three times daily for 15 days. He arrived at the emergency department 15 days after beginning therapy, due to the appearance of herpetic stomatitis. Blood tests showed anemia, leukopenia and thrombocytopenia. He was admitted to the infectious disease department and the next day filgrastim, antibiotic and antiviral therapy was started. Transfusion of one unit of red blood cells was performed. On the fourth day of therapy with filgrastim he presented hemoglobin 8.4 g/dL, platelets 22000/μL, white blood cells (WBC) 450/mm^3, and neutrophils 20/mm^3. The poison control center was contacted and confirmed appropriate therapy had been started. On day six, he presented hemoglobin 7.7 g/dL, platelets 17000/μL, WBC 220/mm^3, and neutrophils 0/mm^3. One unit of platelets and one unit of red blood cells were transfused. He developed respiratory distress and required continuous positive airway pressure (CPAP) oxygen therapy. A chest X-ray showed diffuse pleural thickening and antibiotic therapy was modified. On the eighth day hematology showed hemoglobin 10.5 g/dL, platelets 60000/μL, WBC 530/mm^3, and neutrophils 300/mm^3. On the tenth day, repeat hematology showed hemoglobin 10.3 g/dL, platelets 60000/μL, WBC 9900/mm^3, ad neutrophils 860/mm^3. The patient was discharged after 19 days of hospitalization, with resolving clinical symptoms and haematology parameters (hemoglobin 10 g/dL, platelets 291000/μL, WBC 7600/mm^3, and neutrophils 5300/mm^3).
Conclusion: Monitoring therapeutic errors is important in order to avoid preventable mistakes. This is a serious case due to a misunderstanding of the medical prescription by the patient. It is essential healthcare professionals ensure that patients understand the therapy and dosing regimen to be taken. In this case

treatment with filgrastim restabilized the clinical picture and prevented the development of aplastic anemia.

178. Adult beta-adrenergic antagonist ingestions reported to the US National Poison Data System, 2000-2020

Christopher J. Watson, Michael C. Monuteaux and Michele M. Burns

Boston Children's Hospital, Boston, United States

Objective: Beta-adrenergic antagonists (BAA) are commonplace. We seek to describe clinical characteristics, and rate of serious outcomes amongst adult patients with reported BAA ingestions.
Methods: Retrospective review of United States (US) patients ≥20-years-old with acute single-agent BAA ingestion presenting to a healthcare facility between 2000-2020 for whom a Poison Control Center (PCC) was consulted. Data were abstracted from the US National Poison Data System (NPDS). BAAs were divided into categories: β_1-selective, $\beta_1\beta_2$-non-selective, $\beta_1\beta_2\alpha_1$-non-selective, propranolol, and sotalol. Outcomes were assessed using the following NPDS designations: *no effect*, *minor effect*, *moderate effect*, *major effect*, and *death*.
Results: In total 34,075 cases were identified; 277 patients (0.8%) had hypoglycemia, 6,307 (18.5%) hypotension, and 7,970 (23.4%) bradycardia. Concerning interventions, 11,638 (34.2%) received intravenous fluids, 7,623 (22.4%) received charcoal, 3,970 (11.7%) received glucagon, 1,826 (5.4%) received vasopressors, 961 (2.8%) were intubated, 834 (2.4%) received gastric lavage, 830 (2.4%) received calcium, 781 (2.3%) received dextrose >5%, 740 (2.2%) received high dose insulin, and 1.8% received benzodiazepines. All other interventions were given in <1% of cases. Sixteen patients received lipid emulsion therapy, four patients received extracorporeal membrane oxygenation and 113 patients underwent cardiopulmonary resuscitation (CPR). Amongst intentional ingestions (n = 17,557), 832 (4.7%) had major effects and 89 (0.5%) died. Amongst unintentional ingestions (n = 14,147), 198 (1.4%) had major effects and 19 (0.1%) died. Cases with $\beta_1\beta_2\alpha_1$-non-selective BAAs ingestions had hypotension more frequently (1,486 cases, 28.2%) and bradycardia less frequently (979 cases, 18.6%) than did other BAAs. Of the 5,757 propranolol cases, 23 (0.4%) had QRS prolongation, 8 (0.1%) had ventricular tachycardia/fibrillation, and 69 (1.2%) had seizures. Of the 1,128 sotalol cases, 20 (1.8%) had QTc prolongation, 4 (0.4%) had torsade de pointes, and 31 (2.7%) had ventricular tachycardia/fibrillation.
Conclusion: Reported BAA ingestions in this large US multi-year adult population caused moderate toxicity that was more severe amongst those with intentional ingestions. Overall, mortality was low. Several findings were incongruous with conventional teaching: hypoglycemia was rare overall; and QRS widening, ventricular dysrhythmias, and seizures were infrequent with propranolol ingestions. Ventricular tachycardia/fibrillation was documented much more frequently in sotalol ingestions than was torsade de pointes; this may be due to clinical difficulty in distinguishing between the two dysrhythmias. Interestingly, $\beta_1\beta_2\alpha_1$-non-selective BAAs caused more frequent hypotension and less frequent bradycardia than did other BAAs; this may be due to anti-α_1-associated vasodilation. Overall, future investigation is warranted into the risk of clinically significant illness following reported adult BAA ingestions.

179. Disorders of redox homeostasis and apoptosis in acute poisonings with cardiovascular drugs

Kapitalina K. Ilyashenko, Galina N. Sukhodolova, Maria V. Belova, Elena V. Klychnikova, Natalia V. Borovkova, Anastasia Yu Simonova and Michail M. Potskhveriya

N.V. Sklifosovsky Research Institute of Emergency Medicine of the Moscow Department of Health, Moscow, Russian Federation

Objective: To evaluate indicator violations of the redox homeostasis system and venous blood lymphocyte apoptosis in the early period of acute poisonings with cardiovascular drugs.
Methods: Twenty-five patients (20 women and 5 men, aged 18 to 59 years) with hypotensive and antiarrhythmic drug acute poisoning of moderate severity were examined. Blood samples were taken from patients at hospital admission, and on the 1st and 3rd treatment days. Malondialdehyde (MDA) concentration and total antioxidant activity (TAA) were determined in the patients' blood serum. The coefficient of oxidative stress ($K_{MDA/TAA}$) was calculated as a ratio of normalized values. The total number of blood leukocytes, the absolute and relative number of dead leukocytes, the number of blood lymphocytes ready for apoptosis (CD95), as well as at early (EA, AnnexinV+/7AAD-) and late (LA AnnexinV+/7AAD+) stages were studied. Statistical analysis was performed using the Statistica 10 software (StatSoft, Inc., USA). The threshold level of significant differences was assumed as 0.05.
Results: Oxidative stress was detected at all stages of the study. $K_{MDA/TAA}$ statistically significantly exceeded the norm by 2.0-2.2 times. This was achieved due to an increase in MDA blood content by 1.5 times compared to the norm and a significant decrease by 1.2-1.4 times in TAA. Initially, the total number of leukocytes, as well as the absolute and relative number of dead leukocytes were within the normal range. The proportion of lymphocytes at the EA and LA stages was statistically significantly higher than normal by 1.8 and 2.8 times, respectively. A day later, moderate leukocytosis was detected, accompanied by an increase in the absolute and relative number of dead leukocytes by 1.7 and 1.2 times, respectively. The readiness of lymphocytes for apoptosis was within the normal range, and their proportion at the EA stage continued to increase, being 2.5 times higher than normal. Meanwhile, there was a decrease in the proportion of lymphocytes at the EA stage by 4.7 times compared to the previous value. By the 3rd day of treatment, the total number of leukocytes reached normal values, the absolute content of dead leukocytes decreased, while a moderate increase in their relative number continued. There was a tendency to a decrease in lymphocyte proportion at the EA and its normalization at the LA stage.
Conclusion: We demonstrated that oxidative stress in the early period of acute cardiovascular drug poisoning of moderate severity stimulates apoptosis. This has sanogenetic nature, confirmed by the positive dynamics of lymphocyte apoptosis indicators.

180. Acute toxicity profile of oxybutynin in overdose or accidental exposure: a consecutive case series

Nadine C. Martin, Katharina E. Hofer and Cornelia Reichert

National Poison Centre, Tox Info Suisse, Zurich, Switzerland

Objective: Oxybutynin is an antispasmodic agent, which acts as a competitive antagonist of acetylcholine by inhibiting postganglionic muscarinic receptors. It is approved for hyperactive bladder in adults and enuresis in children >5 years. The oral dose of an immediate/extended release formulation is up to 20/30 mg in adults and up to 15/20 mg in children >5 years. Adverse effects of oxybutynin are frequent and primarily anticholinergic. Information on the clinical features of oxybutynin poisoning is sparse, with only two case reports in the literature [1,2]. The aim of this study was to investigate the clinical features of acute oxybutynin overdose.
Methods: A retrospective review of single-substance acute oral overdose with oxybutynin in adults and children (<16 years), reported to our poison center from 1997 to 2020.
Results: Mono-intoxication occurred in 15 patients; 1 adult (26 years, female) and 14 children (median age 3.5, range 0.3-13 years, 8 females and 6 males). The exposure was accidental in ten children and intentional in four children and the one adult. Absolute dose in mg was known in twelve, dose in mg/kg in nine cases (range 0.2-2.1 mg/kg). Four patients were asymptomatic; eight had mild and three moderate symptoms. All symptomatic patients showed anticholinergic effects with mydriasis (n = 8) and xerostomia (n = 6) as the most frequent symptoms. Moderate symptoms were agitation, urinary retention and tachycardia (Table 1).
Conclusion: Oxybutynin displays an acute toxicity profile comparable to its adverse event profile of an anticholingeric drug. Severe symptoms were not observed in this small case series and also children younger than 5 years of age, for which this drug is not approved. Acute overdose had a favorable outcome in this case series.

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

Amani S. Alrossies[a], Kenzo Motohashi[a], Stephen Wiltshire[b], Simon L. Hill[b], Simon H.L. Thomas[a] and Ruben H.K. Thanacoody[b]

[a]Newcastle University, Newcastle-upon-Tyne, United Kingdom; [b]Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle-upon-Tyne, United Kingdom

Objective: To determine the efficacy of a modified 2-bag 12h acetylcysteine (NAC) regimen ('SNAP') in patients taking large single acute paracetamol overdoses.
Methods: A modified 12h 'SNAP' regimen, consisting of intravenous NAC 100 mg/kg over 2h then 200 mg/kg over 10h, was introduced in October 2016 in our hospital to treat all patients requiring NAC for paracetamol overdose. Patients with an end-of-12h infusion paracetamol concentration >10 mg/L or alanine aminotransferase (ALT) > 40 IU/L receive extended treatment with the 200 mg/kg NAC infusion over 10h. Data was collected prospectively for 5 years (October 2016-October 2021) and compared to published historical data of patients treated with the conventional 21h NAC regimen. Large acute single paracetamol overdose was defined as an extrapolated 4h paracetamol concentration over 300 mg/L.
Results: There were 97 patients above the 300-nomogram line treated with NAC within 24h of ingestion over the 5-year period; 60/97(62%) patients (mean weight 71 Kg) reported a mean ingested paracetamol dose of 27 g, were treated with the 12h 2-bag SNAP regimen only and did not develop acute liver injury at least 24h post-ingestion. 30/97(38%) patients (mean weight 73 Kg) reported a mean ingested paracetamol dose of 39 g and required extended NAC treatment. 22/97 (22.6%) developed acute liver injury (peak ALT >120 IU/L). Hepatotoxicity (peak ALT >1000 IU/L) developed in 16/97 (16.5%) patients, including 4/34

Table 1. Symptoms and severity in 15 patients with oxybutynin overdose.

Case	Sex	Age (years)	Weight (kg)	Dose (mg)	Dose (mg/kg)	Signs and symptoms	Severity	Decontamination and treatment
1	M	0.3	5	1	0.20	None	0	No
21	M	2.9	Not known	10	–	None	0	No
3	M	3.0	15	10	0.67	None	0	Not known
4	M	4.5	20	15	0.75	None	0	No
5	F	0.6	8	3.75	0.47	Somnolence	1	No
6[2]	F	3.0	14	Maximum 70	–	Mydriasis, xerostomia	1	Emesis induced by caregiver
7[2]	F	4.0	14	Maximum 70	–	Mydriasis, xerostomia	1	Emesis induced by caregiver
8	F	9.5	Not known	45	–	Mydriasis, xerostomia, accommodation disorder	1	No
9	M	11.0	56	25	0.45	Mydriasis	1	No
10	M	11.0	Not known	15	–	Mydriasis, somnolence	1	Activated charcoal
11	F	13.6	65	35	0.54	Somnolence	1	No
12	F	26	Not known	Not known	–	Mydriasis, xerostomia	1	No
13	F	2.2	16	5	0.31	Urinary retention	2	No
14	F	2.5	13	27.5	2.12	Mydriasis, xerostomia, tachycardia (148/min), agitation	2	Activated charcoal
15	F	13.3	70	75	1.07	Mydriasis, xerostomia, tachycardia (150/min), hypertension (150/65 mmHg), slightly impaired vision	2	Activated charcoal, physostigmine, esmolol

0 = no effects, 1 = mild effects, 2= moderate effects
[1] Case with extended release formulation, [2] Two children who shared 70 mg

treated within 8h post-ingestion, 4/39 treated within 8-16h and 8/24 treated within 16-24h. 15/16 patients who developed hepatotoxicity had evidence of acute liver injury (ALT >120 IU/L) and the other patient had a paracetamol concentration of 35 mg/L at the end of the 12h infusion. There were no deaths or liver transplants. Compared to a historical UK cohort of 112 patients with acute single paracetamol overdose above the 300-nomogram line treated with the conventional 21h NAC regimen, development of acute liver injury (22.6% versus 33%, difference -10.4%, 95% CI -22%-1.9%, p = 0.09) or hepatotoxicity (16.5% versus 15.2%, difference 1.3%, 95% CI -8.6%-11.5%, p = 0.79) was not statistically different with the SNAP regimen [1].
Conclusion: A simpler 12h acetylcysteine regimen appears to be effective in preventing hepatotoxicity in most patients taking large paracetamol overdoses and allows higher NAC doses (500 mg/kg) to be given within 22h to those at highest risk of developing hepatotoxicity. Larger multi-centre prospective studies are required to risk-stratify patients taking large paracetamol overdoses and optimise their treatment.

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182. Continuous veno-venous haemodialysis (CVVHD) results in low extraction ratio and drug removal after massive sodium valproate overdose

Jason Kwok, Benjamin Cheung and Andis Graudins
Monash Health and Monash University, Melbourne, Australia

Objective: Sodium valproate (VPA) has a small molecular weight and volume of distribution, with concentration-dependent protein binding. At supratherapeutic drug concentrations, free-drug fraction increases and contributes to its central nervous system toxicity. Intermittent haemodialysis (IHD) is recommended for rapid drug removal after overdose. Data on the effectiveness of CVVHD to enhance drug-elimination is limited. We report a case of VPA overdose, treated with CVVHD, with serial blood extraction ratios and dialysate drug recovery.
Case report: A 26-year-old, 70 Kg male was found at home drowsy, 2 hours after suspected ingestion of 200 x 500 mg (100 g, 1.4 g/Kg) enteric-coated VPA tablets. His Glasgow Coma Score (GCS) dropped to 3/15 during transit to hospital. He was emergently intubated in the emergency department and naso-gastric activated charcoal was administered. Three hours post-ingestion, serum [VPA] was 12,402 μmol/L (reference 350-700), ammonia 242 μmol/L (reference 16-50), and ethanol 27 mmol/L. Cerebral-computerised tomography (CT) scan was normal. IHD was recommended to increase VPA and ammonia elimination. Unfortunately, only CVVHD was available at the time. Serum [VPA] peaked 8-hours post-ingestion at 15,144 μmol/L. CVVHD was commenced 11 hours post-ingestion when serum [VPA] was 13,975 μmol/L and serum sodium was 161 mmol/L. Multiple-dose activated charcoal (MDAC) was added to assist VPA elimination and intravenous carnitine was commenced for elevated ammonia. Afferent and efferent serum [VPA] was assayed across the dialysis filter. CVVHD blood flow was 200 mL/min and dialysate flow 1.6 L/h. VPA recovery was measured in recovered dialysate fluid. Serum [VPA] fell to 932 μmol/L over 24 hours of CVVHD. Dialysis filter extraction-ratio averaged 23% when serum [VPA] was more than 8,000 μmol/L, however, this fell to less than 13% when serum [VPA] was below 3,500 μmol/L. Cumulative recovery of VPA in 30 litres of dialysate was 10.8 g. VPA elimination half-life was 26 and 5.4 hours, respectively, pre- and during CVVHD. Serum ammonia peaked at 616 μmol/L, 14 hours post-ingestion. The patient was extubated on day 3 post-ingestion, neurologically intact.
Conclusion: IHD remains the treatment-of-choice to rapidly remove toxins. Sustained low-efficiency haemodialysis is also reported to be superior to CVVHD. Neither modality may be accessible in many hospital ICUs, and CVVHD is used as a replacement or bridging therapy. In this case, CVVHD achieved low extraction ratios and poor total recovery of VPA in dialysate fluid, despite potentially lethal serum VPA concentration, suggesting CVVHD played a moderate role in drug elimination in this patient. It is unclear how much MDAC contributed to VPA elimination in this case.

183. Lamotrigine intoxications reported to the Dutch Poisons Information Center: a prospective study

Saskia J. Rietjens[a], Maaike A. Sikma[b], Dylan W. de Lange[b] and Laura Hondebrink[a]
[a]Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht, Netherlands; [b]Dutch Poisons Information Center, University Medical Center Utrecht; Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, Netherlands

Objective: Lamotrigine is an anticonvulsant drug which is also used in the treatment of bipolar disorders. We investigated the symptoms following lamotrigine overdose and determined the dose-toxicity relationship to improve triage of patients exposed to lamotrigine.
Methods: We performed a prospective follow-up study on isolated lamotrigine overdoses reported to the Dutch Poisons Information Center from April 2014 to October 2016. Patients and physicians were interviewed by telephone to collect information on the exposure, clinical course and treatment. The severity of the intoxication was scored using the Poisoning Severity Score. To study the dose-toxicity relationship, a subset of patients was investigated. We excluded patients with emesis (<1 hour post ingestion) or in whom gastrointestinal decontamination was applied, and patients with multiple lamotrigine ingestions (>2 hours between separate exposures). A literature search on the dose-toxicity relationship of lamotrigine was performed.
Results: We included 29 isolated lamotrigine overdoses (range: 1-85 years). The median self-reported dose was 5.7 mg/kg (range: 0.6-45.0 mg/kg). Most reported symptoms were: sleepiness (72%), dizziness (52%), agitation (41%), headache (34%), nausea (34%), blurred vision (28%), confusion (24%), apathy (24%), tremor (21%) and tachypnea (21%); 10% of the patients remained asymptomatic, 55% developed mild symptoms and 31% moderate symptoms. Severe symptoms occurred in one patient. A 50-year-old woman developed coma (Glasgow Coma Score (GCS) 3-4) after ingestion of 33.1 mg/kg lamotrigine (multiple ingestions; cumulative dose: 2150 mg). Four patients (14%) were examined by a general practitioner, five patients (17%) presented to an emergency department of whom four (14%) were admitted. In the subset of patients suitable to investigate the dose-toxicity relationship (n = 23), the lowest self-reported dose causing moderate intoxication was 1.4 mg/kg, involving a 19-year-old woman who developed agitation, dysarthria, dizziness, tremor, tachypnea and blurred vision. However, in general, moderate effects were

reported from approximately 6 mg/kg in our case series. In literature, moderate to severe symptoms have been reported from 6.5 mg/kg [1].
Conclusion: In our case series (n = 29), 34% of patients developed a moderate to severe intoxication following lamotrigine overdose. In general, moderate poisonings have been observed from 6 mg/kg and at higher doses severe poisonings do occur. Hospital referral of patients with a lamotrigine overdose >6 mg/kg appears indicated, combined with instructions at lower doses about when to call medical assistance to overcome exceptional cases with low-dose toxicity.

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184. Salicylate intoxication can present with a normal anion gap metabolic acidosis depending on the method used for measuring chloride

Laura J. Buisman[a], Ineke J. Riphagen[b], Marieke Kwant[c], Margo D. Themmen[d], Marjan Bouma[e] and Carina Bethlehem[f]

[a]Department of Intensive Care Medicine, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [b]Department of Clinical Chemistry, Certe, Leeuwarden, Netherlands; [c]Department of Emergency Medicine, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [d]Department of Internal Medicine, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [e]Department of Clinical Pharmacy and Pharmacology, Medical Centre Leeuwarden, Leeuwarden, Netherlands; [f]Department of Intensive Care Medicine and Department of Clinical Pharmacy and Pharmacology, Medical Centre Leeuwarden, Leeuwarden, Netherlands

Objective: We present a patient with a remarkable normal anion gap in salicylate intoxication. No rebound effect was seen after treatment.
Case report: A 70-year-old male with a history of bipolar disorder and multiple suicide attempts presented to the emergency department with decreased consciousness, tachypnea and acute renal failure. He had ingested approximately 30 g of acetylsalicylic acid and 35 g of acetaminophen. Time of ingestion was unclear with a maximum of 12 hours before admission. At presentation, salicylate concentration was 594 mg/L (therapeutic range 50-300 mg/L). There was a combined respiratory alkalosis and a normal anion gap metabolic acidosis. He was admitted to the intensive care unit (ICU) because of neurological symptoms and renal failure, and hemodialysis was performed during 4 hours. Intravenous N-acetylcysteine was administered for acetaminophen intoxication. Electrolytes and pH were closely monitored and pH was kept above 7.40. During treatment, breathing pattern and consciousness normalized. The salicylate concentration was 201 mg/L directly after hemodialysis and 138 mg/L 10 hours later. In contrast to previous literature no rebound effect was observed after dialysis [1]. Severe salicylate intoxication usually leads to combined respiratory alkalosis and a high anion gap metabolic acidosis. In this case, anion gap was normal due to a hyperchloremia (122 mmol/L; reference 97-107) measured using a direct ion-selective electrode (ISE) (ABL90-flex). Since earlier case reports have shown that salicylate ions can interfere with chloride measurement using ISE [2], available samples were re-analyzed using an indirect ISE (Roche Cobas 8000), in which salicylate concentrations up to 1000 mg/L were found to cause no significant interference. Actual chloride concentration was found to be 115 mmol/L, corresponding with an elevated anion gap of 17.
Conclusion: In this case, salicylate intoxication was not accompanied by a high anion gap due to overestimation of chloride concentration using a direct ISE. This is an important observation, since a high anion gap metabolic acidosis can be a clue to suspect salicylate poisoning. The patient was successfully treated and no rebound effect was observed after hemodialysis.

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185. Ramipril – how toxic is it?

Dagmar Prasa[a], Jutta Trompelt[b], Sonja Groß[b], Andreas Vagt[c], Eva-Carina Heier[d], Wolfgang Klumb[e], Uwe Stedtler[f], Elke Färber[g], Cornelia Reichert[h], Claudia Zatloukal[i], Dieter Genser[i] and Mandy Gollmann[a]

[a]Poisons Information Centre Erfurt, Erfurt, Germany; [b]Poisons Information Centre Mainz, Mainz, Germany; [c]Poisons Information Centre Berlin, Berlin, Germany; [d]Department of Clinical Toxicology and Poison Control Centre Munich, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Munich, Germany; [e]Poisons Information Centre Bonn, Bonn, Germany; [f]Poisons Information Centre Freiburg, Freiburg, Germany; [g]Poisons Information Centre Göttingen, Göttingen, Germany; [h]National Poisons Centre, Tox Info Suisse, Associated Institute of the University of Zurich, Zurich, Switzerland; [i]Poisons Information Centre Vienna, Vienna, Austria

Objective: Ramipril is an angiotensin-converting enzyme inhibitor, widely used in the management of hypertension and heart failure. Hence, overdose of ramipril is a frequent cause of enquiries to Poisons Information Centres. Its toxicity seems to be relatively low, but available information is limited. The aim of the study was to assess the acute toxicity of ramipril.
Methods: Retrospective analysis of acute overdoses of ramipril reported to nine Poisons Information Centres in Germany, Austria, and Switzerland. Inclusion criteria were single substance ingestion, defined dose, and documented follow-up for at least 8 hours. Severity of symptoms was assessed according to the Poisoning Severity Score.
Results: A total of 141 cases met the inclusion criteria. Patients involved were 71 children (<14 years), 5 adolescents (14-≤18 years), and 65 adults (>18 years). Doses ranged from 1.25 to 85 mg (0.08-1.7 mg/kg) in children, 10 to 495 mg in adolescents, and 5 to 1000 mg in adults. Most patients (62%, n = 88) remained asymptomatic, 32% (n = 45) developed only mild symptoms. In 4% of all cases moderate symptoms were observed (one toddler, one adolescent, three adults). The toddler developed moderate hypotension (75/39 mmHg) after ingestion of 10 mg (0.42 mg/kg). Severe toxicity was only seen in adults (n = 3), after ingestion of at least 250 mg. They developed severe hypotension (minimum 40 mmHg systolic) and bradycardia (minimum 30 bpm). The

lowest dose causing moderate symptoms was 150 mg in adolescents and adults. Adults tolerated up to 1000 mg without any toxicity. In children, asymptomatic cases were observed after ingestion of a maximum dose of 15 mg (1.36 mg/kg). Common clinical features in overdose were hypotension (30.9%), fatigue (14.5%), dizziness (12.7%), vomiting (12.7%), headache (9.1%), and tachycardia (9.1%). Less frequent were somnolence (5.5%), syncope (3.6%), and bradycardia (3.6%).
Conclusion: Most exposures in this study resulted in no or only mild symptoms (94%). Severe symptoms occurred in only three exposures, confirming past experience that severe toxicity is rare. There is no clear correlation between dose and severity of symptoms. Data from this study support the assumption of Balit et al. [1], that children can be observed at home after ingestion of up to 5 mg ramipril.

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186. The challenge of altered mental status: similarities between ziconotide toxicity and baclofen withdrawal

Avery Michienzi, Aaron Frey, Lauren Smaltz, Peter Vandersteenhoven, Heather Borek and Nathan Charlton

Department of Emergency Medicine, University of Virginia, Charlottesville, United States

Objective: To describe a case of altered mental status in a patient with an intrathecal pump containing ziconotide, baclofen and fentanyl. The mechanism and toxicity of ziconotide will be described briefly as it is a medication primarily managed by anesthesiologists.
Case report: A 61-year-old male with a past medical history of ankylosing spondylitis and chronic back pain with an intrathecal pump containing fentanyl/ziconotide/baclofen was admitted to the hospital with five days of worsening confusion. Daily medications included oral baclofen, mirtazapine, duloxetine, amitriptyline, and pregabalin. Two days prior to hospitalization, the patient's intrathecal pump rate was decreased by 6% and then 15% due to concern for ziconotide toxicity. The medications in the intrathecal pump could not be adjusted separately so his baclofen dose was also decreased. On presentation to the hospital, the patient was oriented but exhibited pressured/dysarthric speech, visual hallucinations, upper extremity tremor and mydriasis. Infectious work up did not reveal a cause for his symptoms. The patient's delirium worsened, despite the decreased pump rate, prompting concern for induced baclofen withdrawal. Due to concurrent concern for ziconotide toxicity, the intrathecal pump rate was further decreased by 10% but his oral baclofen dose was increased from 10 mg to 15 mg three times daily. Despite the increase in oral baclofen dose, his agitation progressed, necessitating intubation on hospital day 2. The intrathecal pump rate was increased by 23% at that point as concern for baclofen withdrawal outweighed concern for ziconotide toxicity. On hospital day 5, the patient was extubated with improved mental status. He was discharged home on hospital day 8 at his baseline mental status with no further pump adjustments.
Conclusion: Ziconotide is an intrathecal, synthetic conotoxin derived from the cone snail (*Conus magus*) which inhibits presynaptic N-type calcium channels and interrupts the transmission of pain signals in the spinal cord [1]. Toxicity may present similarly to baclofen withdrawal with confusion, hallucinations, abnormal gait, reduced level of consciousness, dizziness, and double vision [1]. This patient's management was challenging due to the potential for both ziconotide toxicity and baclofen withdrawal. When providing care for patients with mixed medication intrathecal pumps, it is necessary to consider the possibility of toxicity or withdrawal for each of the medications involved during dose adjustments.

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187. Acute overdose of a local anesthetic during suturing of a skin wound

Tinie van't Veen and Dorte F. Palmqvist

Department of Anaesthesiology and The Danish Poisons Information Centre, Copenhagen University Hospital Bispebjerg-Frederiksberg, Copenhagen, Denmark

Objective: Lidocaine overdose can cause local anesthetic systemic toxicity (LAST) and toxicity correlates with serum concentration. Toxicity is caused by sodium channel blockade leading to central nervous system and cardiac effects. The approximate maximum allowable subcutaneous dose is 4.5 mg/kg [1].
Case report: A 70 kg, 82-year-old woman was hospitalized with a large wound (40-50 cm) on her right crus and femur. Comorbidities were chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis. Normal liver function and creatinine (133 μmol/L (habitual)). During suturing of the wound, after a young physician was told to use an abundant quantity of lidocaine, the patient had altered consciousness. She received an injection of 2400 mg lidocaine (8 times the toxic dose). A brain computerised tomography (CT) scan was normal. She was moved to the intensive care unit with suspected LAST. Vital signs were: Glasgow Coma Score (GCS) 10 (E2, V3, M5), free airway, oxygen saturations 95% (with nasal oxygen 2 L/min), heart rate 80, and blood pressure 130/60 mmHg. Electrocardiogram (ECG) showed only first degree AV block. She received a bolus intravenous Intralipid 20% 1.5 mL/kg before the Danish Poisons Information Centre was contacted. They recommended observation for level of consciousness, respiratory depression and cardiac arrhythmias. The next day the patient was discharged from the ICU without sequelae.
Conclusion: Solely the dose determines that a thing is not a poison [2] and in this case, a large dose of lidocaine was administered in a vascular area. Systemic toxicity is usually seen because of unintentional intravascular injection of local anesthesia but in this case was due to an overdose. It is important to communicate precise and clear instructions on administration of a medicine. Data from Denmark states that in healthcare inadequate communication is the cause of up to 70% of severe unintended events [3]. The poor communication in this case resulted in an overdose of lidocaine. It is also important to be alert if a healthcare professional thinks they need to administrate a large number of tablets, ampoules etc. because the pharmaceutical industry usually makes products with the correct dose in one unit. Finally, it is essential that physicians know the symptoms of LAST and that it can also occur with the correct dosage.

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188. Characterizing the clinical toxicity associated with cariprazine, a novel atypical antipsychotic

Varun Vohra

Michigan Poison & Drug Information Center - Wayne State University School of Medicine, Detroit, United States

Objective: Cariprazine is a novel atypical antipsychotic approved in the United States (US) in 2015 for schizophrenia, bipolar disorder, and as an adjunct agent for major depressive disorder [1]. Its pharmacology includes dopamine D2 and D3 receptor partial agonism, partial 5-HT_{1A} receptor agonism, and $5HT_{2A}$ and 5-HT_{2B} receptor antagonism [1]. Cariprazine's unique chemical profile is underscored by its strong affinity and partial agonism for D3 receptors, mitigating extrapyramidal symptoms associated with other antipsychotics [1]. It has a long half-life and two active metabolites [2]. This report reviews the clinical toxicity secondary to cariprazine overdose.
Methods: Retrospective case review of single substance cariprazine overdose cases reported to six US poison control centers from 1 January 2016 to 30 September 2021. Data abstracted included patient demographics, clinical effects, treatment course, and medical outcomes.
Results: Overall, 58 cases were reported involving cariprazine overdose; mean age 30 years (range, 2 to 65), 36 females and 22 males. Most occurred in individuals aged 20-29 years and were intentional suspected suicide attempts (n = 42). Common symptoms were tachycardia (n = 19) and central nervous system depression (n = 19). Seven had electrocardiogram interval disturbances. Thirteen were admitted to the intensive care unit (ICU). Supportive care, including intravenous fluids, activated charcoal, and electrolyte repletion predominated treatment interventions. Two cases involved intubation and mechanical ventilation. Most cases involved a moderate medical outcome (n = 23). No deaths were reported. Since the majority of these cases involved multi-substance exposures, the effects secondary to other substances cannot be ruled out. Of the 58 cases, 17 exposures were cariprazine-only ingestions; mean age 23 years (range, 2 to 57 years), 9 females and 8 males. Most cases were intentional suicide attempts. Common symptoms included tachycardia (n = 3), nausea (n = 2), agitation (n = 2), and QTc prolongation (n = 2). Most patients were evaluated and treated in the emergency department; one patient was admitted to a non-critical care unit and one to the intensive care unit. Supportive care measures including intravenous fluids, activated charcoal, and benzodiazepines were most commonly instituted. The majority of patients in this cohort experienced minor medical outcomes (n = 6) with one experiencing a moderate outcome.
Conclusion: Cariprazine is a relatively novel antipsychotic with a dearth of literature describing its toxicity. This multi-center retrospective review demonstrated the most common effects involving cardiovascular and neurological symptoms treated with supportive care measures with mild-to-moderate outcomes.

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189. Serotonin toxicity following acute lamotrigine overdose: a prospective series

Angela L. Chiew[a], Katherine Z. Isoardi[b], Betty S. Chan[a], Nicholas A. Buckley[c] and Geoffrey K. Isbister[d]

[a]Department of Clinical Toxicology, Prince of Wales Hospital, Randwick, Australia; [b]Clinical Toxicology Unit, Princess Alexandra Hospital, Brisbane, Australia; [c]Clinical Pharmacology & Toxicology Research Group, School of Medical Sciences, University of Sydney, Sydney, Australia; [d]Department of Clinical Toxicology, Calvary Mater Newcastle and Clinical Toxicology Research Group, University of Newcastle, Newcastle, Australia

Objective: Lamotrigine is a broad-spectrum antiepileptic that blocks voltage-gated sodium and calcium channels. In overdose it usually only causes mild or no toxicity, however, large exposures may result in seizures, coma and cardiac conduction delay [1]. Lamotrigine has monoamine oxidase inhibitor activity, however there are few case reports of serotonin toxicity. We aimed to describe the clinical effects, treatments and outcomes in large acute lamotrigine overdoses.
Methods: A prospective observational multi-centre study from July 2020 to October 2021 of acute lamotrigine overdoses of >2 g in patients >14 years, from three toxicology units and via calls to the New South Wales and Queensland Poisons Information Centre. Clinical data and serum lamotrigine concentrations were collected.
Results: Over 15 months, 17 patients were recruited, median age 35 years (IQR: 24-43 years) and 10 were female. The median ingested dose was 4.0 g (IQR: 2.8-6.2 g, range: 2.4-14 g), four were lamotrigine-only ingestions. Median time to presentation was 1.7 hours (IQR: 0.7-3 hours, n = 14). Presenting symptoms included decreased level of consciousness (10), seizure or abnormal movements (2) and agitation requiring sedation (2). Eight had tachycardia on presentation, and four a QRS duration >120 ms; none developed arrhythmias. The median maximum lamotrigine concentration was 17.0 mg/L (IQR: 13.5–22.3, range 8.7– 47.4 mg/L; reference 2.5-15 mg/L) at a median time of 4.3 hours (IQR: 2.5-8.6 hours). Eight patients were intubated, all for decreased level of consciousness, for a median duration of 40 hours (IQR: 16-83 hours) and one was dialysed. Complications included seizures (2) and hypotension (3) of which two received inotropes. Eight (47%) developed serotonin toxicity as per the Hunter criteria, of which seven had moderate to severe toxicity. Those with serotonin toxicity either co-ingested a serotonergic agent (6/8) or took one therapeutically (2/8). Whereas those who did not develop serotonin toxicity 2/9 co-ingested a serotonergic agent and 2/9 took one therapeutically. There was no difference in maximum lamotrigine concentrations in those who developed serotonergic toxicity versus those who did not (18.7 mg/L versus

17 mg/L, respectively). Those with serotonin toxicity were intubated for longer (66.5 hours (n = 6) versus 12.4 hours (n = 2)).
Conclusion: Only a few case reports of serotonin toxicity have been reported after lamotrigine ingestion. Half of patients in our series developed moderate to severe serotonin toxicity, all were exposed to another serotonergic agent.

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190. Toxicity of bisoprolol - overdose in children and adults

Mandy Gollmann, Anabell Wüst and Dagmar Prasa
Poison Information Centre, Erfurt, Germany

Objective: Bisoprolol is the second most frequently prescribed beta-blocker in Germany. However, information on the toxicity of bisoprolol in children and adults is limited. The aim of this study is to provide more data on toxicity and clinical effects of bisoprolol overdose.
Methods: Cases of acute bisoprolol overdose in children and adults were analyzed in a retrospective single-center study. Inclusion criteria were the ingestion of single substance, defined dose and documented follow-up for at least 4 hours. Severity of symptoms was assessed according to Poisoning Severity Score.
Results: A total of 82 cases met the inclusion criteria. Patients involved were 4 infants (0.4-0.58 years), 17 toddlers (1-4.5 years), 2 schoolchildren (7-13 years), 9 adolescents (14-17 years), and 50 adults (18-81 years). Doses ranged between 5-10 mg (0.63-1.43 mg/kg) in babies, 1.25-45 mg (0.10-0.85 mg/kg) in toddlers, 10-50 mg (0.45-1.14 mg/kg) in schoolchildren, 10-375 mg (0.21-7.21 mg/kg) in adolescents and 2.5-515 mg (0.04-6.60 mg/kg) in adults. Overall, 33.0% of patients remained asymptomatic, 41.4% developed mild symptoms. Moderate and severe symptoms occurred in 25.6% and 1.2%, respectively. The following symptoms were observed in intoxication: bradycardia (54.5%), hypotension (34.5%), drowsiness, dizziness and vomiting (14.5%, respectively). In one isolated case an adolescent developed prolonged hypotension and bradycardia after ingestion of 10 mg. In those age groups showing moderate symptoms, symptoms only occurred from a dose of 50 mg and higher. One patient showed severe symptoms after ingestion of 75 mg.
Conclusion: Most bisoprolol overdoses in this study resulted in no or only mild effects (74.4%). Most frequently observed symptoms were hypotension and bradycardia. The already suggested toxic dose of 0.7 mg/kg can be substantiated by our data [1]. However, it can be assumed that there is high variability, and healthcare workers should be aware of individual cases with severe symptoms due to lower doses. Further studies are required in order to be able to comprehensively and conclusively assess the toxicity of bisoprolol, especially in children.

Reference

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192. Isoniazid exposures as reported to the Poisons Information Helpline of the Western Cape, South Africa: June 2015 – May 2020

Catharina E. Du Plessis[a], Gonwayne Voigt[a], Cindy R. Stephen[b] and Carine J. Marks[a]
[a]Stellenbosch University, Parow, South Africa; [b]University of Cape Town, Cape Town, South Africa

Objective: Tuberculosis (TB) is a major health concern in South Africa with an estimated infection rate of more than 350 000 infections per year [1]. Isoniazid (INH), used in combination with other anti-infectives as first-line treatment for TB, can cause severe acute toxicity in overdose by inducing seizures, with resultant metabolic acidosis and coma. Additionally, Isoniazid Preventive Therapy (IPT) is indicated in adult patients diagnosed with Human Immunodeficiency Virus (HIV) and infants born to TB-infected women and INH is therefore readily accessible in many households, for accidental and intentional exposures. The aim of the study was therefore to describe cases of INH exposures reported to the Poisons Information Helpline of the Western Cape (PIHWC).
Methods: We conducted a retrospective review of calls to the PIHWC related to INH exposures during a five-year period (June 2015 – May 2020). All human-related INH exposure data collected were extracted from the database. Key variables included patient demographics, circumstances of exposure, clinical presentation, severity of clinical features according to the Poisoning Severity Score, and treatment advised.
Results: There were 528 enquiries reported to the PIHWC regarding INH exposures. In one case more than one INH containing product was ingested. The majority of the enquiries were received from medical professionals (525, 99.4%), involving more females (388, 73.5%) than males (137, 26.0%). In adults 389 (73.7%) exposures were recorded and 93 (17.6%) in the 13–19-year age group. Only 44 (8.3%) poisoning exposures occurred in children 12 years and under. Overall, self-harming behaviour was the main cause of exposure (479, 90.7%). Severe or life-threatening symptoms and signs (PSS3) were recorded in 80 exposures (15.2%). Seizures were recorded in 254 exposures (48.1%), while 87 patients were asymptomatic at time of enquiry.
Conclusion: Due to increased availability of INH in many households with improving healthcare for TB and HIV patients, there is concern that severe INH exposures may increase in frequency. Clinicians should be aware of the risk and severity associated with INH poisoning. Although exposures in children were infrequent, INH can cause serious toxicity and it should be dispensed in child-resistant packaging and stored safely to prevent accidental exposures.

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193. Survival and recovery of bone marrow following a large colchicine overdose with use of granulocyte-colony stimulating factor

Rachael C. Brookes[a], Hayley A. Williams[a], Stephen Wiltshire[b] and Muhammad E.M.O. Elamin[a]

[a]National Poisons Information Service (Birmingham Unit), Birmingham, United Kingdom; [b]National Poisons Information Service (Newcastle Unit), Newcastle, United Kingdom

Objective: Colchicine is an alkaloid compound extracted from *Colchicum autumnale* and *Gloriosa superba* plants. It is used for the treatment of gout, has a narrow therapeutic window and is highly toxic. Colchicine inhibits cell division and in overdose can significantly affect organs with a high cell turnover such as the gastrointestinal tract and bone marrow, leading to pancytopenia and often death due to secondary infections. We describe a patient who developed bone marrow suppression, 5 days following a large intentional colchicine overdose, which was successfully treated with granulocyte-colony stimulating factor (G-CSF).
Case report: A 25-year-old male with a history of attention deficit hyperactivity disorder, recreational drug use and gout presented to hospital 24 hours after ingestion of 25 mg colchicine with alcohol. On admission he had frequent episodes of vomiting and complained of abdominal pain. Blood investigations revealed a deranged coagulation profile (prothrombin time (PT) 20.7 s, activated partial thromboplastin time (APTT) 44s) and metabolic acidosis (pH 7.28). He was treated supportively with intravenous fluids and sodium bicarbonate, in addition to vitamin K and multiple doses of activated charcoal (50 g). White cell (WCC) and platelet counts declined over the ensuing days reaching a nadir four days following the overdose (WCC 1.8 x 10^9/L; platelets 17 x 10^9/L). Filgrastim (5 μg/kg), a granulocyte-colony stimulating factor was administered for 3 days (from 4 to 6 days post-overdose), and the patient received two platelet transfusions for thrombocytopenia. Despite these measures, the patient developed a bacterial and fungal pneumonia and suffered a respiratory collapse 7 days following the overdose. He was intubated and ventilated and commenced on vancomycin and caspofungin. Bone marrow suppression improved over the subsequent days and resolved by Day 13. His clinical course was complicated by the development of rhabdomyolysis (creatine kinase peak 100,000 IU/L on Day 5), which required treatment with intravenous sodium bicarbonate and haemodiafiltration. In addition, the patient was hypotensive and cardiovascularly unstable, requiring vasopressor and inotropic support (metaraminol, vasopressin, noradrenaline, dobutamine) for several days. The patient also suffered alopecia during the second week of hospital admission. Despite a complicated clinical course, the patient was discharged from hospital 20 days following the overdose.
Conclusion: Colchicine overdose often carries a poor prognosis and bone marrow suppression is one of the most common associated toxicities. Clinicians should consider the use of G-CSF in patients developing bone marrow suppression to help prevent unfavourable outcomes due to secondary infections.

195. Successful use of high dose insulin therapy (HDI) in severe amlodipine poisoning presenting with cardiac arrest

Eleri Thomas[a], James M. Coulson[a] and Muhammad E.M.O. Elamin[b]

[a]National Poisons Information Service (Cardiff Unit), Cardiff, United Kingdom; [b]National Poisons Information Service (Birmingham Unit), Birmingham, United Kingdom

Objective: High dose insulin (HDI) therapy is routinely recommended in the management of calcium channel blocker (CCB) poisoning. We report successful use of HDI in a severe case of amlodipine poisoning presenting with cardiac arrest and severe metabolic acidosis.
Case report: A 47-year-old female, with a background of suicidal ideation, was found in cardiac arrest, hypothermic with fixed, dilated pupils at home. She was intubated at the scene and transferred to an intensive care unit. Her prescribed medications included amlodipine, amitriptyline, atorvastatin, sertraline, omeprazole and hyoscine butylbromide. No tablets were reported missing. An electrocardiogram revealed complete heart block, with abnormal cardiac conduction requiring transcutaneous pacing. She required substantial inotrope and vasopressor support (0.5 μg/kg noradrenaline and 0.5 μg/kg adrenaline) to maintain a mean arterial blood pressure (MAP) of 56 mmHg. She had severe metabolic acidosis (pH 6.87, bicarbonate 7 mmol/L and lactate 28 mmol/L). Bicarbonate infusion and haemofiltration were commenced. Despite supportive care, the patient "lost output" approximately 14 hours post-admission and MAP fell to 52 mmHg. HDI therapy was commenced at 15 hours post-admission. One unit/kg of insulin was administered and titrated up. Vasopressin, noradrenaline and adrenaline were continued. Following 3 hours of HDI therapy, slight neurological improvement was reported, with slight improvement of MAP from 52 mmHg to 56 mmHg, however, urine output remained low. Despite these supportive measures, lactate concentrations (19-20 mmol/L) and urine output remained unchanged. On further discussion, it was recommended to maximise HDI to 10 units/kg/h as the patient remained acidotic (pH 7.02, bicarbonate 8.5 mmol/L). At 36 hours post-admission, adrenaline was weaned off and the patient was only receiving low doses of noradrenaline and vasopressors with 64 mL/h HDI. Her MAP had increased to 72 mmHg, with resolution of metabolic acidosis and improved responsiveness. By day 3, HDI, noradrenaline and vasopressor treatment were discontinued, with successful extubation on day 4. Several "stashes" of medications, including a "calcium channel blocker" were found around her house. A urine toxicology screen confirmed elevated amlodipine and amitriptyline concentrations. The patient was transferred to a medical ward on day 7.
Conclusion: Despite an extremely poor initial prognosis with severe metabolic acidosis and cardiac arrest, the patient made a successful recovery following initiation of HDI therapy in addition to other supportive measures. This case further supports the role of HDI in management of severe calcium channel blocker poisoning with peri-arrest and severe metabolic derangement

196. Rhabdomyolysis due to salinomycin poisoning

Natasa Perkovic Vukcevic, Slavica Vucinic, Jasmina Jovic Stosic, Gordana Vukovic Ercegovic, Olivera Potrebic and Dragan Zivanovic

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

Objective: Salinomycin is an ionophore antibiotic used in veterinary medicine. Acute poisoning of different animal species with damaged skeletal muscles and myocardium has been described.

We report a case of a salinomycin poisoning with prolonged duration of rhabdomyolysis.
Case report: A 58-year-old male chemist was hospitalized for 14 days after an accidental exposure to salinomycin with myalgia and weakness in limbs. The exposure took place in a poultry food and additives factory when a 100 kg sack of salinomycin (100 mg/g), fell from height and burst. The patient inhaled and swallowed a small amount, his face and body were covered with powder. After 3 hours, he had tingling feeling in his fingers and lower legs followed by ataxia. The symptoms persisted and he went to a local hospital the next day. His physical findings were good, he was administered crystalloid solution, but no laboratory analyses were done. His initial difficulties disappeared. The patient, being aware of possible toxic effect of salinomycin, continued on his own with intensive water intake (4 L/d). Ten days after exposure, weakness and muscle pain appear, first in the lower legs, later in his thighs and arms as well as fatigue and palpitations. He noticed dark brown urine, with increased muscle pain. Fourteen days after the exposure he was hospitalised conscious, afebrile, tachycardic, with normal blood pressure. An electrocardiogram (ECG) showed sinus tachycardia, heart rate 120/min, without change to the ST segment and T wave. Musculature was painfully sensitive, and muscle strength reduced with areflexia. Creatine kinase (CK) was 12,579 U/L (normal 32-300), CK-MB was 243 U/L, with normal renal parameters, electrolytes and complete blood count. Therapy included fluids, bicarbonate, diuretics and bisoprolol. Electromyoneurography indicated sensor polyneuropathy of the lower limbs. Echocardiography revealed normal sized chambers with ejection fraction of 65% without any wall motion abnormality. Increased CK values gradually diminished: on 21st day 6960 U/L, on 25th day 4969 U/L, on 28th day 2836 U/L and on 42nd day 245 U/L. The patient was discharged with his muscle strength fully recovered.
Conclusion: Patients who, after being exposed to salinomycin, develop weakness and muscle pain have to be carefully observed both clinically and through laboratory analyses due to possible rhabdomyolysis [1]. Our case contributes to better understanding and more successful treatment of this condition.

Reference

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197. Massive venlafaxine overdose successfully managed with high-dose insulin euglycemic therapy and extracorporeal membrane oxygenation

Friederike Rau[a], Maria Vanezi[b], Riad Al-Khalil[c] and Gesine Liebetrau[a]

[a]Poisons Information Centre, Erfurt, Germany; [b]Clinic for Interventional Cardiology and Intensive Care, Heart and Diabetes Centre North Rhine Westphalia, Bad Oeynhausen, Germany; [c]Clinic for Heart and Thorax Surgery, Heart and Diabetes Centre North Rhine Westphalia, Bad Oeynhausen, Germany

Objective: Overdose with venlafaxine – a serotonin/noradrenaline reuptake inhibitor – may result in severe toxicity and potentially life-threatening serotonin syndrome. Heart failure and serotonin syndrome resulted in death at a dose as low as 2.25 g venlafaxine, according to experiences of the poisons information centre. In the following case report the patient survived a massive intake of 22.5 g venlafaxine due to treatment with high-dose insulin euglycemic therapy (HIET) and extracorporeal membrane oxygenation (ECMO) in conjunction with Impella CP® left ventricular assist device.
Case report: A 22-year-old woman intentionally ingested 22.5 g of sustained-release venlafaxine. Approximately 1.5 hours later, symptoms such as mydriasis and tachycardia were reported to the poisons information centre by the initial caregiving physician. After protecting the patient's airway, gastroscopy was performed. Only a small amount of the ingested tablets could be removed from the stomach, followed by instillation of activated charcoal. Ventricular tachycardia necessitated transfer to the nearby, specialized cardiac centre where the patient developed ventricular fibrillation and required resuscitation approximately 8 hours after ingestion. Therapy with magnesium, lidocaine and high-dose catecholamines was performed, followed by ECMO and an Impella CP® left ventricular support device due to echocardiographic signs of poor biventricular function. Hemodialysis and HIET were also started. ECMO-controlled body temperature was normal at all times and the patient did not show signs of neurological damage. On day 5, the patient had stable blood pressure and no longer required catecholamines, ECMO and cardiac support. The cardiac function as well as kidney and other organ functions returned to normal.
Conclusion: The amount of 22.5 g seems to be one of the highest non-fatal venlafaxine ingestions in the literature [1]. As hemodialysis is unlikely to be effective in venlafaxine overdose due to its high volume of distribution, we assume HIET and ECMO were life-saving treatments in this case. HIET was tolerated without significant side effects, however ECMO was unavoidable. In massive venlafaxine overdose early treatment with ECMO should be considered [2]. Early ECMO may possibly also prevent the patient from developing a serotonin syndrome-associated hyperthermia because body temperature is continuously regulated due to this treatment.

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198. Oral methotrexate poisoning reported to the UK National Poisons Information Service (NPIS)

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

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

Objective: Methotrexate is an anti-proliferative agent that inhibits dihydrofolate reductase. Toxicity is observed in rapidly dividing cells and is dependent on dose, route and duration of exposure. This study was performed to analyse oral methotrexate telephone enquiries to the UK NPIS.

Methods: A retrospective search of the UK Poisons Information Database (UKPID) was performed to identify enquiries relating to oral methotrexate exposures (2015 to 31 October 2020).
Results: During the study period we received 261 enquiries relating to methotrexate; exposure to methotrexate alone occurred in 168 patients. The majority (139; 82.7%) followed oral exposure which is the focus of this study (others were parenteral (27; 16.1%) and unknown (2; 1.2%)). Most exposures occurred in older adults although all age groups were represented: <10 years: 10 patients (7.2%); 10-24 years: 6 (4.3%); 25-39 years: 14 (10.1%); 40-54 years: 26 (18.7%); 55-69 years: 40 (28.8%); 70-84 years: 30 (21.6%); >85 years: 10 (7.2%) and unknown: 3 (2.2%). The majority of ingestions occurred at home (123 patients; 88.5%), followed by hospital (10; 7.2%); and other locations (6; 4.3%). Most exposures were accidental: 81 (58.3%) were due to therapeutic error (e.g. daily ingestion of weekly prescribed dose or single additional dose) and 10 (7.2%) were due to accidental acute ingestion in treatment naïve individuals. Ten cases (7.2%) were classified as adverse reactions to methotrexate therapy (e.g. accumulation in the presence of renal impairment). Deliberate self-harm accounted for 30 cases (21.6%). In 8 cases (5.7%) the reason was unclear.
Most patients were asymptomatic (64; 46.0%) or had minor features only (45; 32.4%). Moderate features were reported in 20 patients (14.4%). Five patients (3.6%) demonstrated severe features; four of these occurred as a result of therapeutic error and in one patient it was due to chronic accumulation. No fatalities were reported. Following therapeutic error and accidental ingestion the majority of patients were asymptomatic or had minor features (72/91 patients; 79.1%). Clinical features included abnormal blood cell counts (33, 47.1%); gastrointestinal upset (22; 31.4%); mucositis (14; 20.0%); abnormal renal function (12; 17.1%); dermal effects (7; 10.0%) and abnormal hepatic function (5; 7.1%).
Conclusion: Oral methotrexate exposures were most frequently reported in older adults and primarily occurred as a result of unintentional exposure with daily ingestion of a weekly preparation or accidental ingestion of additional doses being most common. Reassuringly most patients following therapeutic error or accidental ingestion were asymptomatic or reported minor features only.

199. Haloperidol-associated adverse outcomes in hospitalized non-surgical patients

Ophir Lavon and Amir Wolfovitz
Carmel Medical Center, Haifa, Israel

Objective: To evaluate haloperidol use and adverse outcomes in hospitalized non-surgical patients.
Methods: A retrospective chart review of non-surgical patients hospitalized and treated with haloperidol was conducted. Exclusion criteria included mechanically ventilated patients and patients who were treated with haloperidol regularly before admission. Primary outcomes included in-hospital post-exposure events: mechanical ventilation, cardiac arrhythmia, changes in blood pressure (BP), falls and mortality. Demographic and clinical data were collected and subjected to comprehensive statistical analysis.
Results: In total 200 patients were included in the final analysis. Average age of patients was 83.4 years; 50% were male. The average Charlson Comorbidity Index was 8.3. The main indication for haloperidol was acute agitation (84%) and it was usually given once intramuscularly (92%). The dose was either 5 mg (55%) or 2.5 mg (45%). The average duration of stay was 11 days. Overall, 134 (67%) patients developed an adverse outcome. In-hospital mortality rate was 17.5%. In almost half of the patients (46.5%), a systolic blood pressure change of more than 20 mmHg, within 12 hours post-administration, was recorded. Ten patients (5%) were ventilated and 4 (2%) developed cardiac arrhythmias (ventricular and supraventricular tachycardia) within 24 hours post-administration. Seven falls were recorded, which translated to a rate of 3.15 per 1000 hospitalization days.
A lower pulse rate recorded before haloperidol administration was associated with slightly more adverse outcomes (OR 1.02, 95%CI 1.01-1.03, $p = 0.05$).
Conclusion: Haloperidol treatment in hospitalized non-surgical patients was associated with significant in-hospital morbidity and mortality. Causality is unclear. It can be argued that as high-risk patients with prolonged hospitalizations have higher chance for developing acute agitation secondary to advanced illness and clinical deterioration, haloperidol is sometimes used to suppress the secondary psychoactive state. This practice may mask clinical signs and delay diagnosis and treatment of the underlying cause of agitation. Appropriate evaluation and exclusion of acute organic impairment are vital, before any administration of haloperidol.

200. COVID testing kits – A new source of accidental poisoning in the UK?

Annie Watt[a], 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 (Edinburgh Unit), Edinburgh, United Kingdom; [b]National Poisons Information Service (Newcastle Unit), Newcastle, United Kingdom; [c]National Poisons Information Service (Cardiff Unit), Cardiff, United Kingdom; [d]National Poisons Information Service (Birmingham Unit), Birmingham, United Kingdom

Objective: Self-testing kits for COVID-19 are available to the public and commonplace in households. Kits consist of nasal/throat swabs, absorbent testing strips (including a desiccant sachet) and bottles of extraction liquid. Once samples are collected swabs are placed in the liquid to create a sample for lateral flow (LFT) or polymerase chain reaction (PCR) testing. The liquid is a mixture of water, transport mediums, buffers, preservatives and animal proteins and although not intended for human contact, is considered to be low toxicity. Our objective was to analyse enquiries to the UK National Poisons Information Service (NPIS) regarding COVID-19 test kits to investigate potential toxicity.
Methods: We conducted a retrospective analysis of enquiries from 1 March 2020 until 31 July 2021. Enquiries were identified from the UK Poisons Information Database (UKPID) and filtered to identify those relating specifically to COVID-19 test kits.
Results: In the study period 126 enquiries were received about COVID-19 test kits. One enquiry was regarding ingestion of the desiccant (LFT kit) with all others regarding the extraction liquid. The majority of enquiries (86, 68.3%) related to LFT kits with 9 (7.1%) enquiries regarding PCR kits. In 31 enquiries (24.6%) the test type was not specified. NHS telephone services (NHS 111/Direct/24) accounted for the majority of enquiries (94, 74.6%), with the remaining from hospitals (12, 9.5%), primary care (10, 7.9%), and other sources (10, 7.9%) including ambulance services and nursing homes. Adults accounted for 69 (54.8%) enquiries with 55 (43.7%) regarding children. Age was not specified in 2 (1.6%) enquiries. Most adult exposures were accidental (67, 97.1%) with only 2 (2.9%) intentional exposures. Accidental exposures were due to the liquid being mistaken for eye drops (24, 35.8%), swabs dipped in liquid before taking samples (21, 31.3%),

ingestion of liquid (19, 28.4%), spill of liquid onto skin (2, 3%) and liquid mistaken for ear drops (1, 1.5%). Patients were either asymptomatic (48, 69.6%) or reported mild symptoms only (20, 29%). In 1 enquiry the symptoms were unknown. Paediatric exposures were also accidental with only one intentional ingestion. Enquiries included ingestion of liquid or desiccant (45, 83.3%), liquid mistaken for eye drops (6, 11.1%), and swab dipped in liquid before taking sample (3, 5.5%). Patients were asymptomatic (48, 87.3%) or reported mild symptoms only (7, 12.7%).
Conclusion: Almost all exposures to COVID-19 test kits were accidental with the extraction liquid most commonly being mistaken for eye drops. Reassuringly, serious toxicity has not been reported.

201. COVID vaccines – therapeutic errors reported to the UK National Poisons Information Service (NPIS)

Annie Watt[a], 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 (Edinburgh Unit), Edinburgh, United Kingdom; [b]National Poisons Information Service (Newcastle Unit), Newcastle, United Kingdom; [c]National Poisons Information Service (Cardiff Unit), Cardiff, United Kingdom; [d]National Poisons Information Service (Birmingham Unit), Birmingham, United Kingdom

Objective: The first COVID-19 vaccine was administered in the UK on the 8 December 2020. Since then, the UK has authorised four vaccines for use against COVID-19 (Pfizer/BioNTech, Oxford/AstraZeneca, Moderna and Janssen). Serious adverse effects, including fatalities, have been linked to COVID-19 vaccines [1]. We reviewed all enquiries to the UK National Poisons Information Service (NPIS) related to COVID-19 vaccines.
Methods: We conducted a retrospective analysis of enquiries relating to COVID-19 vaccines to the NPIS from 1 March 2020 until 31 July 2021. Enquiries were identified from the UK Poisons Information Database (UKPID) and filtered to identify those relating specifically to COVID-19 vaccines.
Results: The NPIS received 34 enquiries about COVID-19 vaccines during the study period (Oxford/AstraZeneca: 13, 38.2%; Pfizer/BioNTech: 9, 26.5%; Moderna: 1, 2.9%). Two enquiries were seeking information about two different vaccines (Pfizer/BioNTech and Oxford/AstraZeneca) and in nine enquiries the manufacturer was unknown. Of these enquiries, 29 (85.3%) were specifically patient-related while five (14.7%) were for information only and were excluded from further analysis. The majority of patient-related enquiries were from NHS 111 (17, 58.6%) with the remaining from hospitals (6, 20.7%) or primary care (6, 20.7%). All enquiries were regarding adult patients; 21 enquiries were regarding female patients (72.4%) with 8 regarding male patients (27.6%). The most common enquiries were regarding patients who had received three doses instead of 2 (7, 24.1%), dosing errors due to incorrect dilution/reconstitution of the vaccine (5, 17.2%), doses administered outside the recommended timeframe of 8-12 weeks (5, 17.2%), adverse reactions (4, 13.8%) and patients receiving 2 doses in the same day (4, 13.8%). Nineteen patients (65.5%) were asymptomatic at the time of the enquiry. Four patients had symptoms (13.8%) but these were all deemed to be minor. In 6 enquiries (20.7%) it was unknown if the patient had symptoms. No moderate or severe symptoms were recorded and there were no fatalities.
Conclusion: Serious adverse effects have been rarely associated with COVID-19 vaccines [1]. Enquiries to the NPIS regarding COVID-19 vaccines were generally related to administration or dosing errors. Reassuringly, in this patient population, most patients had no symptoms or mild symptoms only.

Reference

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203. Impact of COVID-19 on the number and type of calls to the Belgian Poison Centre

Dominique Vandijck, Eline Bekaert, Evelien De Smet, Jonas Moens, Pamela Selway, Jonas Van Baelen, Pascale Wallemacq and Anne-Marie Descamps

Belgian Poison Centre, Brussels, Belgium

Objective: The present study provides an overview of the number and type of calls to the Belgian Poison Centre (BPC), and the impact of COVID-19.
Methods: Data of all calls to the BPC (1 January – 31 December 2020) were collected and analysed using appropriate statistics (SAS).
Results: The BPC received 65,308 calls in 2020 (60,668 in 2019, $p < 0.05$). The vast majority (35.9%) of exposures were drug-related (21,151 in 2019 versus 20,666 in 2020, $p > 0.05$), followed by the use of chemical household products (11,836 in 2019 versus 12,247 in 2020 ($p > 0.05$)). A 12.3% increase in the number of cosmetic- and food-related exposures was noted (8,291 in 2019 versus 9,308 in 2020, $p < 0.05$). Within this group, a stable number of exposures (877 in 2019 versus 876 in 2020, $p > 0.05$) due to essential oil exposures were observed. Partly due to the impact of the COVID-19 [1] pandemic, exposures to biocides doubled (104.9%) from 1,964 in 2019 to 4,024 in 2020 ($p < 0.05$). Exposures to type 1 biocides (i.e. human hygiene products, which include alcohol-based hand sanitisers (ABHS)) significantly increased from 322 in 2019 to 1,676 in 2020 ($p < 0.05$), and exposures to type 2 biocides (i.e. disinfectants and algaecides not intended for direct application to humans or animals) from 406 to 902 ($p < 0.05$). In 2020 the BPC received a five-fold increase in the number of calls involving ABHS incidents (both liquid and gel-based, as well as ethanol and isopropanol products) compared to 2019 (1,676 versus 323 in 2019 versus 1,676 in 2020 calls, $p < 0.05$), accounting for 2.6% of all calls in 2020. In 71% of exposures, ingestion was the primary route (1,195/1,676), followed by 28.6% accidental ocular exposures (480/1,676) of which more than half of the incidents involved children (257/480, $p < 0.05$), primarily young children aged 1-4 years (136/257, $p < 0.05$). Finally, as people went into the garden and nature to relax during lockdown, a 28.2% increase in exposures related to the group 'plants, mushrooms and animals' was found, with 3,256 exposures in 2019 and 4,175 in 2020 ($p < 0.05$).
Conclusion: In its history, the BPC has never received as many calls as in 2020. The COVID-19 pandemic contributed to a significant number of additional exposures, and requests for toxicologic advice.

Reference

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204. COVID-19 and methanol poisoning in Azerbaijan

Ismayil Afandiyev
Azerbaijan Medical University, Baku, Azerbaijan

Objective: The global pandemic of coronavirus SARS-CoV-2 has been a serious stress test for healthcare systems in many countries, with a significant impact on the structure and number of acute chemical poisonings. The aim of this study was to examine the impact of the COVID-19 pandemic on the toxic-epidemiological situation in Azerbaijan.
Methods: We conducted a comparative analysis of the database of the Poison Center in Baku during the 9 months of the pandemic period (20 March – 21 December 2020) with the data of the same period in 2019 and the previous decade (2009-2018).
Results: The alarming dynamics of a significant increase in the number of alcohol surrogates, primarily methanol poisoning, was revealed. In the 10-year period 2009-2018, alcohol surrogates intoxication was only 0.09% (18 patients) of total poisoning cases (20,266), but during the study period of 2020 increased to 3.4% (32 patients of 946 poisoning cases). The mortality rate in the ethanol and alcohol surrogate intoxication group in 2019 was 7.5% (8/106) versus 28.3% (30/106) in March-December 2020. All fatal cases in the alcohol surrogate poisoning cohort were related to methanol, thus, the mortality rate of this pathology was 61.5% (16/26). At the same time, no case of methanol poisoning was recorded in March-December 2019, and in the previous decade (2010-2018), only 1 case of methanol intoxication was recorded. The source of methanol during the pandemic was ingestion of counterfeit medical alcohol and alcohol-containing disinfectant products purchased by the victims themselves in the pharmacy network.
Conclusion: The COVID-19 pandemic and quarantine measures had a significant impact on the epidemiology of poisoning in Azerbaijan, with an increase in cases and mortality of methanol poisoning. The outbreak of methanol poisoning in Azerbaijan revealed many shortcomings and weaknesses in the country's public health system. Late or erroneous diagnosis, lack of knowledge and clinical experience in the diagnosis and management of poisoned patients, difficulties with laboratory and diagnostic confirmation of the diagnosis, restrictions in the treatment of patients, relating to the lack of an effective antidote (fomepizole) resulted in high mortality. Considering the almost complete absence of methanol poisoning in Azerbaijan over the previous decade, the question of the source of the methanol is raised. Until a few years ago, the only methanol plant in the Caucasus was opened in Azerbaijan with a production capacity of more than 400 thousand tons per year. The plant stores more than 48 thousand metric tons of finished product, and should be investigated for possible leakage to the illegal market.

205. Increased risk of COVID-19 mortality in patients with opioid use disorder across an academic urban hospital system

Jonathan Schimmel, George Loo, Gordon Ngai and Alex F. Manini
Icahn School of Medicine at Mount Sinai, New York, United States

Objective: As the world copes with the pandemic caused by the 2019 novel coronavirus (COVID-19), there is concern it could disproportionately affect some populations with substance use disorders. For example, increased COVID-19 severity in patients with opioid use disorder (OUD) is biologically plausible based on several mechanisms (respiratory effects, immune mechanisms, social/environmental factors, drug-drug interactions). Therefore, we examined a health system-wide database to evaluate clinical outcomes from COVID-19 in patients with OUD. We hypothesized that among Emergency Department (ED) patients with COVID-19, OUD and opioid overdose would be associated with a higher incidence of COVID-19 mortality.
Methods: Retrospective data collection was obtained across one large urban academic healthcare system (5 hospitals) via automated chart abstraction over 2 years (since 19 January 2021). Adult (age 18-104 years) ED patients with positive COVID-19 PCR testing were included. The study database was extracted with waiver of consent from a data warehouse located on a high performance computing cluster which contains details of the electronic medical record. The study outcome, COVID-19 mortality, was defined as in-hospital all-cause mortality. OUD was defined by either ICD-10 diagnostic codes or medication for opioid use disorder (MOUD) prescriptions in the healthcare record. Opioid overdose (OD) was defined as naloxone administration within the first 24 hours of hospitalization or ED stay. We performed multivariable logistic regression models using SAS v 9.4. With a fixed sample size of 19,769, assuming 2% had OUD, and 10% baseline outcome rate, we had 84.9% power to demonstrate a 5% increase in mortality risk.
Results: We analyzed 19,769 patients (52.6% male, 24.5% Black, 26.7% Hispanic, 6.8% Asian) meeting study criteria, of whom 374 (1.9%) had OUD, and 21 (0.1%) had opioid OD. The study outcome occurred in 2103 (10.6%) patients. Additionally, 835 had acute respiratory distress syndrome (ARDS), 1671 required invasive ventilation, and 936 non-invasive ventilation. On bivariate analysis, both opioid OD (OR 1.27, $p = 0.012$) and OUD (OR 2.2, $p < 0.001$) were associated with the study outcome. Using multivariable logistic regression controlling for demographics (age, sex, race/ethnicity), smoking, and obesity, OUD was an independent predictor of COVID-19 mortality (aOR 3.5, CI 2.6-4.7).
Conclusion: In this large health system analysis of ED patients with COVID-19, OUD was an independent predictor of COVID-19 mortality. Additionally, opioid OD was associated with COVID-19 mortality but its rarity prevented robust modeling. Future studies should focus on these high-risk subgroups for targeted therapeutic interventions.

206. The impact of the COVID-19 pandemic on substances of abuse poisoning in adolescents

Viorela Nitescu, Diana Usurelu, Teodora Turcu, Irina Coman and Coriolan Ulmeanu
Pediatric Poisoning Centre Bucharest, Bucharest, Romania

Objective: To evaluate the impact of the COVID-19 pandemic on the epidemiological features of substances of abuse poisoning in adolescents.
Methods: We performed a comparative analysis of all adolescents diagnosed with substances of abuse poisoning during two periods of 20 months each: one before and the other after the onset of the COVID-19 pandemic. We analyzed the medical records (T40 ICD -10-CM code) taking into consideration the following criteria: age, gender, environment, incriminated substance from the case history and urinary toxicological screening tests, route of exposure, hospitalization period, chronic consumption in antecedents. The patients were divided into two samples: Sample 1 patients before the COVID-19 pandemic onset

(September 2018-February 2020) and Sample 2 patients after the onset of the pandemic (March 2020-September 2021).
Results: The analysis of the two samples revealed that there were significantly fewer patients with substances of abuse acute poisoning admitted after the COVID-19 pandemic onset (56 versus 106). Analyzing the data regarding age, gender, environment, route and length of hospitalization, there were no statistically significant differences between the two groups of patients (Table 1). The percentage for cannabis is quite similar in both categories while for new psychoactive substances and benzodiazepines it is higher in the second sample. The percentage of chronic consumers was significantly higher in sample 2 compared to sample 1 (66.7% versus 50.9%).
Conclusion: There were significantly fewer hospitalized adolescents with substances of abuse poisoning during the pandemic period. The percentage of poisoned patients that were chronic consumers of substances of abuse was higher during the pandemic. The COVID-19 pandemic did not influence the popularity of cannabis which was the most commonly used substance in both sample groups.

207. Paraquat ingestion and COVID-19 infection: deadly double hit

Ashish Bhalla, Tukaram P, Neha Sharma and Manoj Goyal

Postgraduate Institute of Medical Education and Research, Chandigarh, India

Objective: To describe two cases of intentional paraquat ingestion as self-harm in patients with COVID-19 infection.
Methods: We retrospectively analysed poisoning cases (accidental and suicidal), admitted to a dedicated COVID-19 care facility at our institute. As a protocol, all patients coming to our emergency department were reverse transcriptase-PCR tested for novel coronavirus disease 2019 (nCOVID-19) before being admitted to a high dependency unit (HDU) intensive care unit (ICU). If they tested positive for COVID they were transferred to a dedicated COVID care facility. These patients were treated according to the protocol developed for poisoned patients. All patients were followed until discharge or death. We describe the details of 2 patients with intentional paraquat ingestion.
Results: We received nine patients at our dedicated COVID care facility created at our institute during the pandemic. Of these 9, 2 patients had ingested paraquat and presented with acute respiratory distress syndrome (ARDS). Both patients were in the third decade of life and the economic crisis due to the pandemic was the trigger for the ingestion of paraquat. Both had ingested a significant amount of commercially available paraquat. They had significant acute kidney and liver injury at presentation and required dialysis. Haemoperfusion was not performed as the charcoal filters were not available. The clinical picture and chest X-rays were similar to the findings observed in severe COVID-19 patients. Since patients were hypoxic at presentation, monoclonal antibodies were not indicated and were not administered. Both patients were given dexamethasone (6 mg daily), as per the "COVID treatment protocol". We did not administer pulse doses of methylprednisolone or cyclophosphamide due to concerns over exacerbating COVID infection. One of the patients developed significant oesophageal ulceration leading to massive haematemesis. Both developed spontaneous pneumomediastinum and succumbed to their illness after an average stay of 8 days in the HDU.
Conclusion: During the pandemic, paraquat ingestion for self-harm with COVID-19 infection poses a challenge to treating physicians. Since the clinical picture of ARDS, is similar to severe COVID infection, the management with immunosuppressive agents becomes difficult.

208. Increased occupational exposure to disinfectants during the COVID-19 pandemic in 2020

Esther Feistkorn, Nina Glaser, Michael Reuser and Herbert Desel

German Federal Institute for Risk Assessment (BfR), Berlin, Germany

Objective: Health authorities' recommendations for containment of COVID-19 have led to a wide spread availability and use of disinfectants in Germany. The study investigates if the frequency and characteristics of poisonings with disinfectants at the workplace have changed in 2020 in comparison to previous years.
Methods: The German Federal Institute for Risk Assessment (BfR) receives reports on workplace poisonings on a legal basis (German Chemicals Act §16e). Occupational exposures with disinfectants between 2018 and 2020 were evaluated in terms of frequency and characteristics (Poisoning Severity Score (PSS), route of exposure, product category).
Results: The BfR received 19,431 cases of workplace exposures in 2018-2020. Biocidal disinfectants were involved in 1,066 cases

Table 1. Substances of abuse poisoning in adolescents before and after the onset of the COVID-19 pandemic.

Criteria	SAMPLE 1 Prepandemic period (n = 106)	SAMPLE 2 Pandemic period (n = 56)
Gender	Male 57 patients (53.7%)	Male 20 patients (35.7%)
	Female 49 patients (46.2%)	Female 36 patients (64.2%)
Age	15.4 years ±1.34 (minimum age 12 years and a maximum of 18 years)	15.5 years ±1.22 (minimum age 12 years and a maximum of 18 years)
Environment	Urban 84 (79.24%)	Urban 46 (82.1%)
	Rural 22 patients (20.7%)	Rural 10 (17.8%)
Length of hospitalisation	1.52 ± 0.8 days	1.46 ± 0.9 days
Incriminated substance	Cannabis 68 (64.1%)	Cannabis 34 (60.7%)
	New psychoactive drugs 19 (17.9%)	New psychoactive drugs 14 (25%)
	Cocaine 3 (2.8%)	Cocaine 3 (5.3%)
	Opioids 12 (11.3%)	Opioids 2 (3.5%)
	Benzodiazepines 6 (5.6%)	Benzodiazepines 6 (10.7%)
	Hallucinogens 8 (7.5%)	Hallucinogens 2 (3.5%)
	Unidentified substance 2 (1.8%)	Unidentified substance 2 (3.5%)
Route	Smoking 80 (75.4%)	Smoking 42 (75%)
	Ingestion 26 (24.5%)	Ingestion 17 (30.3%)
	Inhalation 3 (2.8%)	Inhalation 2 (3.5%)
	Intravenous 3 (2.8%)	Intravenous 1 (1.7%)
Chronic consumers	54 patients (50.9%)	37 patients (66.7%)

(5.5%). Due to variations in the total number of annually notified cases, the proportion of cases involving biocidal disinfectants in relation to all cases was calculated for each year. With 6.9%, the highest percentage of cases involving biocidal disinfectants was registered for 2020, compared to 4.9% in the two previous years. In the majority of cases (83.5%) only minor symptoms (PSS1) were registered, mostly eye irritation (78.4%). The distribution of PSS assigned to cases showed no significant differences between 2020 and previous years (Table 1).

Conclusion: The COVID-19 pandemic has led to an increase in general disinfection measures. Professional publications from numerous poison information centres around the world report an increase in the number of cases of disinfectants. This trend is also reflected in our study, analysing exposures with disinfectants at workplace. While the total number of reported cases decreased in the "shutdown year" 2020, the proportion of cases with disinfectants increased. The distribution of severity remained almost the same. In the work environment too, care should be taken to handle disinfectants and, if necessary, appropriate protective clothing, should be worn.

209. Effects of the COVID-19 pandemic on the Finnish Poison Information Center call records

Elina T. Karhu[a], Terhi Lampinen[a] and Tuomas O. Lilius[b]

[a]Poison Information Center, Department of Emergency Medicine and Services, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [b]Poison Information Center, Department of Emergency Medicine and Services, Helsinki University Hospital and University of Helsinki; Department of Pharmacology and INDIVIDRUG Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland

Objective: To investigate calls made to the Finnish Poison Information Center (FPIC) before and during the COVID-19 pandemic. We hypothesized that the number of calls concerning COVID-related drugs and disinfectants would have increased, as well as the number of calls regarding intentional poisonings, due to the social and economic stress caused by the pandemic.

Methods: We analysed the FPIC call records to assess the impact of the COVID-19 pandemic on our statistics. The pandemic started in Finland in March 2020 and the highest peaks were experienced during April 2020, December 2020, March 2021 and August 2021. We compared the mean number of calls per month from the same time period (March-June) before the pandemic (years 2018–2019) and during the pandemic (years 2020–2021).

Results: The FPIC receives approximately 40,000 calls yearly from healthcare professionals and the public. The total number of calls was not significantly changed by the pandemic. Compared with 2018–2019, we observed a mean 161% increase (2018, n = 24; 2019, n = 25; 2020, n = 61; 2021, n = 67) in calls concerning hand disinfectants during the pandemic. Respectively, there was a 180% increase concerning hydrogen peroxide (2018, n = 3; 2019, n = 2; 2020 n = 9; 2021, n = 5) and a 24% increase in calls concerning vitamin D (2018, n = 38; 2019, n = 50; 2020, n = 60; 2021, n = 49). Hydrogen peroxide (1%) was used at the dentist as a mouth disinfectant during the pandemic, so the abundant use was seen in our call records. Most of the vitamin D and hand disinfectant exposures were accidental and concerned toddlers. There was also an increase in cases of intentional drinking of hand disinfectants due to their easy availability. Calls regarding intentional poisonings (including drug of abuse and suicide attempts) experienced a slight (13%) increase (2018, n = 342; 2019, n = 351; 2020, n = 369; 2021, n = 413), which has also been the trend for the past few years. There was no increase in calls concerning drugs (such as antivirals) used in the treatment of COVID-19.

Conclusion: The total number of calls to the FPIC was not affected by COVID-19. Some of the most prominent changes during the pandemic were the increase in calls concerning hand disinfectants and hydrogen peroxide. There was no increase in calls concerning COVID-related drugs, which has been the case in some Poison Information Centers in the United States.

210. The increase in accidental exposures to disinfectants and antiseptics related to the COVID-19 pandemic during the second lockdown and the first months of 2021

Anna Celentano[a], Giacomo Genesi[b], Marcello Ferruzzi[a], Paolo Severgnini[b], Giovanni Milanesi[a], Fabrizio Sesana[a] and Francesco Scaglione[a]

[a]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [b]Università degli Studi dell'Insubria, Varese, Italy

Objective: Numerous national and international publications highlight an increase in enquiries for exposures to disinfectants and antiseptics related to the COVID-19 pandemic. The data published in the literature, however, are limited to analyzing the months corresponding to the first period of confinement, while data relating to the second and third pandemic waves are lacking. Our aim was to analyse these exposures in the months following the wave of the pandemic.

Methods: We used descriptive statistics to analyse toxicology consultation volumes to hypochlorite bleaches, disinfectants and antiseptic products for the period 1 February 2020-3 May 2020 (first lockdown), 1 October 2020-31 December 2020 (second lockdown) and we compared these data with that relating to the same periods of 2019 and the period 1 February 2021-3 May 2021.

Results: Compared to 2019, accidental exposures to all the products considered in the study showed an increase of 67.9% in the period February-May 2020, an increase of 26.3% in the period October-December 2020 and an increase of 16.9% in the period February-May 2021. (Table 1). During the period February-May 2020 the respective increases compared to the same period of 2019 were: bleaches (+45.7%), antiseptics (+61.7%), disinfectants (+140.2%); for the period October-December 2020 the respective

Table 1. Distribution of cases and severity of occupational disinfectant exposure.

				Biocidal disinfectants: distribution of severity (PSS)			
Year	All cases	Cases with biocidal disinfectants	Biocidal disinfectants, proportion	No symptoms	Minor	Moderate	Unknown
2018	6,436	313	4.9%	2.9%	85.3%	4.5%	7.3%
2019	7,240	354	4.9%	3.1%	82.2%	5.4%	9.3%
2020	5,755	399	6.9%	0.7%	83.5%	4.5%	11.3%
TOTAL	**19,431**	**1,066**	**5.5%**				

increases compared to the same period of 2019 were: bleaches (+0.3%), antiseptics (+43.2%), disinfectants (+113%). During the period from February to May 2021 compared to 2019 changes were as follows: bleaches (-9.7%), antiseptics (+44.3%), disinfectants (+59%). Respiratory symptoms were present in the majority of cases, followed by gastrointestinal, oropharyngeal, ocular and other routes.
Conclusion: The data highlight how the effect of the COVID-19 pandemic on exposures to antiseptic and disinfectant products in Italy did not end with the first wave, but persists, although with smaller numbers, even in the period of the second wave and in early 2021.

211. Pre- and post-COVID-19 pandemic: acute poisoning among patients in an Emergency Department

Juan Ortega Pérez[a], Jordi Puiguriguer Ferrando[a], Antonio Caballero Bermejo[a], Catalina Homar Amengual[a], Bernardino Barceló Martín[b] and Bernardino Comas Díaz[a]

[a]Hospital Universitario Son Espase, Palma de Mallorca, Spain; [b]Servicio de Análisis Clínicos, Hospital Universitari Son Llàtzer, Palma de Mallorca; Instituto de Investigación Sanitaria de las Islas Baleares (IdISBa), Palma de Mallorca, Spain

Objective: The COVID-19 pandemic has affected daily life in unprecedented ways. Many studies have found dramatic changes in individuals' physical activity, sleep and mental health [1]. This study aimed to analyze retrospectively demographic and clinical characteristics of patients with acute poisoning presenting to the Emergency Department (ED) [2] in three different periods of time (June-July): pre-pandemic (2019), after strict confinement of the Spanish population (2020) and post-pandemic (2021) [3].
Methods: All cases of poisoning in the study periods were reviewed. Demographic variables and the type of intoxication were studied. A comparison was made between the three periods.
Results: All cases of acute poisoning were included (n = 1182, 528 in June-July 2019; 299 in June-July 2020, 355 in June-July 2021). Patients with acute poisoning presenting to the ED decreased during the pandemic (2019: 1.9%, 2020: 1.5%; $p < 0.01$). The ratio male/female increased during the pandemic (2 versus 1.4, p = 0,02). The mean age of the patients increased during the pandemic (2019: 31.4, 2020: 41.3, $p < 0,001$), this tendency was maintained in 2021 (38.3). Poisoning in suicide attempts increased during the pandemic (2019: 8.71%, 2020: 21%; $p < 0.01$), as well as poisoning due to commercialized drugs (2019: 14.20%; 2020: 28.76%, $p < 0.01$), while recreational drug poisoning decreased (2019: 76.1%, 2020: 62%; $p < 0.01$), in 2021 these increased again (69%, p 0.07).
Conclusion: This study has found significant changes in some clinical patterns in patients attending the ED due to acute poisoning in the context of COVID-19, in line with the already described psychological impact of the pandemic.

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212. The impact of the first two waves of COVID-19 on the activities of the Estonian Poisoning Centre (EPIC): the need for quick learning

Mare Oder

Estonian Poisoning Information Centre, Estonian Health Board, Tallinn, Estonia

Objective: Coronavirus disease (COVID-19) reached Europe in March, including Estonia (population 1.3 million) with two waves in 2020. Suddenly all citizens needed new information about cleaning and disinfectants including the need for information on safe usage. People remained at home while almost 90% of poisonings occur at home, therefore an increase in poisonings was expected. In addition to advising on toxicity, the EPIC was also expected to provide constant media information to target groups. Previously planned Poisoning Prevention Week (in March) rapidly required new content. The aim is to analyze the effects of the COVID-19 on EPIC's hotline in order to be better prepared for poisoning prevention in the future.
Methods: A retrospective study analyzing the data from the EPIC's hotline 2019-2020. We compared the number of monthly

Table 1. Comparison of clinical cases relating to hypochlorite bleaches, disinfectants and antiseptic products during the period 1 February 2020-3 May 2020 (first lockdown), 1 October 2020-31 December 2020 (second lockdown) and the period 1 February 2021-3 May 2021.

Agents	Feb-May 2019	Feb-May 2020	Feb-May 2021	Oct–Dec 2019	Oct–Dec 2020	Total 2019	Total 2020
Hypochlorite bleaches	339 (56%)	494 (48.6%)	306 (43.3%)	323 (57%)	324 (45.3%)	662 (56.5%)	818 (47.2%)
Antiseptics	149 (24.6%)	241 (23.7%)	215 (30.4%)	183 (32.3%)	262 (36.6%)	332 (28.3%)	503 (29%)
Disinfectants	117 (19.3%)	281 (27.7%)	186 (26.3%)	61 (10.8%)	130 (18.2%)	178 (15.2%)	411 (23.7%)
Total	605	1016	707	567	716	1172	1732
Symptoms	**Feb-May 2019**	**Feb-May 2020**	**Feb-May 2021**	**Oct-Dec 2019**	**Oct-Dec 2020**	**Total 2019**	**Total 2020**
Respiratory	84	165	103	83	121	167	286
Gastrointestinal	82	85	71	74	73	156	158
Oropharyngeal	54	97	68	67	58	121	155
Ocular	15	40	36	20	48	35	88
Cutaneous	14	24	13	6	11	20	35
Central nervous system	12	17	6	8	12	20	29
Other symptoms	3	9	5	2	3	5	12
Total symptomatic	264 (41.9%)	437 (41.3%)	302 (46.6%)	260 (44.4%)	326 (43.5%)	524 (43.1%)	763 (42.2%)
Total asymptomatic	366 (58.1%)	622 (58.7%)	441 (59.4%)	326 (55.6%)	423 (56.5%)	692 (56.9%)	1045 (57.8%)
Total	630	1059	743	586	749	1216	1808

calls in 2020, as well the number of yearly calls in 2020/2019. The information collected included: type of caller, age group, reason for exposure (accident, intentional), specific type of exposure. Increases or decreases of 10% in parameters with N > 5 were considered a change.
Results: The average number of monthly calls in 2020 was around 325 (an increase of 32% from 2019), with rapid change in 2020 from March compared with February (increased by 65%). The number of calls remained high until the end of 2020. Compared to annual average statistics 2019/2020: there were more calls concerning adults (39%, 1069/1483), while calls regarding children (0-3 years/4-17 years) increased modestly (28%/26%). There was a small change in calls regarding drug poisoning (increasing 17%). Poisoning from chemicals increased 33%, including a marked increase in calls about disinfectants of 505% (22/133 compared 2019/2020), while exposures to mixed chemicals markedly decreased (-97%, 30 poisonings 2019/1 call 2020). Accidents with button batteries increased 76% (38/67 comparing 2019/2020). Many people visited woodland to avoid crowded places and this was associated with an increase in enquiries about mushrooms (149%), snakes (62%), and plants (46%) following the first COVID-19 wave. There was no significant change in the ratio of accidental/intentional poisoning or the ratio of caller type (public/medical professionals), compared 2019/2020.
Conclusion: The COVID-19 pandemic impacted the activity of EPIC significantly and trends were identified. It is possible to assume that the EPIC's active role in the crisis with a strategic communication may be related to the higher number of calls through increased awareness. The identified toxicity trends need more precise targeting in the media for subsequent coronavirus outbreaks.

213. Suicide attempts by overdose of paracetamol and ibuprofen in adolescents and young adults in Switzerland before and after the beginning of the COVID-19 pandemic

Katrin Faber and Colette Degrandi

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

Objective: Paracetamol and Ibuprofen are popular over the counter analgesics and frequently involved in suicidal overdose in adolescents. The aim of the study is to determine trends of paracetamol and ibuprofen overdose in adolescents and young adults before and during the COVID-19 pandemic.
Methods: A retrospective descriptive study of suicide attempts by poisoning in adolescents and young adults (10-25 years) reported to the Swiss National Poison Center before and after the beginning of the COVID-19 pandemic (1 January 2016 to 30 June 2021). Intervention date was defined as end of Q1 2020 (lockdown in Switzerland started on 16 March 2020). Preintervention period was determined as Q1 2016-Q1 2020, postintervention period as Q2 2020-Q2 2021. Data collected included age, sex, time of call (month, year), and substances. Trends for cases involving paracetamol and/or ibuprofen were analysed per quarter (Q), and by patient age.
Results: Overall 7697 cases met inclusion criteria (females n = 5883, males n = 1808, unknown n = 6). Paracetamol was involved in 1864 cases (24.2%), ibuprofen in 1021 cases (13.3%), including 394 cases combining both substances. We recognized a higher proportion of exposures in 13 to 17-year-olds (paracetamol 28.4%, ibuprofen 16.2%), with a maximum proportion in 15-year-olds (paracetamol 30.7%, ibuprofen 18.3%). Comparing the average number of cases per quarter of the preintervention period to the postintervention period revealed an increase of 1.2 with an overproportional rise in paracetamol exposures of 1.4. Suicide attempts by paracetamol were even more common in the 13 to 17-year-olds (rate 1.7) (Table 1). Due to the small numbers in 10 to 12-year-olds trends are not determined.
Conclusion: Paracetamol is involved in a quarter of suicide attempts in adolescents and young adults, even up to a third in the 15-year-olds, whereas ibuprofen plays a less prominent role. The observed increase in paracetamol overdoses in the 13 to 17-year-olds during the postintervention period requires close observation.

214. Suicide attempts by poisoning in adolescents and young adults in Switzerland before and after the beginning of the COVID-19 pandemic

Colette Degrandi and Katrin Faber

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

Objective: Suicide attempts among adolescents and young adults are a significant concern in many countries. The aim of the study was to describe trends in rates of suicide attempts by poisoning in adolescents and young adults before and during the COVID-19 pandemic.
Methods: Retrospective descriptive study of suicide attempts by poisoning in adolescents and young adults (10 to 25 years) reported to the Swiss Poisons Center before and after the beginning of the COVID-19 pandemic (1 January 2016-30 June 2021). Intervention date was defined as end of Q1 2020 (lockdown in Switzerland started on 16 March 2020). Preintervention period was determined as Q1 2016-Q1 2020, postintervention period as Q2 2020-Q2 2021. Data collected included age, sex and time of call (month, year). Trends were analysed per quarter (Q), and by patient age.
Results: Overall, 7697 cases met inclusion criteria (females n = 5883, males n = 1808, unknown n = 6). Most calls were reported for 15-year-olds (n = 936), followed by 17 (n = 732), 16 (n = 712), 18 (n = 673) and 14-year-olds (n = 631). The number of cases per quarter was stable until Q3 2020. From Q4 2020 the number of cases started to increase (Table 1). Comparing average number of cases per quarter of the preintervention period to the postintervention period revealed an increase of 1.4 in the 13 to 17-year-olds (1.4 in 13y, 1.5 in 14y, 1.3 in 15y, 1.3 in 16y, 1.3 in 17y). No increase (rate 1.0) was seen in the 18 to 25-year-olds (1.1 in 18y, 1.3 in 19y, 0.9 in 20y, 1.1 in 21y, 1.3 in 22y, 0.8 in 23y, 0.7 in 24, 0.9 in 25y).
Conclusion: The frequency of suicide attempts by poisoning among 13 to 17-year-olds started to increase two quarters after the intervention date, whereas the frequency among the 18 to 25-year-olds remained stable. The observed trend in the 13-17-year-olds is concerning and requires close observation.

215. Comparison of selected epidemiological features of acute poisoning in young people between 2019 and 2020

Table 1. Trends in suicide attempts by paracetamol and ibuprofen in 13 to 17-year-olds and 18 to 25-year-olds during the preintervention and postintervention period. Q = quarter, y = years.

				13-17y			18-25y		
	Total	Paracetamol	Ibuprofen	13-17y	Paracetamol	Ibuprofen	18-25y	Paracetamol	Ibuprofen
Preintervention Period Q1 2016-Q1 2020 Number of cases, average/Q, median/ Q, range	5707, 336, 339	1322, 78, 78	752, 44, 46	2401, 141, 143	636, 37, 39	384, 23, 21	3148, 185, 185	650, 38, 37	340, 20, 21
Postintervention Period Q2 2020-Q2 2021									
Q2 2020, n	322	79	37	149	44	23	164	30	13
Q3 2020, n	329	81	49	143	47	28	181	33	21
Q4 2020, n	391	120	56	187	69	31	200	48	23
Q1 2021, n	446	125	73	227	76	41	206	46	28
Q2 2021, n	502	137	54	269	85	40	213	45	12
Rate (preintervention period/ postintervention period)	1.2	1.4	1.2	1.4	1.7	1.4	1	1.1	1

Zanina Perevska, Natasha Simonovska, Aleksandra Babulovska, Afrodita Berat-Huseini, Kiril Naumovski and Kristin Kostadinovski

University Clinic of Toxicology, University Ss Cyril and Methodius, Skopje, North Macedonia

Objective: COVID-19 has changed the social life-style of young people. The aim of our study was to assess the difference in selected demographic and clinical characteristics of adolescents and young adults (14-24 years) treated at the Clinic of Toxicology during 2019 and 2020.
Methods: The study was retrospective, observational and cross-sectional, analyzing data from the Poison Information Center at the University Clinic of Toxicology during 2019 and 2020. The observed variables were age (divided into 2 groups with 19 years old as the cut off value), in/outpatient treatment, circumstances of poisoning (suicide, accidental, abuse and unknown), outcome (recovery, postponed) and agents (medicine, alcohol, psychoactive substances (PAS), chemicals and others).
Results: Poisoning in young patients presented a percentage decrease of 20.4% in 2020 and without lethal outcome. There was no significant difference in gender distribution in the two study years (X^2=1.456, df =1, P = 0.228, RR =0.917), with an increased number of male patients of 9% in 2020 and their presentation of 57% in the total number of patients. Significant association was registered between the circumstances of poisoning and 2020 (X^2= 5.607, df =1, P= 0.001) with increased accidental poisoning in patients younger than 19 years (X^2=9.694, df =1, P = 0.002). Suicidal poisonings in those above 19 years increased by 32.9% (X^2= 3.610, df =1, P = 0.057) from 2019 to 2020 and abuse decreased in both age groups, but was significantly reduced in those aged over 19 years (X^2=7.921, df =1, P = 0.008). There was an association of gender with suicide in patients under 19 years old (X2 = 4 5.483, df =1, P < 0.001) with males at 3.51 higher risk for suicide (RR =3.52, 95%CI 2.283-5.400) compared to the over 19 years group, where females were at increased risk for suicide (X^2=26.923, df =1, P < 0.001). Poisoning with medicines were decreased by 38.9% in the under 19 years group (P = 0.837) in 2020. There was no significant association between distribution of type of poisoning and the two observed years (X^2= 10.673 df= 6, P = 0.099). Poisoning with medicines (P < 0.001), inpatient treatment (P < 0.001), and increasing age (P = 0.006) were associated with increased likelihood of suicidal poisoning ($\chi^2(12) = 583.057$, P < 0.001).
Conclusion: Acute poisoning in patients aged 14-24 years during the pandemic in 2020 decreased with increased male patients and without registered lethal outcome. There were increased accidental poisonings in patients under 19 and suicidal poisoning in patients above 19 years. Males younger than 19 years were at higher risk of suicide compared to males aged over 19 years.

216. Methanol intoxication outbreak during the COVID-19 pandemic in Cape Town, South Africa: a case series

Cindy R. Stephen[a], Kate H. Balme[a], Cathrin Bissbort[b], Bronwen Davies[c] and Lorna J. Martin[c]

[a]Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa; [b]False Bay Hospital, Western Cape Department of Health, Cape Town, South Africa; [c]Division of Forensic Medicine and Toxicology in Department of Pathology, University of Cape Town, Cape Town, South Africa

Objective: Methanol poisoning may result in significant morbidity and mortality, particularly during poisoning outbreaks in low-and-middle-income countries (LMIC) [1]. Although not readily available to the public in South Africa, methanol may be used as a substitute for ethanol in alcoholic beverages or to fortify illicit spirits. Following the announcement of the global COVID-19 pandemic, the South African government declared a State of Emergency in March 2020 which amongst other things prohibited the consumption, sale and transportation of alcohol [2]. We aim to describe the clinical presentation, diagnosis, treatment and outcome of a series of cases presenting to a Cape Town hospital after reportedly drinking illicit alcohol.
Case series: We performed a retrospective case record review using the available records for 19 of 24 patients presenting to False Bay Hospital during June 2020 with presumed methanol poisoning. Almost all the patients were male (n = 18), with a mean age of 35.1 years (SD =7.3). At least half of the patients had central nervous system effects (n = 12; headache, ataxia, confusion, weakness), as well as gastrointestinal symptoms (n = 10; abdominal pain, nausea, vomiting), and 5 patients reported visual loss. Time from exposure to presentation varied from 12 hours to 8 days, with 47.4% (n = 9) presenting within the first 24 hours. On admission, venous blood gas samples from the patients showed the following mean values: pH of 7.14 (SD =0.23); serum bicarbonate 17.4 (SD =8.5) mmol/L; base deficit of -7.8 (SD =11.6) mmol/L, and lactate concentration of 4.1 (SD =4.0) mmol/L. Assays to measure methanol or formate concentrations were

Table 1. Trends in suicide attempts by poisoning in 13 to 17-year-olds and 18 to 25-year-olds during the preintervention and postintervention period.

	Time period (quarter)	Total	13-17 years	18-25 years	10-12 years
Preintervention period	Q1 2016-Q1 2020	5707	2401	3148	158
Number of cases					
Average/Q		336	141	185	9
Median/Q		339	143	185	8
Range		296-378	99-172	163-214	6-16
Postintervention period	Q2 2020	322	149	164	9
Q2 2020-Q2 2021	Q3 2020	329	143	181	5
Number of cases	Q4 2020	391	187	200	4
	Q1 2021	446	227	206	13
	Q2 2021	502	269	213	20
Rate (preintervention period/postintervention period)	–	1.2	1.4	1.0	Not determined due to small numbers

not performed as these are not routinely available. Ten patients (52.6%) received both ethanol via nasogastric tube and intravenous sodium bicarbonate. Haemodialysis was considered for one patient but never started due to intensive care unit (ICU) resource constraints with COVID-I9 admissions. The mortality rate was 26.3% (n = 5) and one patient had ongoing visual loss.
Conclusion: To the authors' knowledge, this is the first published data concerning a methanol poisoning outbreak in South Africa. As described in other LMICs, the mortality rate was high, diagnosis was difficult, and access to ethanol antidote and supportive care was challenging, particularly during the COVID-19 pandemic.

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217. Poison Center hand sanitizer exposure characterization peri- and during the COVID-19 pandemic

Shireen Banerji and Christopher O. Hoyte
Rocky Mountain Poison & Drug Safety, Denver, United States

Objective: Poison centers frequently manage calls involving ethanol-containing hand sanitizers. During the 2020 COVID-19 pandemic, our Specialists in Poison Information sensed rising numbers of cases. The increased use was not surprising due to the desire to sanitize skin and reduce transmission of COVID-19. We sought to compare hand sanitizer trends pre-pandemic and during the pandemic including a sub-analysis for children 0-5 years.
Methods: We queried the National Poison Data System for human exposures of all ages within our 4-state poison center from 1 January 2015 to 31 October 2021. Generic codes for all types of hand sanitizers were included plus 2 product codes for methanol-containing hand sanitizer. Data captured included age range, product type, reason, gender, route, clinical effect, medical outcome, month, management site, and therapies. The query was repeated for the same parameters in children 0-5 years old. Descriptive statistical analyses were utilized.
Results: Our poison center managed 5,819 human hand sanitizer exposures during the study period; 67% occurred in children 0-5 years old. From 2019 (n = 723) to 2020 (n = 1,272), hand sanitizer exposures increased by 76%, 38% [all ages, children 0-5 years]; 52% were male. Most [77%, 99%] of these exposures were unintentional and [89%, 96%] involved ingestion as the primary route and exposures in children 0-5 years represented 64% of the total number of ingestion cases. Exposures in 2020 occurred throughout the year with higher volumes in March and July through December. Most cases were managed on-site (non-hospital) [81%, 89%], with [18%, 11%] evaluated in or referred to a hospital. Most [87%, 89%] clinical outcomes were minor or no effect overall, with similar numbers in 2020 [82%, 87%]. The top clinical effect in children 0-5 years was vomiting. For all ages, the most common effects were vomiting, nausea, and drowsiness. There was one death involving an adult who intentionally consumed hand sanitizer as an alcohol substitute. The product was contaminated with methanol and he died from methanol intoxication. Non-ethanol or isopropanol hand sanitizers were involved in 10% of exposures during the study period and 19% of exposures in 2020.
Conclusion: We confirmed our suspicion that hand sanitizer exposures rose significantly in 2020. Explanations include increased usage and availability in the home paired with more time spent at home overall due to coronavirus school restrictions, working from home, and quarantine. Fortunately, even during 2020, most medical outcomes resulted in none or minor effects. Additional sub-analyses are needed to characterize other aspects including non-ethanol hand sanitizer exposures.

218. Occurrence of adverse drug reactions after Comirnaty® vaccine administration against SARS-CoV-2 in healthcare workers: a pilot study

Lucia Bernasconi[a], Valeria M. Petrolini[a], Cristina Grazioli[a], Valentina Negrini[a], Benedetta Brolli[a], Paola Baiardi[b], Anna Losurdo[c], Luisa Gervasio[d], Letizia Borra[a], Elisa Roda[a], Fabio Blandini[e], Saverio Robustelli Della Cuna[d], Valentina Tibollo[f], Olha Maystrova[a], Eleonora Buscaglia[a] and Carlo A. Locatelli[a]

[a]Pavia Poison Control Centre - National Toxicology Information Centre - Clinical and Experimental Lab, Toxicology Unit, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [b]Scientific Directorate, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [c]Hospital Pharmacy, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy; [d]Hospital Pharmacy, Mondino Foundation IRCCS, Pavia, Italy; [e]Scientific Directorate, Mondino Foundation IRCCS, Pavia, Italy; [f]Laboratory of Informatics and Systems Engineering for Clinical Research, Maugeri Clinical and Scientific Institutes IRCCS, Pavia, Italy

Objective: A prospective observational study aimed at monitoring adverse drug reactions (ADR) in healthcare workers after a SARS-CoV-2 vaccination campaign was started in January 2021. We report preliminary results obtained from the pilot study.

Methods: The first 300 Sars-CoV-2 vaccinated subjects (2 Comirnaty® (BioNTech, Pfizer) doses administrated 21 days apart) that signed informed consent were enrolled in the pilot study. For each patient, age, sex, body-mass-index (BMI), ADRs after vaccination and SARS-Cov-2-antibodies titer (quantitative evaluation of the neutralizing S1-RBD-IgG using Anti-SARS-CoV-2 QuantiVac ELISA (IgG)® Euroimmun diagnostic assay) were collected. The evaluation of SARS-Cov-2-antibodies was performed at the time of first dose administration (T0) and followed by four subsequent evaluations at different time-points. ADR developed within the first 8 days after the first and second dose were recorded. Exclusion criterion were cases with incomplete data. ADRs were divided into local (at injection site) and systemic, and their occurrence was correlated to sex, BMI and presence of SARS-Cov-2-IgG at T0. Fisher's exact test, Wilcoxon-Mann-Whitney test and multivariate logistic regression models were used for statistical analyses; $p < 0.05$ was considered significant.

Results: In total 297 subjects (72.4% females; 98.9% Caucasians, mean age 47 years) were included. Fifty (16.5%) subjects were positive for SARS-CoV-2-antibodies at T0. ADRs were reported in 67% and 74.1% of subjects after the first and second dose, respectively. Systemic ADRs were more common after the second dose (59.1% of subjects) compared to the first dose (31.4%). Systemic ADRs were reported in 44% of subjects positive for SARS-CoV-2 antibodies (22/50) and in only 28.9% of negative subjects (71/246) ($p = 0.044$); this correlation was significant for fever ($p = 0.017$) and lymphadenopathy ($p = 0.008$). Systemic ADRs after the first dose occurred in 36.7% (79/215) of females and in 17.1% (14/82) of males ($p = 0.0012$), while they occured in 63.7% (137/215) and 46.34% (38/82) after the second dose, respectively ($p = 0.0082$). No correlation was found between ADR and BMI after both doses.

Conclusion: These preliminary results demonstrate higher prevalence of systemic ADRs after a second dose and a positive correlation between female and ADRs after both the first and second doses. Moreover, there was a positive correlation between the presence of SARS-CoV-2-antibodies and systemic ADRs after the first dose. These data support the hypotheses that systemic reactions (fever, lymphadenopathy) could be a clinical expression of immune system reactivity to vaccination, which is greater in subjects with SARS-CoV-2-antibodies at the time of the first administration. These results will require confirmation from a greater sample size.

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