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North American Congress of Clinical Toxicology (NACCT) Abstracts 2017

1. Effect of methylene blue on mortality in a porcine model of amlodipine toxicity

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Background: Cardiovascular medication overdose causes significant morbidity and mortality in the US. In 2015, the National Poison Data System responded to over 2.1 million exposures, 103,339 related to cardiovascular drugs. Cardiovascular drugs were the seventh most frequently involved substance and rated as the fourth category with the greatest rate of increase in exposure. Despite maximal supportive pharmacologic therapy (including vasopressor administration, high-dose insulin therapy, lipid emulsion therapy, and extracorporeal life support), there are still cases of refractory shock leading to death. *In vitro* studies on canine arteries exposed to amlodipine have shown that it stimulates release of nitric oxide (NO) leading to peripheral vasodilation. Amlodipine overdose could therefore be managed by scavenging NO. Methylene blue (MB) inhibits NO directly but also inhibits NO production by inhibiting guanylyl cyclase and endothelial NO synthase activity. We developed a porcine model of amlodipine toxicity and compared the effects of MB versus traditional vasopressor therapy with norepinephrine (NE), with time to death as the primary outcome.
Methods: Animals were anesthetized and instrumented with monitoring devices according to previous protocols in our institution and a pilot study was first completed to establish a lethal model of amlodipine toxicity. Each of the two groups of animals received a toxic dose of amlodipine. A continuous infusion of amlodipine with accelerating doses was given to mimic overdose and continuing gastrointestinal absorption. After 70 min of amlodipine infusion, each group was resuscitated with 20 mL/kg of normal saline. Animals in each group were then randomized to receive either MB or NE therapy. Hemodynamic parameters, including mean arterial pressure, cardiac output, were measured every 10 min.
Results: The primary outcome was time to death. Survival times were compared using a Kaplan–Meier analysis, and the two groups were compared with the log-rank test. The study was powered at 80% to detect a hazard ratio of 0.2 (MB versus NE), assuming a two-sided log-rank test with alpha = 0.05. Nine animals per group were required for adequate power. An interim analysis was conducted after 15 of the initially planned 18 animals were completed (seven MB and eight NE). This revealed that, for the primary outcome, MB was clearly not superior to NE. Furthermore, it would be impossible to achieve a statistically significant effect for the MB hazard ratio with the addition of three pigs, regardless of the outcome. Therefore, the study was ended prematurely. Overall, one of the seven (14%) animals in the MB group survived to 300 min compared with two of the eight animals (25%) in the NE group. Median survival time was 100 min for the MB group and 177 min for the NE group. Survival time did not differ by group (log-rank test, $p = .29$) but there was a non-significant trend toward longer survival in the NE group.
Conclusions: In this newly developed porcine model of amlodipine toxicity, MB did not lead to increased time to death as compared with NE poisoned animals. Whether MB is beneficial in combatting distributive shock in amlodipine toxicity remains unclear and requires further study.

KEYWORDS Amlodipine; overdose; methylene blue

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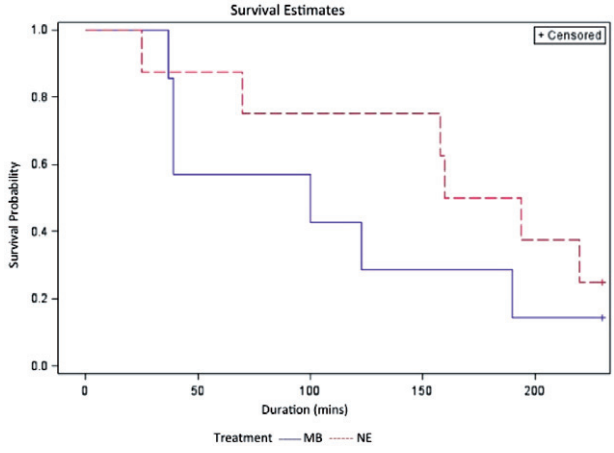

2. A regional poison control center's role in the public health response to multiple harmful algal blooms

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Background: Harmful algal blooms (HAB) are large densities of cyanobacteria that pose a risk to public health. At present, HAB-associated illness is likely underreported and poorly understood. We describe a collaborative effort between a regional poison control center (PCC), the state's department of environmental quality (DEQ), and department of health (DOH) in responding to and tracking public health concerns during an unprecedented HAB season.
Methods: Following a smaller-scale HAB, the PCC, DOH, and DEQ developed signage and a communication plan for future HAB. During the summer of 2016, three bodies of water, and numerous secondary waterways used for irrigation and recreation in the PCC service area were closed as a result of HAB. The public was encouraged to contact the PCC with HAB-associated questions or

potential exposures through posted closure signs and news releases. Throughout the HAB season the PCC, DOH, and DEQ participated in regular conference calls. DEQ requested PCC gather data on location of exposure and recreation activity. DOH granted PCC staff access to CDC's One Health Harmful Algal Bloom System (OHHABS), a database created to track HAB-associated illness.
Results: The PCC immediately began taking HAB-associated exposure and information calls following closure of the first body of water. On the day of the first waterway closure, the PCC experienced a 200% increase in average case volume, documenting 246 (32.5%) HAB-associated cases. Throughout the duration of the HAB season, the PCC documented 758 HAB-associated cases from all impacted waterways. There were 642 (84.7%) exposures to HAB and 116 (15.3%) HAB-associated information cases. Human exposures accounted for 609 (94.9%) cases and animals for 36 (5.6%). There were 231 (30.5%) cases of HAB-associated illness that met criteria for input into OHHABS. Specific exposure location was captured in 222 (96.1%), and recreation activity in 217 (93.9%) of cases reporting HAB-associated illness. Regular communication successfully alerted PCC staff of key messages and water body status. Identifying reopening of waterways was more challenging, as these decisions were not made at the state level. Regular communication also provided a venue to address unanticipated consequences of the HAB such as using contaminated water for irrigation/agriculture, consuming food irrigated with the water, or consuming fish caught from contaminated waterways.
Conclusions: Collaboration between the PCC and state agencies resulted in an immediate response to public health concerns during a busy HAB season. Coordination between organizations allowed for standardized data collection, increased understanding of the impact of HABs on public health, and will inform decision making during future HABs.

KEYWORDS Harmful algal bloom; cyanobacteria; cyanotoxins

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3. Efficacy of intramuscular cobinamide in a swine model of severe hydrogen sulfide poisoning: a prospective trial

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Background: Hydrogen sulfide (H2S) is one of the leading causes of unintentional workplace gas inhalation deaths and is a chemical terrorist threat. Significant exposures (50–400 ppm) may produce difficulty in breathing, agitation, confusion, nausea and vomiting, elevated blood pressure, and loss of consciousness. Several potential antidotes have been used for hydrogen sulfide poisoning, but none have been consistently successful. We previously reported that intravenous cobinamide successfully rescues severely NaHS-poisoned swine from apnea in the absence of assisted ventilation; however, intramuscular administration is preferred in a workplace or mass casualty scenario.
Objective: To compare hemodynamic variables and survival of swine with acute NaHS-induced apnea treated with intramuscular (IM) cobinamide or control (no treatment) in a swine model that replicates a clinically relevant prehospital/mass casualty scenario.
Methods: Eleven swine (five cobinamide/six control), weighing 45–55 kg were anesthetized, intubated, and instrumented with continuous femoral and pulmonary artery pressure monitoring. After stabilization, anesthesia was adjusted such that animals would spontaneously ventilate with a FiO2 of 0.21. NaHS (concentration 8 mg/mL) solution was administered at 0.9 mg/kg/min and continued until apnea or mean arterial pressure less than 45 mmHg, at which time 3 mL of cobinamide (concentration 200 mM) was administered intramuscularly to the treatment group. Immediately after treatment, the NaHS solution was decreased to 0.4 mg/kg/min for 1 min, then decreased to 0.2 mg/kg/min for 10 min. Animals were observed for 60 min post-treatment. A priori, death was defined as a mean arterial pressure less than 20 mmHg for 10 min. Survival time was analyzed by developing Kaplan–Meier curves for each group and the survival distributions were compared using a 3-sample log-rank test using Kaplan–Meier analysis. Repeated measures ANOVA was used to calculate 95% confidence intervals of hemodynamic variables. A sample size of five animals per group were needed for a beta of 0.8 and an alpha of 0.05 to detect an 80% difference in survival.
Results: There were no significant differences in baseline hemodynamics, weights or blood chemistries, and arterial blood gases were normal in both groups. There were no significant differences in the mg/kg dose of NaHS required to produce apnea or MAP less 45 mmHg (9.04 ± 6.16 mg/kg cobinamide versus 5.90 ± 5.54mg/kg control (95% CI of difference 11.32, −5.04). All cobinamide-treated animals survived (5/5), none of the control (0/6) animals survived. Kaplan–Meier method of survival analysis clearly showed a significant difference by group (log rank $p < .001$) with almost all control animals dying at 10–15 min after the trigger. Mean systolic blood pressure 10 min post-treatment was 101.20 ± 17.06 mmHg for cobinamide treated animals versus 37.75 ± 19.08 mmHg for control (95% CI difference 2.94, 123.96). Lactate concentrations were greater in the control group (95% CI difference −5.18, −1.32).
Conclusions: Intramuscular cobinamide successfully rescued the severely NaHS-poisoned swine in the absence of assisted ventilation or vasopressor support in our clinically relevant prehospital swine model.

KEYWORDS Hydrogen sulfide poisoning; cobinamide; swine model

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4. Graft failure rates of organs transplanted from poisoned patients compared with other causes

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Introduction: In 2015, the number of organ transplants in the United States surpassed 30,000 but the waiting list for an organ transplant exceeded 120,000 patients. Deaths from poisoning and overdose has increased over the past two decades largely due to the ongoing opioid epidemic. Despite fears of transmission of poisons and associated infectious diseases from organs transplanted from these patients, little is currently known about outcomes of organs procured from poisoned patients as they compare with those procured from patients with other causes of death.
Methods: This is a retrospective cohort analysis of one region's organ donation registry utilizing the Gift of Hope Organ & Tissue Donor Network. Gift of Hope is a not-for-profit organ procurement

Table 1. Types of Organs Transplanted by Mechanism of Donor Death and Graft Failure Rate

	Kidney	Liver	Lung	Heart	Pancreas	Intestine	Total	Graft Failure
Drug Intoxication	133	61	22	37	12	0	264	3 (1.15%
Brain	89	72	29	30	12	2	234	5 (2.14%
Cardiac	142	31	2	0	6	0	181	10 (5.2%

Table 2. Organs Donated per Donor Patient for Select Organ Types

	Drug Intoxication (n=81)	Brain (n=81)	Cardiac (n=81)
Kidneys	1.64	1.10	1.75
Liver	0.75	0.89	0.38
Lung	0.27	0.36	0.02
Heart	0.46	0.37	0.00
Pancreas	0.15	0.15	0.07
Total Organs	3.36	2.89	2.23

organization that is a one of the 58 organizations that make up the US organ procurement system and covers an area including two states. Registry data of organ transplants from September 2015 to March 2017 for organs procured from drug-intoxication deaths (DD) was compared with the same number of donors with non-drug causes of brain deaths (BD) and cardiac deaths (CD). Proportions of graft failures between groups were compared using Fisher's exact test. For the purposes of analysis, double lung procurement and transplantation was counted as a single organ.

Results: Over the study period, there were 81 DD organ donors and 264 individual organs transplanted from these donors. These were compared with 81 donors each from the BD and CD groups with 234 and 181 organs transplanted, respectively. Total numbers of organ types transplanted and graft failures per group are shown in Table 1. The number of organs donated per donor patient was 3.36 organs, 2.89 organs, and 2.23 organs for the DD, BD, and CD groups, respectively. Organ donation rates per individual donor are shown in Table 2. The DD group had three graft failures (1.15%) compared with five (2.14%) and 10 (5.52%) graft failures in the BD and CD groups, respectively. The difference in graft failure rates between the DD and BD groups was less than 1% ($p = .48$) and the difference in graft failure rates between the DD and CD groups was 4.37% ($p = .01$). The three graft failures in the DD group were lung (one), kidney (one), and liver (one). The five graft failures from the BD group were lung (three), liver (one), and pancreas (one). The 10 graft failures from the CD group were kidney (eight) and liver (two).

Conclusions: Utilizing existing organ procurement and transplantation methods, organs procured from patients with drug-intoxication deaths had a similar graft failure incidence compared with those from non-drug brain deaths and a decreased graft failure incidence compared with those from non-drug cardiac deaths. Additionally, it appears that the total number of organs donated per donor patient is greater in the drug death group. Reasons for these findings may be due to the lower age and improved relative health of this group prior to death. These data support the argument that patients that die from poisoning are suitable organ procurement candidates.

KEYWORDS Organ donation; graft failure; transplant

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5. Passive poison center exposure identification using the electronic medical record

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Background: Poison Control Centers (PCC) perform a vital public health surveillance role. PCC data is frequently cited in epidemiologic reports. However, PCC data suffers limitations including the need for active reporting and reliance on verbally communicated clinical information which may be inaccurate or misunderstood. PCC call volumes have demonstrated an increasing percentage of hospital-based calls and case complexity. Nevertheless, many hospital cases are not reported to PCCs. As a designated public health authority and source of data which contributes to policy development, PCCs are granted the capability of performing surveillance without violating HIPAA. We hypothesized that by performing a regular query of a health system electronic medical record, cases could be identified and accurately coded in our database thereby enhancing our public health capabilities and increasing the value of our PCC's data.

Methods: A regional PCC incorporated within a healthcare system was granted access to the electronic medical record of that system with "read-only" privileges. After review by legal and privacy offers, a process of daily case review was approved for surveillance and quality assurance purposes. A list of "Primary Diagnosis" search terms was developed. A daily search of 17 EDs, all within the PCC service area, using the system electronic medical record (EMR) was

performed and a spreadsheet sent securely to poison center staff. Cases were then divided among staff members. Using the EMR, including clinical notes, vital signs, electrocardiograms, and laboratory results, the cases were reviewed and entered in the local PCC database. Cases in which the PCC had already been called or clearly not associated with a poison exposure were removed. Specialists were encouraged to contact the care team to provide recommendations when appropriate.

Results: In the first 173 days of this process, 6703 additional cases were identified. Of those, 2127 (32%) involved opioids including prescription opioids, heroin, and fentanyl. Fifty percent (3321/6703) involved toxicity and complications of ethanol use. The remaining 18% of cases included a variety of medications, environmental toxins, and illicit drugs. A majority of staff indicated that they had called healthcare providers to give treatment recommendations based on these case reviews, but that statistic was not prospectively tracked.

Conclusions: Passive collection of exposures through the use of EMR is feasible. A large majority of exposures that are not reported to PCCs include commonly encountered toxins. It is likely that the common nature of these exposures leads to underreporting by healthcare providers as immediate assistance in management is typically not required. However, given the current public health implications of these poisons, particularly opioids, and the need for substantive information related to overdose survivors, gathering this data is critical to fulfilling our public health role and maintaining the value of PCCs. Patients may also directly benefit through poison center intervention in hospitalized patient care. Efforts to develop similar programs at poison centers throughout the country as well as appropriate case definitions in NPDS may improve patient care and overall volume and quality of poison center data.

KEYWORDS Poison center; data collection; electronic medical record

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6. Early FabAV treatment improves time to full limb function recovery in patients with copperhead envenomation

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Background: Nearly half of all US crotaline envenomations are by copperhead snakes. A recent Phase IV clinical trial demonstrated improved recovery of limb function with administration of Fab antivenom (FabAV) compared with placebo. However, it remains unclear if time to antivenom administration impacts recovery.
The objective of this study is to determine if early administration of FabAV reduces the time to full recovery of limb function in patients with mild or moderate copperhead envenomation.

Methods: A secondary analysis of the multi-center, Phase IV, randomized, double blind, placebo controlled trial of FabAV in copperhead envenomation was performed. Patients ≥12 years with a mild or moderate copperhead envenomation were randomized to FabAV or saline placebo. Mild envenomation was defined as swelling crossing 0-1 major joints and moderate envenomation as swelling crossing two major joints. Patients with severe venom effects, envenomations proximal to the elbow or knee or on >1 extremity, and those presenting >24 h post-envenomation were excluded. Patient recovery was assessed using the Patient Specific Functional Scale (PSFS), which collects patient reported functional impairment on outcomes the patient has identified as important. The PSFS was administered every 3–4 d post-envenomation until day 28. Patients that were not recovered by day 28 were followed up to an additional 3 months. A survival analysis was conducted to determine if time to treatment had a significant effect on time to full recovery through 28 d post-envenomation.

Results: Forty-five patients received FabAV. The mean age was 43.9 years, 93% were adults, 51% were male, and 89% had a mild severity envenomation. The median time to treatment was 5.47 h post-envenomation. Twenty-two (49%) patients were treated early (<5.47 h) and 23 (51%) late. A greater proportion of patients treated early had recovered at each time point compared with those treated late (Table). Overall, patients treated with FabAV early had a significantly shorter time to full recovery than those treated late ($p = .03$).

Conclusions: Early administration of FabAV to patients with mild and moderate copperhead envenomation resulted in faster full recovery compared with late treatment with FabAV.

KEYWORDS Copperhead; antivenom; snakebite

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Table. Recovery by Days Post-Envenomation

Day Post-Envenomation	Early (<5.47 hours) (%)	Late (=5.47 hours) (%)	Total (%)
3	4.5	4.3	4.4
7	22.7	8.7	15.6
10	36.4	8.7	22.2
14	40.9	17.4	28.9
17	54.5	21.7	37.8
21	68.2	34.8	51.1
24	72.7	43.5	57.8
28	86.4	65.2	75.6

7. A randomized trial of intramuscular olanzapine versus oral clonidine for symptomatic treatment of opioid withdrawal in the emergency department

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Background/Objectives: Patients experiencing withdrawal from opioids may present to the Emergency Department (ED) for symptoms associated with this clinical syndrome. Although outpatient programs can implement long-term opioid withdrawal treatment with agents such as methadone or buprenorphine, currently most EDs do not have the resources or infrastructure to initiate such treatments. Therefore, ED management of opioid withdrawal generally entails symptomatic control. The alpha-2 agonist clonidine is often considered the first-line agent for ED treatment of acute opioid withdrawal symptoms, but we hypothesized that intramuscular olanzapine would be superior to clonidine in this clinical scenario.

Methods: This was a prospective, randomized clinical trial comparing 10 mg of intramuscular olanzapine to 0.3 mg of oral clonidine for the symptomatic treatment of acute opioid withdrawal in the ED. All adult ED patients reporting a history of ongoing opioid

use with symptoms consistent with withdrawal necessitating medical treatment were screened for eligibility Patients were excluded if they had already received any treatment during the ED encounter. If enrolled, patients were randomized 1:1 to receive either olanzapine or clonidine for their initial medical treatment. A baseline Clinical Opiate Withdrawal Scale (COWS) score was calculated, and information regarding opioid use history was recorded. After 30 min post-study medication administration, the patient could receive any additional treatment at the ED physician's discretion. The primary efficacy outcome was need for any rescue medication within 1 h of study medication administration. Secondary outcomes included additional rescue medications needed after 1 h, change in COWS score from baseline, time in department, and any adverse reactions from the study medications.

Results: We present preliminary data on the first 46 subjects enrolled. The target enrollment for adequate power is 56 patients based on *a priori* sample size calculations. Thus far, 28 patients were randomized to receive olanzapine and 18 patients were randomized to receive clonidine. All 46 enrolled subjects received study medications and were analyzed on an intention-to-treat basis. Baseline and demographic characteristics of the two groups are depicted in Table 1. Regarding the primary outcome, in the olanzapine group, 8/28 (29%) patients required rescue medication within 1 h of treatment, and in the clonidine group, 12/18 (67%) patients required rescue medication within 1 h of treatment, yielding a difference between the two groups of 38% (95% confidence interval of the difference 11–66%). Details of rescue medications administered as well as secondary outcomes are depicted in Table 2.

Conclusions: The ED treatment of symptomatic acute opioid withdrawal with 10 mg of intramuscular olanzapine results in a lower incidence of rescue medication administration and improved symptoms (utilizing the COWS scale) at 1 h when compared with 0.3 mg of oral clonidine. Adverse events were uncommon, and occurred at a similar rate for both groups. Total time in the ED was similar for both groups.

KEYWORDS Opioid; withdrawal; antipsychotic

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Table 1. Demographic and Baseline Data on Study Subjects

Variable	Olanzapine Group (n=28)	Clonidine Group (n=18)
Age (Standard Deviation)	39 (12)	41 (12)
Gender (male)	19 (67%)	9 (50%)
Chronicity of Opiate Use		
Less than 6 months	4 (14%)	2 (11%)
Between 6 months and 1 year	2 (7%)	3 (17%)
Between 1 year and 5 years	9 (32%)	5 (28%)
Greater than 5 years	13 (46%)	8 (44%)
Previously Received Naloxone	7 (25%)	3 (17%)
Previous Opioid-Related ED Encounter	14 (50%)	9 (50%)
Previous Treatment/Detoxification Program	13 (46%)	67 (39%)
Opiates Used Within Last 7 Days		
Heroin	18 (64%)	9 (50%)
Methadone	6 (21%)	5 (25%)
Oxycodone/Hydrocodone	5 (18%)	4 (22%)
OxyContin®	2 (7%)	1 (6%)
Buprenorphine	1 (4%)	1 (6%)
Hydromorphone	0	1 (6%)
Hours Elapsed Since Last Use (median, range)	48 (3-96)	48 (2-120)
Baseline COWS Score (median, range)	12 (4-23)	11 (5-22)

Table 2. Primary and Secondary Outcomes

PRIMARY OUTUCOME	Olanzapine (n=28)	Clonidine (n=18)	Difference
Rescue Medication within 1 Hour	8 (29%)	12 (67%)	P=0.01
Rescue: Clonidine	4 (14%)	1 (6%)	NA
Rescue: Olanzapine	4 (14%)	7 (39%)	NA
Rescue: Ondansetron	2 (7%)	6 (33%)	NA
Rescue: Ibuprofen/Acetaminophen	2 (7%)	2 (11%)	NA
Rescue: Diphenhydramine	1 (4%)	0	NA
Rescue: Benzodiazepines	0	0	NA
SECONDARY OUTCOMES			
Rescue Medication, within 2 Hours	11 (39%)	14 (78%)	P=0.01
Rescue Medication, entire encounter	14 (50%)	15 (84%)	P=0.02
Change in COWS score, 1 hour	9.6	6.4	P=0.04
Change in COWs score, disposition	10.6	9.4	P=0.52
Time in Department (mean minutes)	318	308	P=0.70
Adverse Reactions			
Akathisia	0	0	NA
Dystonia	0	0	NA
Hypotension	0	1 (6%)	p=0.21
Allergic Reaction	0	0	NA
Respiratory Depression	0	0	NA

Patients may have received more than one rescue medication

8. A prospective study of the QTc prolonging effect of intravenous ondansetron administered to children with gastroenteritis

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Background: In 2011, the US FDA reported the potential for ondansetron to cause QT prolongation and fatal dysthrhythmia. Numerous case reports suggest that QTc prolongation and dysrhythmias resulting from intravenous ondansetron are of concern. Little data regarding the QT prolonging effect of ondansetron in children exists, and no thorough QT studies on this topic have been published.

Objective: We seek to evaluate the effect of intravenous ondasetron on QT by conducting a prospective study on the effect of a standardized dose of intravenous ondansetron on the QTc duration of children aged 2–14 years treated for gastroenteritis in a pediatric ED. This study model and outcome variables are based on recommendations of the US FDA for conduct of a "thorough QT study".

Methods: In children treated in our pediatric ED, EGCs were obtained before and 15, 30, 45, and 60 min after a 0.15 mg/kg IV dose of ondansetron given for gastroenteritis associated vomiting. QT intervals were measured manually with digital calipers, and the QTc interval calculated both by Bazett's (QTcB) and Fridericia's (QTcF) correction. A paired *t*-test comparing QTc was conducted, and categorical outcomes of absolute prolongation >30 ms, >60 ms, and prolongation >450 ms, >480 ms, and >500 ms were evaluated at these time intervals.

Results: In a 4-month period, 134 patients were included in the study, 46% were male. The average QTc prior to ondansetron administration was QTcB 415ms (95% CI 343–565) and QTcF 373ms (95% CI 304–499). The mean difference in QTc after ondansetron was 0.4 ms for QTcB (95% CI −35 to 45 ms) and 0.1 ms for QTcF (95% CI −40 to 18 ms). Figures and tables for the 15-min interval are presented because this ECG timing for which the greatest QT-proloning effect is expected, and results at other time intervals did not show greater effect.
Conclusions: In these children, 0.15 mg/kg of intravenous ondansetron did not cause prolongation of QTcB or QTcF measured 15 min after administration, nor at later times.

KEYWORDS QTc; ondansetron; dysrhythmia

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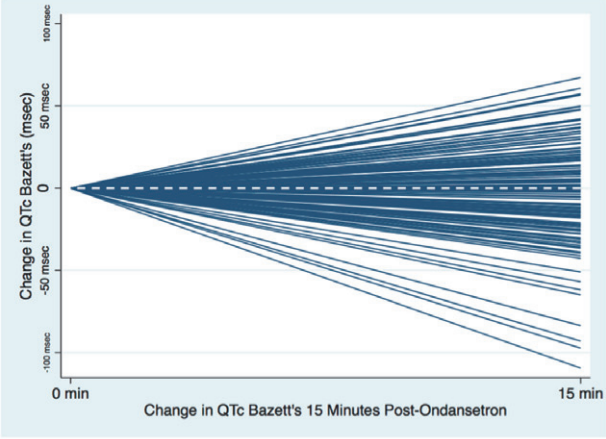

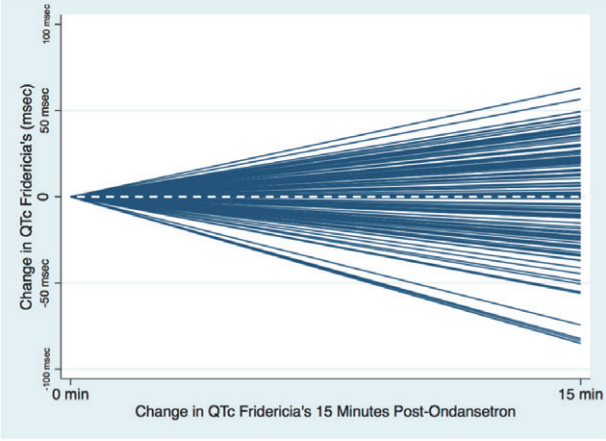

Figure 1. **Effect of IV Ondansetron After 15 Minutes on QTc Calculated By Bazett and Fridericia's Formulas**

Table 1. Paired t-test comparison of pre and 15 minutes post-ondansetron QTc

	Mean difference	95% CI	p value
QTcBazett	.4 msec	-.36 - .45 msec	0.83
QTcFridericia	0.1 msec	-.4msec -.18msec	0.37

Table 2. Summary "Thorough QT Study" Outcome Variables

	x̄	95% CI
QTcBazzet		
QTcB baseline	415 msec	343-565 msec
QTcB prolongation >30msec	7.5%	2.9-12%
QTcB prolongation >60msec	0	-
QTcB absolute prolongation >450 msec	5.2%	1.4-9-3.5%
QTcB absolute prolongation >480 msec	0.7 %	- 0.7 - 2.2%
QTcB absolute prolongation >500 msec	0	-
QTcFridericia		
QTcF baseline	373 msec	304-499 msec
QTcF d30msec	3.7%	0.5 – 7%
QTcF d60msec	0	-
QTcF absolute prolongation >450 msec	6.7 %	2.4-11%
QTcF absolute prolongation >480 msec	0	-

9. When lipid rescue is not the magic bullet

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Objective: While anecdotal reports suggest that intravenous lipid emulsion (ILE) therapy is effective in a large variety of overdoses, the few controlled human trials published to date have disappointing results. Additionally, because of potential publication biases there is a paucity of reports concerning failure of ILE, either when used as a "rescue" therapy or as primary therapy of local anesthetic systemic toxicity. The primary aim of this study was to identify fatal poisoning cases in the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS), in which, ILE was administered. These cases represent ILE treatment failures by definition. Secondary aims include demographic data of cases, description of substances and routes involved, timing of ILE administration, and adverse effects of ILE.
Methods: Following IRB approval, data release from AAPCC, NPDS fatality narratives for years 2010–2015 were systematically searched for the words "lipid" and "fat". Cases were excluded if ILE therapy was not performed, if it was unclear whether ILE therapy was performed, or if search terms represented unrelated cases (such as patients with hyperlipidemia). Duplicates were removed if the patient demographics, date of death, and substances exposed were identical. Only descriptive statistics were used.
Results: The initial search yielded 826 case narratives. After exclusions and duplicates were eliminated, 462 cases remained. The most common substances were calcium channel blockers (183; 39.6%), beta blockers (102; 22.1%), bupropion (53; 11.5%), tricyclic antidepressants (48; 10.4%), citalopram/escitalopram (36; 7.8%), quetiapine (26; 5.6%), and flecainide (21; 4.5%). Prescription local anesthetics were found in nine cases of parenteral and five cases of oral administration. Return of spontaneous circulation (ROSC) in close proximity to ILE therapy was noted in 7% of cases, while no effect was clearly noted in 45%. Another 7% had transient or minimal response, and 3% had immediate hemodynamic worsening. In the remaining cases, documentation was too limited to determine an effect of ILE. The most notable adverse effect possibly attributed to ILE was acute respiratory distress syndrome and/or fluid overload.
Conclusions: The AAPCC NPDS data contain a large number of treatment failures of ILE therapy outnumbering all successful

cases cited in the published literature. The clinical presentation and management of these ILE failures also resemble the ILE successes described in the recent published systematic review, other than their obvious outcomes. This first and large collection of failed responses to this increasingly used therapy lends support to the need for randomized controlled studies to better define its efficacy and place, if any, in therapy. In addition, careful consideration of the contribution of ILE to fluid balance and acute respiratory distress syndrome is warranted in patients with serious hemodynamic instability due to poisoning.

KEYWORDS Lipid emulsion; calcium channel blockers; beta blockers

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10. Prognostic factors for patients with hemolysis from brown recluse spider envenomation

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Background: Brown recluse spider (*Loxosceles reclusa*) envenomation may cause local dermonecrotic lesions and constitutional symptoms such as fever, generalized exanthema, and malaise. Less frequent but more severe systemic reactions include hemolytic anemia. Multiorgan failure and death have occasionally been reported, more commonly in pediatrics than adults. Hemolytic anemia is due to direct toxin-induced erythrocyte damage and complement-mediated immune destruction, and may be Coombs positive or negative. The objective of this study was to investigate the individual factors predictive of hemolysis onset and duration.
Methods: A retrospective chart review of patients hospitalized for brown recluse spider bite [BRSB] between 2008 and 2015 was performed. Only cases confirmed by a medical toxicologist were included. Demographics, history of present illness, clinical course, laboratories, and interventions were assessed. Fisher's exact test and Mann–Whitney *U* test were used to assess potential predictors of hemolysis in the univariate analyses. Spearman's rank-order correlation was used to assess time factors. Logistic regression was used to assess the independent contribution in a multivariate analysis.
Results: There were 97 patients with BRSB of which 40% ($n = 39$) developed hemolysis. The incidence of constitutional symptoms was significantly different between the hemolysis and non-hemolysis groups (see Table 1). Additionally, patients in the hemolysis group were more likely to present with leukocytosis (16.5 versus 9.4; $p < .001$). In patients with hemolysis, the onset of constitutional symptoms occurred in 23% ($n = 9$) on the day of envenomation and 77% ($n = 30$) the next day. Hemolysis developed earlier in patients with same-day onset constitutional symptoms than those with next-day onset (0.6 versus 2.4 d; $p < .001$). Age did not correlate with hemolysis onset time ($r_s = 0.279$; $p = .104$). However, increasing age was associated with prolonged hemolysis duration ($r_s = 0.563$; $p = .001$). Hemolysis was prolonged in patients with positive direct antiglobulin for IGG antibodies (DAT IGG) (7.1 versus 4.8 d; $p = .042$). Multivariate analysis demonstrated that the independent predictors for hemolysis were malaise, myalgia, initial hematocrit, and initial white blood cell count (area under the curve [AUC] = 0.937).
Conclusions: Constitutional symptoms have been reported in BRSB patients without hemolysis, but their presence is highly suggestive that a potentially life-threatening hemolytic reaction may occur. Malaise, myalgia, initial hematocrit, and initial white blood cell count had the largest prognostic effect. Patients whose constitutional symptoms appeared shortly after BRSB were more likely to develop early onset hemolysis than patients whose symptom onset was delayed. Increasing age and positive DAT IGG were associated with prolonged hemolysis duration.

KEYWORDS Loxosceles; hemolysis; statistical model

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11. Pediatric sedation weaning protocol decreases prescriptions for high risk opioids

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Background: For both safety and comfort, critically ill pediatric patients are often sedated with multi-agent pharmacologic regimens, placing them at risk for iatrogenic withdrawal when these agents are discontinued. At baseline, sedation weaning practices at our tertiary care children's hospital were widely variable and a subset of patients were discharged to complete weans at home. In the context of several adverse events related to home sedation weans, a quality improvement effort was initiated to standardize weaning protocols across hospital units.
Objective: Our primary objective was to decrease the number of patients discharged on high-risk (defined as multiple agent or methadone) sedation weaning regimens.
Methods: A multidisciplinary taskforce including nurses, nurse practitioners, physicians and pharmacists from ICUs, pertinent surgical and medical units and the Pain Treatment Service wrote a sedation weaning protocol based on the RESTORE trial. Dissemination of the protocol was achieved using educational outreach in pertinent clinical settings and changes to hospital policy. In addition, changes were made to the documentation of

Table 1. Comparison of Constitutional Symptoms

	Hemolysis (% [n])	Non-Hemolysis (% [n])	Odds Ratio (95% CI)	p-value
Malaise	97.4% (38)	48.3% (28)	40.7 (5.2 – 316.7)	< 0.001
Myalgia	82.1% (32)	31.0% (18)	10.2 (3.8 – 27.3)	< 0.001
Fever/Chills	92.3% (36)	58.6% (34)	8.5 (2.3 – 30.7)	< 0.001
Nausea	71.8% (28)	34.5% (20)	4.8 (2.0 – 11.7)	< 0.001
Tachycardia	66.7% (26)	31.0% (18)	4.4 (1.9 – 10.6)	0.001
Exanthema (Rash)	94.9% (37)	67.2% (39)	9.0 (2.0 – 41.4)	0.001
Headache	17.9% (7)	12.1% (7)	1.6 (0.5 – 5.0)	0.557

withdrawal assessment scores (WAT-1) in the electronic medical record to include baseline and target WAT-1 Scores. From 1 July 2013 through 31 December 2016, patients were identified for inclusion in the measurement of this quality improvement effort using two primary criteria: (1) Intubated for ≥5 d and (2) Received three decreasing doses (= "weaning") of one or more of the typical sedation medications (clonidine, dexmedetomidine, diazepam, fentanyl, hydromorphone, lorazepam, methadone, midazolam, morphine). The primary outcome measure was a prescription for a sedation medication at the time of discharge. Balancing measures included WAT-1 scores and length of stay. Results were assessed quarterly.
Results: A total of 626 patients were identified for inclusion in this study, 358 prior to the interventions and 268 post-interventions. Prior to the interventions, 36–40% of "weaning" patients per quarter were discharged with a methadone prescription. Over the course of the study period, this percentage has steadily declined, and as of the most recent measurement (Quarter 4 of 2016), no weaning patients were discharged home with methadone. In addition, the percentage of patients discharged with multiple sedative prescriptions (≥2) decreased from 26% to 11%. Over this same time period, the percentage of moderate WAT-1 scores (4–7) increased from 9.6% to 22.7%, but the percentage of severe WAT-1 scores (≥8) remained stable. Length of stay (LOS) did not increase, with a median LOS of 52.8 d (mean = 67.6 d) pre-interventions and 51.2 days (mean = 67.1 d) post-interventions.
Conclusions: Standardizing a weaning protocol for opioid, benzodiazepine and alpha-agonist medications in pediatric patients decreased the number of patients discharged home on methadone and multiple-agent sedation weans without increasing length of stay or episodes of severe withdrawal. This effort has implications for toxicologists given the potential to decrease medication errors and unintentional ingestions of these high risk medications in young children.

KEYWORDS Pediatric; opioids; withdrawal

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12. Assessment of simulated naloxone administration by community members

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Background: Opioid-related deaths have increased in the last decade. Naloxone is distributed to first-responders, law enforcement officers, and community members to reduce accidental overdose deaths. There is limited data assessing community members' ability to administer naloxone. We conducted a randomized usability assessment of intramuscular (IM), intranasal atomized (IN), and nasal spray (SP) administration of simulated naloxone by community members.
Objectives: *Primary*: Successful administration of simulated naloxone, defined as administration within 10 min and without critical errors. *Secondary*: Time required for successful administration.
Methods: This was a randomized usability assessment of IM, IN, and SP administration of simulated naloxone by community members. This study was approved by the SUNY Upstate Medical University institutional review board. Adult subjects (≥18 years of age) were enrolled in a convenience sample over a two day period at a State Fair. Subjects with visual or hearing impairment, previous naloxone administration training, who were non-English speaking, or pregnant were excluded. Enrolled subjects were randomized to administer IM, IN, or SP-simulated naloxone using a predetermined randomization list created in SPSS with block randomization every six subjects (up to 150). Each subject viewed a 2-min video showing proper administration for their randomized route. Subjects were then given a kit and asked to administer the simulated naloxone to a mannequin head or flesh pad. Subjects were observed for successful administration and time to successful administration.
Results: About 138 subjects were enrolled with a mean age of 48 years ($n = 135$), 79% were female, and 89.1% were right handed. There were no significant differences in age, handedness, or education between groups. The rate of successful administration was significantly higher in the SP (100%) and IN (89.1%) groups as compared with the IM (69.6%) group ($p < .05$). The median time to successful administration for the SP group (34.3 s) was significantly shorter than the IN (110.3 s, $p < .001$) and IM groups (99.9 s, $p < .001$).
Conclusions: Broad distribution of naloxone is one measure that may reduce mortality from accidental overdose. Community members with limited medical training may not be able to successfully administer naloxone by all available routes of administration. Our results suggest that intranasal kits may have a higher success rate than IM kits when administered by community members. Additionally, SP devices may allow for more rapid administration of naloxone than IN devices.

KEYWORDS Naloxone; opioid; overdose

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13. Treating valproic acid intoxication using conventional hemodialysis combined with protein binding displacers: an *in silico* analysis

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Background: Although small molecular weight drugs can diffuse through a hemodialysis (HD) filter, the clinical applicability of HD for poisoning is limited in many by high-protein binding. We used a novel *in silico* model to test the efficacy of increasing the free (dialyzable) valproic acid (VPA) concentration by displacing VPA from albumin with the addition of low-toxicity drugs in the extracorporeal circuit.
Methods: VPA binds to two drug binding sites on albumin, with assumed binding affinities of 2×10^4 M^{-1} for site I and 1×10^4 M^{-1} for site II. Using the law of mass action, these equilibrium association constants result in free drug fractions for VPA of 6.5% at 50 mg/L and 81.5% at 1000 mg/L. The following parameters were entered as into the model: albumin 4.32 g/dL; apparent $t_{1/2}$ of VPA 25 h for toxic concentration; $t_{1/2}$ of free VPA of 0.9 h. We then used two displacers: acetylsalicylic acid (2000 mg in 100 mL saline) for site I and ibuprofen (1600 mg in 400 mL saline) for site II, with respective binding affinities of 1.9×10^5 M^{-1} and 1.76×10^5 M^{-1}, infused into the arterial line of the extracorporeal circuit. We then simulated VPA removal by HD combined with displacers. The simulation begins at an initial VPA concentration of 500 mg/L and an albumin binding of 64% calculated using aforementioned parameters. The model comprises a spatiotemporal representation of the dialyzer and a three-compartmental

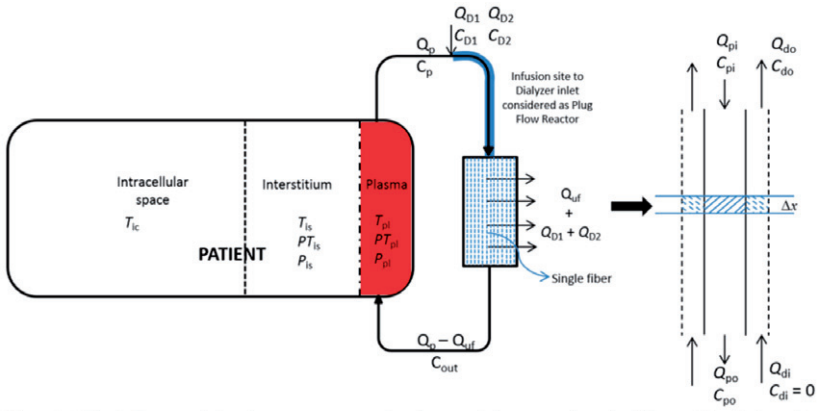

Figure 1: A block diagram of the three-compartmental patient model connected to the dialyzer. Albumin-bound valproic acid (VPA) is distributed in the interstitial and plasma compartments, while free VPA is distributed in all three compartments. The same distribution spaces are assumed for ibuprofen and acetylsalicylic acid. Plasma, interstitial, and intracellular fluid volumes were set to 3, 12 and 28 L, respectively. Q_b = 300 and Q_d = 800 mL/min were used. The mass transfer coefficient for VPA and displacers was 300 mL/min between intracellular and interstitial space and 1000 mL/min between interstitial and plasma compartments. The dialyzer K_oA was assumed to be 1000 mL/min for both VPA and displacers.

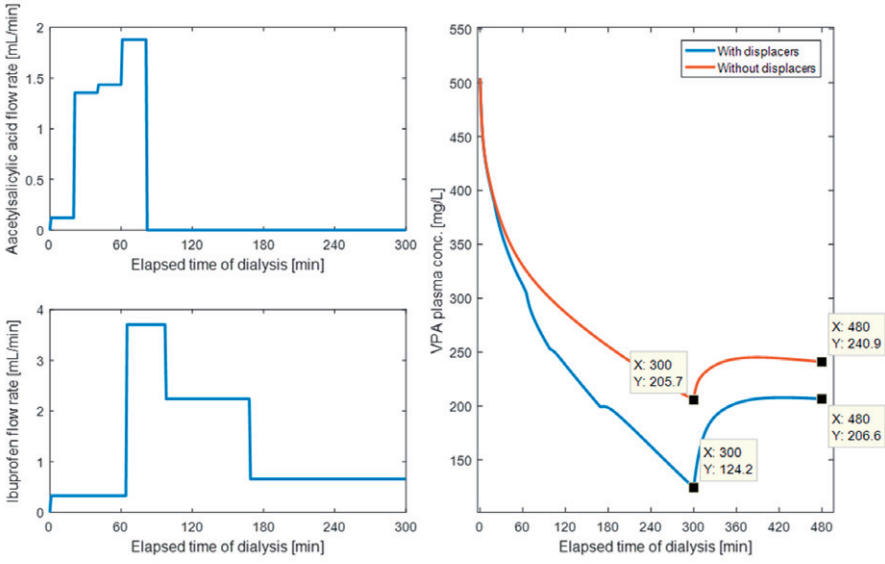

Figure 2: Left panel: displacer (acetylsalicylic acid and ibuprofen) infusion profiles during HD. Both profiles are optimized to maximize valproic acid removal during 300 minutes of HD. Conventional HD requires 390 minutes to achieve the same removal. Right panel: total valproic acid plasma concentrations during and after dialysis, without and with displacers.

patient model accounting for dynamic equilibrium between albumin, drug, displacers, albumin-drug complex, and albumin-displacer complexes (Figure 1). Displacer infusions were optimized such that maximum toxin removal is achieved during a 300-min HD session.

Results: The total amount of VPA removed during 300 min of HD with displacers was 11.4 g (75% of initial VPA load) versus 10 g in in standard HD. The total removal also includes removal by drug metabolism. With displacers, the absolute dialytic removal was 10.3 g versus 8.7 g in standard HD. The end-dialysis VPA concentration was 124.2 mg/L with displacers versus 205.7 mg/L in standard HD. Standard HD of 390 min would be required to achieve the same total removal as in 300 min of displacer-augmented HD. Owing to the displacers' action in the extracorporeal circuit, the displacers primarily influence the plasma VPA concentration; a significant reserve of VPA is present outside the vasculature, as indicated by the post-HD rebound: at 2 h post-HD, plasma VPA concentration was 206.6 mg/L with and 240.9 mg/L without displacers (Figure 2). As VPA is removed, the patient moves from toxic concentrations into the therapeutic range where $t_{1/2}$ is shorter (≈12 h). This will lead to shorter HD time. In the absence of any literature evidence, we did not change the $t_{1/2-}$ in the results presented here.

Conclusions: Although VPA is only moderately bound to albumin in the toxic range, displacer-augmented HD reduces the dialysis time by 90 min (a 23% reduction in time). For more strongly bound toxins, the impact of displacer-enhanced HD would be even more pronounced.

KEYWORDS Displacers; mathematical model; valproic acid

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14. Retrospective assessment of desmopressin effect on hematoma expansion and safety in antiplatelet-treated patients with intracranial hemorrhage

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Background: Hematoma expansion (HE) is associated with increased mortality following intracranial hemorrhage (ICH). Desmopressin (DDAVP) improves platelet function and may prevent HE in antiplatelet-treated patients with ICH. There are limited studies assessing the safety of DDAVP or its effect on HE. The objective of this study is to assess DDAVP effect on HE and safety in antiplatelet-treated patients withICH.
Methods: This retrospective chart review was performed in a single academic medical center between February 2014 and February 2017. This project received exemption from the institutional review board. Adult patients age 18 years and older were included if they were treated with at least one antiplatelet agent and had evidence of ICH on cerebral computed tomography (CT). Patients were excluded for the following reasons: (1) repeat cerebral CT scan not performed within first 24 h; (2) non-comparative repeat cerebral CT scan; (3) chronic anticoagulation; (4) administration of fibrinolytic medications; (5) concurrent ischemic stroke; (6) neurosurgical intervention. The primary outcome was HE on repeat cerebral CT scanning. Safety outcomes were venous thromboembolism (VTE) in the first seven hospital days and largest absolute decrease from initial serum sodium in the first three hospital days. Continuous variables were compared using Mann–Whitney *U* or Student's *t*-test. Categorical variables were compared using Chi-square or Fisher exact test. All tests were two tailed and a *p*-value $< .05$ was considered statistically significant. Odds ratio (OR) and 95% confidence interval (CI) were calculated when applicable.
Results: One-hundred and thirty-three patients were included in this study, of which 59 received DDAVP and 74 did not. Patients were most frequently on aspirin alone (74.4%, 99/133) or the combination of aspirin and clopidogrel (15.8%, 21/133). Those receiving DDAVP were less likely to be on aspirin alone (DDAVP 66.1% versus non-DDAVP 75.9%, $p = .049$) and more likely to be on at least one antiplatelet agent for secondary prevention of stroke or myocardial infarction (DDAVP 37.2% versus non-DDAVP 20.3%, $p = .030$). Mean ± standard deviation (SD) DDAVP dose was 0.34 ± 0.10 mcg/kg. Demographics, platelet transfusion, time between cerebral CT scans, and systolic blood pressure at repeat CT scan were similar between groups. HE occurred less frequently with DDAVP (DDAVP 27.1% versus non-DDAVP 48.6%; OR 95% CI 0.58 (0.37–0.92)). VTE frequency (DDAVP 1.7% versus non-DDAVP 1.4%; OR 95% CI 1.12 (0.28–4.45)) and median (IQR) absolute decrease from initial serum sodium (DDAVP 1.0 mEq/L (0.0–5.0 mEq/L) versus non-DDAVP 1.0 (0.0–4.0), $p = .874$) were similar between groups.
Conclusions: DDAVP reduced the frequency of HE in a cohort of antiplatelet-treated patients with ICH. DDAVP did not increase the frequency of VTE or cause a larger absolute decrease in serum sodium. Although more clinical outcomes research is still required, DDAVP appears to be a safe and viable treatment option for antiplatelet-treated patients with ICH.

KEYWORDS Desmopressin; antiplatelet; intracranial hemorrhage

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15. Dosing strategies of *N*-acetylcysteine for acetaminophen overdose in patients greater than 100 kg. An evaluation of dosage capping

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Background: Acetaminophen (APAP) is the most commonly used antipyretic and pain-reliever worldwide. Generally safe at therapeutic doses, large ingestions (typically acute dosages >150mg/kg) are frequently associated with hepatotoxicity. N-Acetylcysteine (NAC) dosing to prevent hepatotoxicity is protocolized and typically based on actual body weight (ABW). Although there are no validated dosing guidelines for patients whose weight exceeds 100 kg, the package insert for Acetadote®, intravenous (IV) NAC, describes limiting the NAC dose at a maximum body weight of 100 kg with the assumption that all patients should have equivalent hepatic blood volumes and metabolic capacity regardless of ABW.
Methods: This is a multicenter, retrospective review of patients who present to the emergency department with APAP overdose requiring treatment with IV NAC. The study period is from 1 January 2009 to 1 January 2016. Patients are identified by pharmacy charges or international classification of disease codes (ICD) 9 or ICD 10 codes. Inclusion criteria are met if a patient received IV NAC for the treatment of an acute APAP overdose, has an ABW >100kg, and is ≥18-years-old. The primary endpoint is to compare the prevalence of hepatic injury evidenced by either AST or ALT >100 IU/L (or a doubling during admission) or hepatotoxicity defined as a peak serum AST or ALT >1000 IU/L after receiving either NAC dosing utilizing ABW (traditional) versus NAC dosing capped at 100 kg (capped). Secondary endpoints include the prevalence (or no worse) of adverse events (cutaneous, gastrointestinal, respiratory, angioedema or cardiovascular) during NAC administration, patient cost, time to resolution of APAP levels (defined as an APAP level ≤20 mcg/mL), length of hospital stay, length of intensive care unit stay, and mortality.
Results: Enrollment is ongoing. To date across 10 sites, 81 patients have been identified for study inclusion. In an interim analysis, there are no differences in instances of hepatic injury or hepatotoxicity between groups ($p = .363$). Statistically significant differences are seen between groups with respect to mean weight, where weight was higher in the traditional dosing group (120 kg versus 109 kg; $p = .0234$). There are no differences in past medical history, total duration of hospital stay, or mortality.
Statically significant differences in patient cost (USD$1524 traditional versus USD $725 capped; $p = .0001$) and cumulative dose (49.5g traditional versus 30 g capped; $p = .0004$) were observed between groups. The traditional dosing group experiences more adverse events and requires more doses of rescue medications

although results are not significant (9.1% traditional versus 0% capped). Time to resolution of APAP levels was not significantly different between groups ($p = .9106$) and is unreported in approximately 20% of patients.
Discussion: During interim analysis, there are no observed differences between instances of hepatic injury and hepatotoxicity between the groups. Patient cost and cumulative dose is higher with traditional NAC dosing compared with capped dosing.
Conclusions: Limiting the dose of NAC to a maximum body weight of 100 kg does not appear to have any adverse consequences. Hepatic volume and metabolic capacity in patients exceeding 100kg may be clinically insignificant for NAC dosing. Dosing in this patient population warrants continued study.

KEYWORDS *N*-acetylcysteine; acetaminophen; overdose

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16. Is intravenous silibinin a failed antidote for the fulminant hepatic failure treatment of amatoxin mushroom poisoning? Interim results of the North American clinical trial

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Objectives: Amatoxin mushroom poisonings (AMP) treated in Developing Country Hospitals or on North American/Australian/European tertiary transplant units are both documented to have poor outcome (death/liver transplant) rates of >50% that are linked to early oliguric Acute Kidney Injury (AKI). Multiple Italian retrospective series demonstrate the efficacy of Forced Diuresis in mild-moderate AMPs, but ~20% still suffer a poor outcome in severe (peak ALT>2000) cases. Many treatment failures with IV silibinin have recently been reported from Turkey, Australia, Germany, and France. Silibinin has been licensed in Europe since the 1980s but has never been evaluated prospectively. Is IV silibinin a failed antidote? What circumstances determine silibinin success or failure?
Methods: Prospective uncontrolled open label IND nationwide clinical study of IV silibinin using "The Santa Cruz Protocol," which has a rationale based on well-documented amatoxin toxicokinetics. About 97 amatoxin poisoning patients enrolled since 2007. Includes (1) rapid aggressive ED volume replacement and sustained aggressive IV hydration to reverse presentation prerenal AKI, restore urine output, enhance elimination, protect kidneys, and prevent oliguric AKI. (2) Strict NPO status + octreotide infusion to stop gallbladder contraction, close the Sphincter of Oddi, and prevent amatoxin laden bile from reaching the GI tract. (3) IV silibinin to occupy the hepatocyte sinusoidal membrane transporter OATP1B3, block enterohepatic re-penetration, divert reabsorbed amatoxin into the general circulation, and promote hepatic recovery.
Results: Of the enrolled 54 males and 43 females (age range 18 months to 94 years), 78 had a peak ALT>2000 and 68 had a peak INR>1.5 (49>2.0). Twelve of 97 suffered a poor outcome (death/liver transplant). One death; late presentation, pH 6.8, irreversible oliguric AKI, rapidly progressing fulminant hepatic failure (FHF). One transplant; serum lactate remained uncorrected despite aggressive hydration after a very late presentation. One death, two transplants; silibinin initiated >120 h post-ingestion. Four deaths, four transplants; IV hydration interruption/restriction, usually upon arrival to a tertiary transplant unit from a community hospital (6/8), triggered precipitous serum lactate elevation, f/b oliguric AKI and malignantly progressing FHF. Among 84 adherent to the protocol (silibinin begun <120 h post-ingestion; sustained aggressive IV hydration), INR correction began by silibinin infusion hour 30, heralding full recovery in 83 (99%). ED presentation to hospital discharge ~5 d. Occasional mild warmth/flushing during silibinin bolus. ICU care rarely required. Uncorrected serum lactate elevation sensitively predicted silibinin treatment failure and the need for liver transplant. Sustained serum lactate correction augured recovery. Silibinin effective initiation window was ~120 h post-ingestion. Treatment success or failure predominantly determined by IV fluid management.
Conclusions: Silibinin is reliably effective in severe AMP cases when combined with sustained aggressive IV hydration. Inadequate volume replacement at presentation or subsequent interrupted/restricted IV hydration predisposes a patient to treatment failure.

KEYWORDS Amatoxin; mushroom; silibinin

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17. Eye see an EpiPen®: complications from a pediatric ocular epinephrine injection

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Background: Unintentional administration of epinephrine auto injectors has been well described, but data are limited regarding direct exposures to the eye. We report a case of ocular morbidity in a toddler from unintentional direct epinephrine auto injector discharge.
Case report: A 15-month-old male was brought to an emergency department after his 4-year-old sibling stabbed an EpiPen® Junior (1:1000 of .15mg) through the upper temporal eyelid into the right eye. Initial vitals were a temperature of 36.8 °C, a heart rate of 180 BPM, a respiratory rate of 20 BPM, and an O_2 saturation of 98%. The patient was crying on exam, and noted to have a 6mm dilated right pupil that was unreactive to light with an eyelid hematoma, normal pressures measurements, mildly erythematous conjunctiva, intact visual fields, foveal fixation, and tracking appropriately for age. Initial ED evaluation by an ophthalmologist revealed a retinal tear, so the patient was transferred to a tertiary hospital for better evaluation and intervention under anesthesia in an operating room. By the time of arrival to the second hospital 6 h later, the tachycardia had resolved. Examination under anesthesia revealed a traumatic retinal tear, a self sealing corneal injury from the 22-gauge needle tract, a traumatic iridectomy, suspected lens capsule violation, and multilayered retinal hemorrhages. Laser retinopexy, and external cryopexy were performed. No optic nerve or vascular ischemia were noted. The patient was discharged with outpatient ophthalmology follow up. During the most recent visit a month after the event, the patient was noted to have normal dilated examination, age appropriate tracking, with intact visual fields and foveal fixation.
Case discussion: Unintentional exposures to epinephrine from EpiPen® auto injectors are an increasingly common phenomenon because they are so readily available in homes, schools, camps, and other public places. This case describes a rarely reported injection into the eye. The initial consult to our service was for questions regarding damaging vasoconstrictive effects from epinephrine on the eye. While this patient exhibited some local

effects to epinephrine such as mydriasis, fortunately no vascular or optic nerve ischemia from epinephrine were noted on ophthalmological examination. The main complications instead appeared to be secondary to the force of the sibling's jab and the force of the spring-loaded needle in the auto-injector.
Conclusions: EpiPen® autoinjectors are generally safe and life-saving when used as indicated, but can result in significant morbidity if directly injected in the eye itself. Although the force of the needle in this case was likely primarily responsible for the abnormal ocular findings, it is worrisome this was done by 4-year-old sibling and additional safety measures need to be investigated to prevent future ocular injuries from auto-injectors.

KEYWORDS Epinephrine; ocular; EpiPen

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18. Too much milkshake: acute chylous ascites following intralipid treatment for flecainide overdose

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Background: There has been a growing "mission creep" in the use of intravenous lipid emulsion (ILE) therapy, from the treatment of local anesthetic systemic toxicity (LAST) to that of many other lipophilic drugs, with mixed results. As several recent reviews have emphasized, the evidential basis for ILE therapy for most acute poisonings relies predominantly on case reports and other small studies, subject to considerable publication bias. Optimization of dosing regimen is based upon "titration to effect" with maximal doses inferred from animal studies. Treatment duration is also not well established. Risk benefit clinical calculations are influenced by clinical severity. As acceptance of ILE therapy expands beyond its "last resort" rescue status, potential interference with other established antidotes and serious complications takes on more importance. We describe a case of chylous ascites associated with high-volume ILE in the treatment of massive flecainide overdose.
Case report: A 31-year-old man with a history of suicide attempts was transferred from an outside hospital after intentionally ingesting 9 g of his own flecainide. Prior to transfer, he receive calcium, 300 mEq of sodium bicarbonate, and a bolus of Intralipid. After transfer he was placed on venoarterial ECMO following a PEA arrest. He was subsequently twice bolused with 1000 mL of 20% Intralipid. Overnight, the patient's abdomen became progressively distended, prompting laparotomy to exclude abdominal compartment syndrome. Profuse chylous ascites was removed via peritoneal drains. The patient improved and was decannulated after 6 d. He was discharged after prolonged hospitalization to a psychiatric facility with good neurological outcome.
Case discussion: Lipid is transported as chyle through the lymphatic system to the thoracic duct, the most inferior part of which is the cisterna chyli. Chylous ascites may occur secondary to trauma, iatrogenesis, and conditions producing inflammation or stasis within the thoracic duct or venous system. In our patient's case, the combination of a low-flow shock state coupled a large lipid load caused rupture of the thoracic duct. While not life-threatening, the chylous ascites prompted clinicians to perform a laparotomy.
Conclusions: To our knowledge, chylous ascites has not been previously reported as a complication of ILE therapy. In light of limited clinical experience, caution should be exercised when considering ILE for non-LAST poisonings except as a last resort rescue agent.

KEYWORDS Flecainide; intralipid; chylous ascities

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19. Two cases of ventricular dysrhythmias from aconitine poisoning

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Background: Aconitine is a deterpenoid alkaloid found in plants of the Aconitium genus that contain potent cardiovascular and neurological toxins. Most reported cases of aconitine poisoning have been related to the use of traditional Chinese medications. These herbs are used in the treatment of rheumatism, arthritis, and other ailments. Aconitine acts as a voltage-sensitive sodium channel opener that results in paresthesias, muscle weakness, ventricular ectopic rhythms, heart block and ventricular arrhythmias.
Case reports: Patient 1: A 56-year-old female presented with chest pain and weakness 1 h after preparing and drinking an herbal tea. On arrival, she was found to have rapidly evolving tachydysrhythmias including bidirectional ventricular tachycardia. She was treated with adenosine, diltiazem, cardioversion, amiodarone, lidocaine, and ultimately developed hypotension requiring a dopamine infusion and intubation. Given her persistently unstable hemodynamics, she was started on extracorporal membrane oxygenation. She had multiple complications including a retroperitoneal hemorrhage, right leg ischemia requiring an above the knee amputation, spinal cord ischemia with paralysis, and prolonged ventilation requiring tracheostomy. The patient died from her complications approximately one month after initial presentation. Serum concentrations of aconitine on presentation and at 4 h were 3.4 ng/mL and 5.6 ng/mL. Patient 2: A 36-year-old male presented with paresthesias approximately 1 h after preparing and drinking an herbal tea. He had witnessed syncope prior to presentation. Clinical course was complicated by rapidly evolving tachydysrhythmias including polymorphic ventricular tachycardia, superventricular tachycardia, bigeminy, and bidirectional ventricular tachycardia. The patient had progressively worsening altered mental status and hypotension requiring intubation and norepinephrine. Treatments also included calcium, sodium bicarbonate, magnesium, cardioversion, and amiodarone. The patient was extubated on hospital day 2, and subsequently discharged in good condition. Serum concentration of aconitine was 1.8 ng/mL approximately 3.5 h after initial presentation.
Case discussion: These two patients presented to separate hospitals in the same city within a one-month period triggering a public health investigation. Samples of the original herbs used in the tea preparations were obtained from each patient's homes and also confirmed positive for aconitine. Both products were ultimately traced back to the same vendor.
Conclusions: Aconitine is commonly used in traditional Chinese herbal medicines and is a potential source of significant cardiovascular toxicity.

KEYWORDS Aconitine; aconite; herbal preparation

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20. Massive dosing error of iron dextran in a newborn

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Background: Iron dextran is one of three parenteral formulations of iron on the market. Each milliliter contains 50 mg of complexed iron. After administration and uptake within the reticuloendothelial system, iron leaves the dextran complex and binds to storage proteins. Most infusions are very well tolerated with few adverse events, the most common being allergic reactions. Overdose is rarely associated with toxicity.
Case report: A 7 week old male infant with gastroschisis received 500 mg (131.6 mg/kg) of iron dextran in his total parental nutrition over an 18 h period, resulting in a 100-fold overdose. When the error was recognized, the patient was hemodynamically stable. Despite down-trending iron levels, an in-house consultant recommended deferoxamine (DFO) at 5 mg/kg/h on day 5 post-iron infusion. The DFO infusion was increased to 10 mg/kg/h after 48 h and further increased to 15mg/kg/h on the seventh day of treatment (see Graph). The patient soon developed respiratory distress, a pneumothorax, pneumomediastinum, and possible sepsis. DFO was stopped, antibiotics were started, and he was transferred to a higher level of care. Twenty-five days after iron infusion, a whole body MRI showed moderate iron deposition in the liver and spleen. DFO was restarted for a total 3-d treatment without recurrent liver dysfunction, acidemia or hemodynamic instability. The child was discharged home 63 d post-iron dextran infusion, and was reportedly doing well.
Case discussion: Toxicity from iron dextran overdose is rare. The clinical course of this case suggests that manifestations more closely relate to iron deposition disease than to direct toxicity from elemental iron. Kinetics suggest that the iron level at the end of iron dextran infusion exceeded 1200 mcg/dL (see Graph). There was a temporal relationship between clinical decompensation and escalation of continuous DFO therapy.
Conclusions: Exogenous overdose with iron dextran may lead to iatrogenic toxicity including hemosiderosis. The package insert states that overdosage is "unlikely to be associated with any acute manifestations." Overly aggressive attempts at chelation may be deleterious. Caution should be exercised in the treatment of these symptomatic patients.

KEYWORDS Iron dextran; medication error; overdose

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21. The characterization of carfentanil sales on a major darknet cryptomarket

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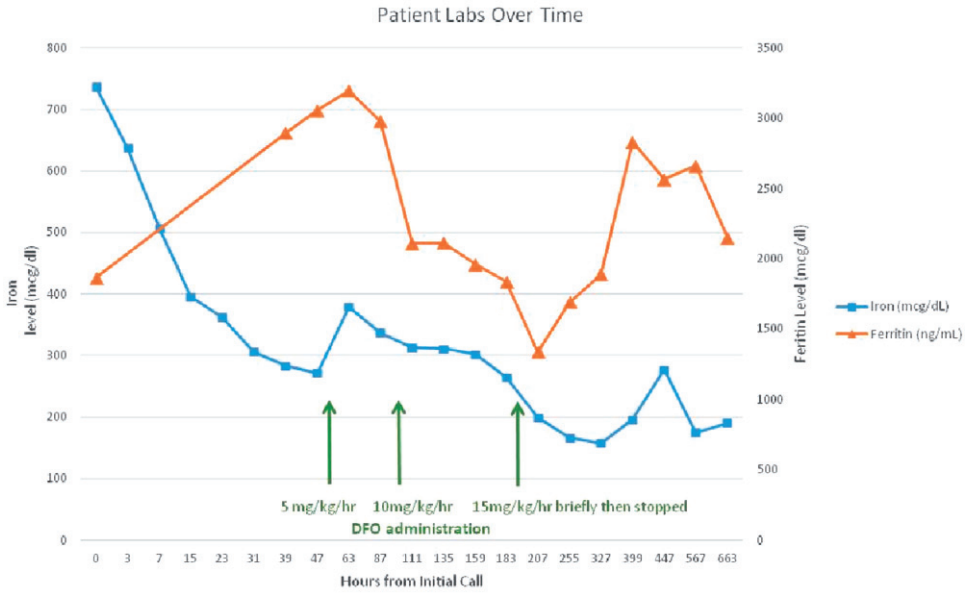
Background: Carfentanil is a synthetic fentanyl analogue approximately 100 times more potent than fentanyl. It is is marketed as a veterinary anaesthetic for large animals, but has recently become a drug of abuse in the United States. Carfentanil has been associated with multiple outbreaks over the past year. Though carfentanil has been available on darknet cryptomarkets since 2015, its sale and distribution is not described. Darknet cryptomarkets serve as anonymous exchange sites for the purchase of illicit products, including drugs of abuse. The purpose of this study is to characterize the sale of carfentanil on the largest darknet cryptomarket, *Alphabay*, over the past year.
Methods: Utilizing a virtual private network (VPN), the darknet cryptomarket, *Alphabay*, was accessed via the Tor browser. *Alphabay* was first accessed on 29 February 2015, and again on 4 April 2017. Sellers with listings containing "carfentanil" or the misspelling "carfentanyl" were identified. Sellers' profiles were accessed to document individual carfentanil listings. For each listing, dose, price, seller location, allowed shipping destinations, and number sold were recorded dating back to March 2016. Customer feedback, a reliable indicator of completed sale, was used as a proxy for number sold from 1 March 2017 to 4 April 2017. *Alphabay's* reported 'number sold' was used for data prior to March 2017.
Results: A total of 11 vendors were identified as selling carfentanil within the past year. A total of 6310 g were reported sold for



525,674 US dollars (USD). From 1 March 2017 to 4 April 2017, 100.24 g of carfentanil were sold for 124,915.16 USD. The vendor bigjule33 generated 220,490 USD in revenue from carfentanil since March 2016, the highest among vendors. Price per milligram varied significantly from 0.02 for Chinese bulk to 516.07 for parenteral grade restricted to sale in Australia. The majority of sales involved quantities less than 100 mg (Figure 1). Summary of carfentanil sales on *Alphabay* over the past year is reported in Table 1. Data for March 2017 only are reported in Table 2.

Conclusions: Carfentanil has emerged as a contributor to the current opioid epidemic. It is associated with several recent outbreaks, including 19 deaths in Wayne County, Michigan, eight deaths in Hamilton County, OH, and five deaths in Minnesota. To date, its use, sale, and distribution have been poorly described. The majority of sales are for quantities less than 100 milligrams. These findings favor personal use and small-scale distribution compared with large scale operations. The U.S. vendor, "FENTSTORE", accounted for more than 70% of seller volume in March. This could indicate increased domestic, clandestine production of carfentanil in an effort to bypass interdiction by law enforcement. It may also reflect increased consumer confidence in local sources. In this study, 23.8% of the revenue from the prior 12 months was generated in March of 2017 alone. Sales continue to increase and public health officials and clinicians should be aware of the increasing availability of carfentanil.

KEYWORDS Carfentanil; darknet; opioids

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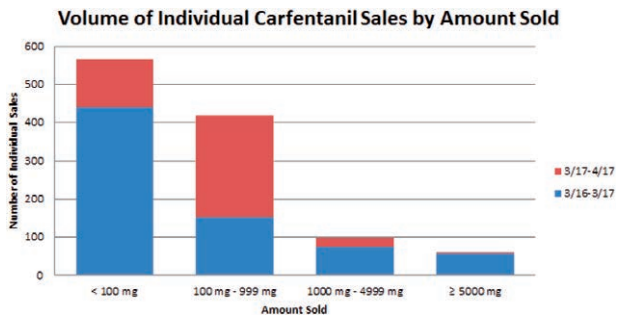

22. How sweet it is: sodium glucose co-transporter 2 inhibitor ingestions reported to U.S. poison centers

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Background: Sodium–glucose co-transporter two inhibitors (SGLT2Is) are a new class of oral agent for type 2 diabetes that lower glucose (GLU) by blocking renal reabsorption and increasing glycosuria. The three agents available in the US are now in widespread use but the literature offers little guidance on

Summary of Carfentanil Sales on *Alphabay* : March 2016 to Present

Vendor	Origin	Destination	Total Revenue (USD)	Total Amount (mg)	Price (USD) / mg
Bigjule33	Worldwide	Worldwide	$ 223,950.00	133550	$ 1.68
Alaurizen	China	Worldwide	$ 121,040.00	5305000	$ 0.02
FENTSTORE	USA	Worldwide	$ 89,225.00	51250	$ 1.74
UKBargins	Worldwide	Worldwide	$ 26,767.26	37400	$ 0.72
GermanTeam	Germany	Europe	$ 19,140.00	22600	$ 0.85
carfentanil	China	Worldwide	$ 15,808.00	702000	$ 0.02
TheLittleGuys	Australia	Australia	$ 13,005.00	25.2	$ 516.07
WWCookiefromGermany	Germany	Worldwide	$ 8,778.00	17200	$ 0.51
Chemical_usa	Worldwide	United States	$ 6,745.00	24000	$ 0.28
DougFish44	Canada	North America	$ 990.00	1000	$ 0.99
WellnessCenter	United States	United States	$ 226.00	52.5	$ 4.30
Totals			$ 525,674.26	6294077.7	

Summary of Carfentanil Sales During March 2017

Vendor	Total Amount (mg)	Total Revenue (USD)	Individual Sales
FENTSTORE	51250	$ 89,225.00	251
UKBargins	37400	$ 17,084.16	70
Bigjule33	7180	$ 10,640.00	27
GermanTeam	2350	$ 2,160.00	25
TheLittleGuys	4.55	$ 2,190.00	20
WellnessCenter	52.5	$ 226.00	12
Chemical_usa	1000	$ 2,400.00	1
DougFish44	1000	$ 990.00	10
Total	100237.05	$ 124,915.16	

management of acute overdose or pediatric exploratory ingestion (PEI).
Methods: The primary aim of this study was to determine the extent of hypoglycemia in PEI involving an SGLT2I. A secondary aim was to characterize the effects in adult overdose. We obtained data on single substance exposures to canagliflozin, dapagliflozin, and empagliflozin, January 2013–January 2017 (all ages, all intents) from the American Association of Poison Control Centers' (AAPCC) National Poison Data System. For all cases with > minor effects, we requested de-identified case narratives. Adult cases were included based on the assumption that they were more likely to involve larger ingestions and potentially more serious effects.
Results: AAPCC provided data on 627 cases for the study period (231 age ≤6 years, 394 age >6, 2 unknown age). About 262/627 were not followed because judged to be minimally toxic. Other outcomes were: no effect 245, minor effect 26, moderate effect 33 (7 age ≤6), major effect 4 (0 age ≤6), unrelated effect 15, unable to be followed 38, and confirmed non-exposure 4. There were no fatalities. Case narratives were requested for all cases with moderate or major effects. AAPCC provided 24/37 narratives (4/7 age ≤6) requested. Of the four narratives obtained for children age ≤6, two were coded for hypoglycemia. GLU nadirs were 67 (treated with IV D10) and 73 mg/dL (treated with a snack). Both nadirs appear to have occurred within a few hours of ingestion. Twenty narratives were obtained for patients >6 (range 33–72) years old with moderate or major effects. The most common effect was diabetic ketoacidosis (13/20) with none of these related to acute overdose. One adult taking dapagliflozin as well as insulin had hypoglycemia (18 mg/dL), coded as an adverse drug reaction after apparently forgetting to eat.
Discussion: Although "hypoglycemia" was reported in PEI, the lowest documented GLU was 67 and no mental status changes were noted. D10 was given, but the child might have done well with oral treatment. Based on mechanism of action, profound hypoglycemia is not expected. This study was limited by the fact that >40% of cases reported to poison centers were not followed because they were deemed to be minimally toxic, and narratives for some cases with moderate or major effects were unavailable.
Conclusions: Most exploratory SGLT2I ingestions result in no more than minor effects. Mild hypoglycemia without CNS effects has occurred, however optimal management remains unclear and larger prospective studies are needed.

KEYWORDS SGLT2 inhibitors; oral diabetes drugs; poison centers

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23. Multi-center analysis of self-reported drug and ethanol use in sexual assault patients taken prior to, or during an assault

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Background: Drug facilitated sexual assault is implicated in approximately 20% of sexual assault. Minimal recent literature exists which describes the self-reporting of drugs and ethanol taken prior to or during an assault. We aim to provide descriptive data from an on-going NIH-funded multi-center study across the United States to examine the substances involved prior to, or during an assault.
Methods: This is a secondary analysis of data collected from 2015 June to 2017 March as part of an on-going NIH-funded trial evaluating the mechanisms of chronic musculoskeletal pain following sexual assault among females presenting to 13 emergency department and clinical-based sexual assault programs across the United States. Female survivors ≥18 who presented to a sexual assault program within 72 h of assault, received a SANE exam, and who met other inclusion criteria were eligible to participate. Subjects completed a short self-report assessment at time of exam, followed by self-report assessments at 1 week, 6 week, 6 months, and 12 month time periods. Data from the initial self-report at time of exam was utilized for this analysis. Data are reported in frequencies, percentages and confidence intervals.
Results: About 283 patients were included in the analysis, 4 cases had no recorded result. 115 (41% [35–46%]) reported no drugs or alcohol were taken before or during the assault, 58(21% [16–26%]) reported drugs or alcohol were taken before or during the assault, but not to the point of incapacitation, 106 (38% [32–43%]) reported drugs or alcohol were taken before or during the assault, to the point of incapacitation and that they were unable to give consent. The total number of ingestions reported was 189. Substances reported included the following: 134 (71% [64–77%]) ethanol, 14 (7% [4–12%]) other agents (over-the-counter(otc)/home meds), 12 (6% [4–11%]) THC, 8 (4% [2–8%]) benzodiazepines, 5 (3% [1–6%]) cocaine, 5 (3% [1–6%]) heroin/narcotics, 4 (2% (1–5%) amfetamines, 1 (1% [0–3%]) zolpidem, 1 [1% (0–3%]) MDMA, and 5 (3% [1–6%]) reported no known agents taken.
Conclusions: Limitations include self-reporting, lack of validation of agents by conformational screening, and exclusion of non-English speaking patients. This analysis revealed that 38% of patients reported drugs or alcohol were taken to the point of incapacitation and 71% reported using ethanol, which is consistent with published data. Self-reported use of ethanol continues to be a notable factor in this type of assault with OTC, THC, and benzodiazepines following. Education and intervention should continue to focus on ethanol use; however, given the ubiquitous nature of OTC, THC, and benzodiazepines these agents should also be considered in outreach efforts.

KEYWORDS Drug; sexual assault; ethanol

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24. Safety and efficacy of idarucizumab in clinical practice

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Introduction: Idarucizumab (IDZ) is a monoclonal antibody fragment used to reverse dabigatran-induced coagulopathy. IDZ received accelerated regulatory approval in 2016 but its capacity to affect patient-relevant outcomes remains unclear. Our study aimed to identify the mortality trends, adverse events, and functional outcomes associated with IDZ administration across three Canadian tertiary care hospitals.
Case series: All cases of IDZ administration between 1 June 2016 and 30 March 2017 at the Royal Victoria Hospital, Montreal General Hospital, and Montreal Neurological Hospital were identified through pharmacy records. Ethics approval was obtained

through the McGill University Health Centre. Our primary outcomes were mortality and thrombotic events at thirty days following IDZ administration. Two investigators independently abstracted patient data on a standardized data collection tool. We identified six patients who received IDZ (Table 1). Four patients received IDZ for active bleeding (group A) and two patients for peri-procedural anticoagulation reversal (group B). In group A, all three patients with intracranial hemorrhage (ICH) died by day 15 while one patient with a post-traumatic chest wall hematoma survived past 30 d without requiring transfusion (Figure 1). Two of three patients with ICH had a goals-of-care discussion leading to de-escalation of care within 2 h of IDZ administration; the third patient was de-escalated following discussion on his eighth hospital day. Both patients in group B survived past thirty days. No thrombotic events were observed in either group. IDZ reduced partial thromboplastin time (PTT) in the four patients with repeat values.

Case discussion: Our patients were older than those previously reported. Two of three ICH patients had a documented de-escalation of care after IDZ administration but before a meaningful clinical reassessment could be performed. The impact of these decisions on each patient's outcome is unclear but their prognoses were considered dismal by the treating team. The variability in time-elapsed between ED presentation and IDZ administration suggests that clinicians remain unfamiliar with this new drug and its indications. IDZ was only administered six times in ED's with a combined volume of ~100,000 visits per year. We cannot say from our study whether this was due to decreased dabigatran use, the rarity of major dabigatran-associated bleeding, underrecognition of IDZ's availability, or a combination of these factors. No patient with ICH survived past 15 d, suggesting that IDZ's efficacy ability to affect long-term neurological outcomes in closed-space neurologic bleeds may be limited or that it was administered too late.

Conclusions: IDZ administration is a rare event. Although a single patient with large-volume hemorrhage did well, all three patients in our study who received IDZ for dabigatran-associated ICH died within fifteen days of its use. Although IDZ may have been given in futility, it may not be possible for physicians to have a patient-centred goals-of-care discussion prior to making a decision on antidote administration. Our data suggest the need for institutional protocols for IDZ administration, ongoing study of its safety and efficacy, and future efforts to identify patients who would benefit the most from this antidote.

KEYWORDS Idarucizumab; dabigatran; anticoagulation

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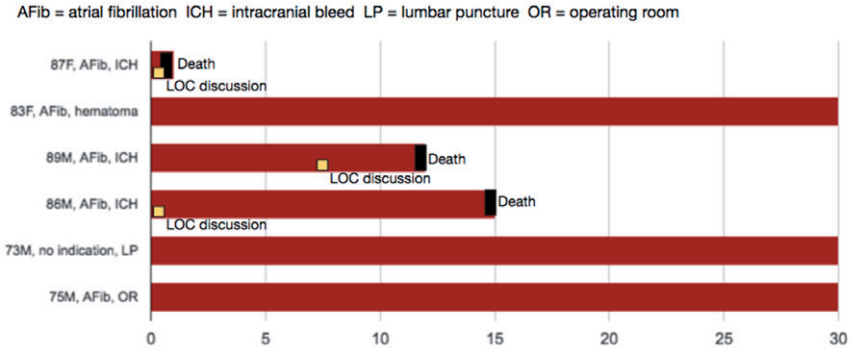

Figure 1: Death, thrombotic events, and level of care (LOC) discussions in the 30 days following idarucizumab (IDZ) administration. Included are the patient's age and sex, indication for dabigatran, and indication for IDZ administration. No thrombotic events were observed in our study population.

Table 1: Patients who received idarucizumab (IDZ) were divided into two groups based on the indication for IDZ administration: Group A = active bleeding, Group B = pre-procedural reversal. Abbreviations: partial thromboplastin time, PTT.

Characteristic	Patient A1	Patient A2	Patient A3	Patient A4	Patient B1	Patient B2
Age	87	83	89	86	73	75
Sex	Female	Female	Male	Male	Male	Male
Creatinine (umol/L)	89	75	60	119*	90	65
Dose of dabigatran	Not reported	110mg twice daily	110mg twice daily	Not reported	110mg twice daily	110mg twice daily
Indication for dabigatran	Atrial fibrillation	Atrial fibrillation	Atrial fibrillation	Atrial fibrillation	No indication	Atrial fibrillation
Indication for IDZ	Spontaneous intracranial bleed	Traumatic chest wall hematoma	Traumatic intracranial bleed	Traumatic intracranial bleed	Lumbar puncture	Operating room for Fournier's gangrene
PTT before IDZ (seconds)	68.2*	36.6*	39.7*	56.9*	30.6*	41.7*
PTT after IDZ (seconds)	Not performed	23.3	27	31.2*	Not performed	27.9
Time to IDZ administration (minutes)	110	475	694	332	1247	235

25. Palatability of effervescent versus standard oral *n*-acetylcysteine: Is it worth all the fizz?

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Background/objectives: Acetaminophen overdose is a common exposure reported to US Poison Centers. Standard *n*-acetylcysteine's (NAC) strong sulfur taste and smell makes oral administration challenging in the treatment of acetaminophen overdose. Traditionally oral NAC has been mixed with a variety of beverages to a 5% concentration for improved tolerability. The FDA recently approved a lemon-mint flavored, effervescent NAC (eNAC) tablet for treatment of acetaminophen poisoning, with increased palatability. The package insert for the eNAC recommends mixing with water prior to administration. Noteworthy, eNAC contains significant amounts of sodium and bicarbonate which may be concerning in a critically ill patient. We conducted a palatability study to determine how eNAC compares to standard oral NAC diluted in different beverages.
Methods: Pharmacy students and faculty were asked to participate an IRB approved prospective, cross-over, palatability study. A power calculation determined 45 participants were necessary to detect a difference in taste/smell of 2 points on the visual analog scale. Forty-five healthy volunteers, after informed consent, were recruited and completed the study. Participants took part in three sessions; Session 1: Tasting standard NAC in Fresca, Coca-Cola, and cranberry juice, Session 2: Tasting effervescent NAC in water and lemonade, and Session 3: smelling all the mixtures. Each of the sessions were conducted at least 24 h apart. Solutions were prepared in a 5% concentration to reflect accepted practice when administering oral NAC. Ten milliliters were placed in an opaque cup with lid and straw for tasting sessions, to maintain anonymity. Participants evaluated each mixture using a visual analog scale (VAS) with 0, and 10, being the least and most offensive taste/smell, respectively. Visual analog scale scores from all sessions were collected using the secure data system RedCap. Data analysis was completed using t-test and Kruskall Wallis ANOVA with Bonferroni correction.
Results: eNAC mixed in lemonade had the lowest average taste VAS score (4 ± 2.4), followed by standard NAC mixed in Fresca (4.91 ± 2.1). Standard NAC mixed in Coca-Cola had the highest taste VAS score (5.76 ± 2.0), and eNAC mixed in water had the second highest VAS score (5.57 ± 2.3). eNAC mixed in lemonade and water had the two lowest average smell VAS scores, 3.83 ± 2.1 and 3.87 ± 2.5, respectively. Standard NAC mixed in cranberry juice had the highest average smell VAS score (7.09 ± 1.9). The taste of standard NAC (all mixtures) (5.38 ± 2.3) was not statistically significantly different from the taste of eNAC (all mixtures) (4.78 ± 2.5), $p = .06$. The smell of all the eNAC mixtures was statistically different than the standard NAC mixtures (3.85 ± 2.3 versus 6.56 ± 1.9, $p < .01$).
Conclusions: The taste of eNAC is not superior to standard NAC and needs to be mixed with a beverage similar to standard oral NAC to improve palatability. Fresca best mitigated the taste of standard NAC in increasing palatability. The eNAC product smelled better than standard NAC.

KEYWORDS *n*-Acetylcysteine; acetaminophen; palatability

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26. Adjunct ketamine use in the management of severe ethanol withdrawal

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Background: Ketamine offers a plausible mechanism with favorable kinetics in treatment of severe ethanol withdrawal. The purpose of this study is to determine if a treatment guideline using an adjunctive ketamine infusion improves outcomes in patients suffering from severe ethanol withdrawal.
Methods: This is a retrospective observational cohort study of patients identified from the medical toxicology patient database admitted to the ICU at a tertiary care academic hospital for treatment of severe ethanol withdrawal from January 2008 to March 2011 (pre-guideline) and April 2011 to January 2015 (post-guideline). Patients were included if admitted to the ICU, diagnosed with delirium tremens (DT) by *Diagnostic and Statistical Manual of Mental Disorders V* criteria, and had complete medical records available for review. During the study period (pre and post-guideline) all patients were treated in a symptom-triggered fashion with benzodiazepines and/or phenobarbital under the direction of medical toxicology, critical care, and clinical pharmacy. Post-guideline, standard symptom-triggered dosing continued as pre-guideline, plus, the patient was initiated on an intravenous ketamine infusion at 0.15–0.3 mg/kg/h continuously until delirium resolved. On occasion, a ketamine bolus (0.3 mg/kg) was provided prior to continuous infusion. Pearson-correlation coefficients were determined for association between all outcomes (ICU days, hospital days, and need for intubation). Factors with significant correlation coefficients were included in a multivariable linear regression analysis for the outcomes of ICU days and hospital days, and in a multivariable logistic regression for intubation need.
Results: A total of 63 patients were included (29 pre-guideline; 35 post-guideline). Patients treated with ketamine were less likely to be intubated (OR = 0.14, $p < .01$, 95% CI 0.04, 0.49) and had a decreased ICU stay by 2.83 d (95% CI = −5.58, −0.089; $p = .043$). For ICU days outcome, correlation coefficients were significant for alcohol level and total benzodiazepine dosing. For hospital days outcome, correlation coefficients were significant for patient age, AST and ALT level. Regression revealed the use of ketamine was associated with a non-significant decrease in hospital stay by 3.66 d (95% CI = −8.40, 1.08; $p = .13$).
Conclusions: Mechanistically, adjunctive therapy with ketamine may attenuate the demonstrated neuroexcitatory contribution of NMDA stimulation in severe ethanol withdrawal, reduce the need for excessive GABA agonist mediated sedation, and limit associated morbidity. A ketamine infusion in patients with DT was associated with shorter ICU length of stay, lower likelihood of intubation, and a trend toward a shorter hospitalization.

KEYWORDS Ketamine; ethanol; withdrawal

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	No Ketamine (n=29)	Ketamine (n=35)
Mean Age (SD)	53.3 (12.2)	47.0 (9.6)
Number Men (%)	28 (96.6)	23 (67.7)
Mean MCV (SD)	96.2 (5.4)	96.3 (6.6)
Median AST (IQR)	85 (43,122)	69 (43,156)
Median ALT (IQR)	53 (30,88)	48 (29, 80)
Median EtOH (IQR)	19 (0,224)	0 (0,43)

27. Physostigmine versus standard cares for anticholinergic toxicity: a prospective study of efficacy and adverse events

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Background/objectives: Poison centers frequently consult on patients with anticholinergic poisoning. However, controversy surrounds the use of physostigmine, the antidote for the anticholinergic toxidrome. The purpose of the study was to prospectively investigate physostigmine versus standard care in the treatment of anticholinergic toxicity through a single regional poison center.
Methods: This was a non-interventional, prospective analysis of patients with anticholinergic delirium treated in consultation with a regional poison center. We aimed to quantify the rate of successful delirium reversal with physostigmine use compared with standard. We also described reported adverse effects (bradycardia, vomiting, seizures) and resource utilization (intubation and restraint) in the groups. Case details regarding patients identified to have an anticholinergic toxidrome requiring medical intervention were collected over a nine-month period. The anticholinergic toxidrome was identified by either the calling provider or the certified specialist in poison information (CSPI) based on clinical presentation, history, and reported exam findings. Demographics, vital signs, substances involved, and case details were collected initially, along with a previously validated altered mental status score (AMSS). The CSPI recommended treatment based on preexisting poison center guidelines. A callback was made to the patient's provider at 2 h and further information was collected, including whether physostigmine was given, other medications given, vital signs, and an updated AMSS. Episodes of bradycardia, vomiting, restraint, or intubation were collected during a subsequent phone calls. Cases were then followed to outcome as per normal poison center guidelines.
Results: A total of 214 cases were identified over the study period. 80 cases were excluded for a total of 134 cases (Figure 1). The patients were predominately female ($n = 80$, 60%) with a median age of 26. The most common substance classes were antihistamines ($n = 91$, 68%), followed by analgesics ($n = 26$, 19%), and antipsychotics ($n = 23$, 17%) (Table 1). Physostigmine was recommended in 107 cases (80%), and given in 51 cases (38%). Of the cases where physostigmine was given, delirium was controlled in 71.4% of cases versus 35.9% of cases in the group that did not receive physostigmine at the 2-h follow-up. Delirium control was more than four times more likely in patients receiving physostigmine than in patients treated with standard care alone (odds ratio 4.46). Vomiting occurred in three of the physostigmine cases, while no occurrences of bradycardia or seizures were observed following physostigmine administration (Table 2). Using a logistic regression model, physostigmine was neither associated with increased incidence of adverse events, nor decreased rate of intubation/restraint.
Conclusions: In this prospective poison center study, physostigmine was observed to be superior to standard care for control of anticholinergic delirium. Adverse effects related to physostigmine were minimal. Physostigmine was not shown to decrease the rate of restraint or intubation. Although this study is limited by small sample size, it provides further evidence of both the safety and efficacy of physostigmine in the treatment of anticholinergic delirium.

Table 1. Substance exposures in patients given physostigmine or not given physostigmine

Medication Class[1]	Total (%)	Patients given physostigmine (%)	Patients not given physostigmine (%)
All	134 (100)	51 (100)	83 (100)
Antihistamine	91 (67.9)	35 (68.6)	56 (67.5)
Stimulant	13 (9.7)	5 (9.8)	8 (9.6)
Analgesic	26 (19.4)	11 (21.6)	15 (18.1)
Benzodiazepine	7 (5.2)	1 (2.0)	6 (7.2)
TCA	4 (3.0)	2 (3.9)	2 (2.4)
SSRI/SNRI	11 (8.2)	6 (11.8)	5 (6.0)
Bupropion	4 (3.0)	1 (2.0)	3 (3.6)
Dextromethorphan	10 (7.5)	1 (2.0)	9 (10.8)
Antipsychotic	23 (17.2)	10 (19.6)	13 (15.7)
Muscle relaxant	7 (5.2)	3 (5.9)	4 (4.8)
Ethanol	16 (11.9)	6 (11.8)	10 (12)
Antiepileptic	2 (1.5)	2 (3.9)	0 (0)
Sedative	5 (3.7)	0 (0)	5 (6.0)
Blood pressure medication	2 (1.5)	1 (2.0)	1 (1.2)
Unknown	9 (6.7)	4 (7.8)	5 (6.0)
Other[2]	7 (5.2)	4 (7.8)	3 (3.6)

1. Patients may be counted more than once due to exposure to multiple drugs
2. Other includes antibiotics, blood thinners, proton pump inhibitors, diabetes medications, and non-pharmaceutical exposures

Table 2. Delirium control, adverse effects, and resource utilization at 2 hour call

	Total	Patients given physostigmine (%)	Patients not given physostigmine (%)
All patients	134	51 (38.1)	83 (61.9)
Delirium control	68	40 (78.4)	28 (33.7)
Seizure	0	0 (0)	0 (0)
Vomiting	3	3 (5.9)	0 (0)
Bradycardia	1	0 (0)	1 (1.2)
Restraint placement	9	3 (5.9)	6 (7.2)
Intubation	5	2 (3.9)	3 (3.6)

KEYWORDS Physostigmine; anticholinergic; poison center

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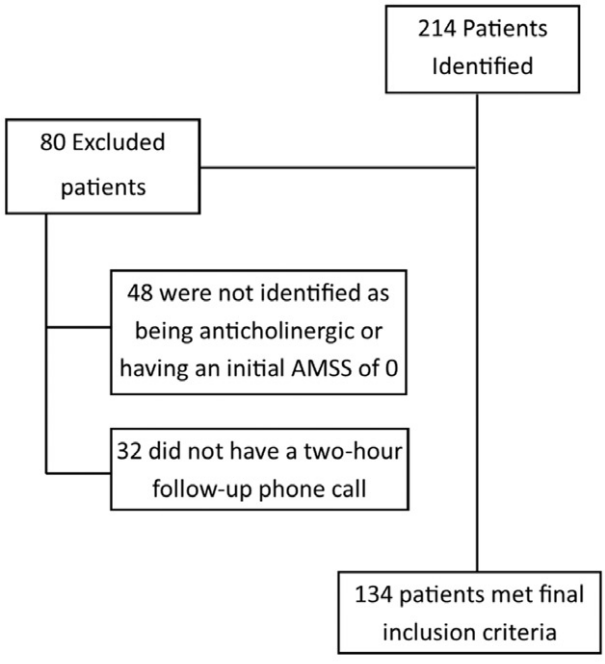

Figure 1. Study Enrollment

28. ReCAP2: reducing childhood admissions to the PICU for poisoning by predicting unnecessary PICU admissions after acute ingestion

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Background: Most children admitted to a Pediatric Intensive Care Unit (PICU) after acute ingestion never require PICU intervention. We recently developed a model that accurately predicts which children need intensive care using data from the entire hospital course as recorded in the American Association of Poison Control Centers National Poison Data System.
Objective: To evaluate this model, considering only factors known to the poison center from initial emergency department (ED) evaluation.
Methods: We reviewed the charts of 700 sequential patients <19 years old admitted to a hospital following acute ingestion. Demographics, substance(s) ingested, and clinical signs/symptoms were reviewed independently by two toxicology physicians and discrepancies were reconciled before analysis. Vital sign and laboratory parameters were compared with standards for age. The need for PICU admission predicted by the model was compared with actual admission data and need for PICU interventions.
Results: Of the 700 patients reviewed, 414 were admitted to PICU (59.1%). Only 64/414 (15.5%) of the patients received one or more PICU interventions. Using only clinical findings documented in the ED, the model successfully predicted all 64 patients that required PICU intervention. Out of the 350 remaining patients admitted to a PICU, our model correctly predicted 110 patients as not needing PICU intervention; therefore, reducing unnecessary PICU admissions by 31.4%.
Conclusions: Prediction of which patients presenting to the ED with acute ingestion will need a PICU intervention will improve resource utilization. Our refined predictive model would have reduced overall demand for PICU beds by 27% without missing any patient who needed PICU intervention. Further prospective model validation is needed.

KEYWORDS Poisoning; ingestion; PICU

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29. Flibanserin toxicity in a toddler

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Background: Flibanserin is a medication approved by the US Food and Drug Administration in 2015 to treat hypoactive sexual desire disorder in women. It is a 5-HT(1A) agonist, 5-HT(2A) antagonist, and weak partial agonist of dopamine D4 receptors. Effects at these receptors in the prefrontal cortex may promote sexual desire by increasing dopamine and norepinephrine and decreasing serotonin levels. The risk–benefit ratio is currently under debate. Given its recent approval, flibanserin toxicity has not yet been well described. We present a case of flibanserin toxicity in a child.
Case: A 2-year-old boy presented to the emergency department (ED) 2 h after ingesting six 100 mg tablets of his mother's flibanserin. He was transported to the ED after being found limp and minimally responsive. On presentation, vital signs were: temperature, 37.4 °C; heart rate, 91 beats per minute; blood pressure, 111/61; respirations, 22/min; O2 saturation, 99% on room air. Blood glucose was 90 mg/dL. Examination was notable for an unresponsive child with dilated pupils, abnormal facial movements, normal skin, and the absence of clonus. Providers were concerned for seizure, so he received 1.5 mg of lorazepam. Subsequently, he began responding to painful stimuli and appeared postictal. EKG, non-contrast head CT, and radiographs of the chest and abdomen demonstrated no abnormalities. Laboratory studies, including BMP, venous lactate, ammonia, EtOH level, salicylate level, and acetaminophen level, were within reference ranges. Anion gap was 9. After transport to the children's hospital, mental status was improved. Exam was notable for dilated pupils, hypotonia, purposeful movements, and spontaneous eye opening. Urine drug screen (UDS) by immunoassay was positive for benzodiazepines. UDS by gas chromatography and mass spectrometry was positive for caffeine, paraxanthine, and 1-(3-trifluoromethylphenyl)-piperazine (TFMPP). The patient was admitted to the PICU where he developed a fever to 38.4 °C. He was discharged the next day with a much-improved exam.
Discussion: The reported history and positive UDS for TFMPP highly suggest that this patient's presentation was a result of flibanserin toxicity.
Flibanserin is primarily metabolized by CYP3A4 in the liver where it is de-ethylated to produce TFMPP, a piperazine. At toxic doses, effects of piperazine toxicity may occur. These include symptoms seen in our patient, such as seizure, mydriasis, hypertension, and fever. Piperazines can also lead to serotonin syndrome, muscle rigidity, psychosis, and tachycardia.
Conclusions: Presented here is a case of flibanserin toxicity in a toddler. The patient demonstrates a syndrome indicative of piperazine toxicity, consistent with the proposed mechanism of flibanserin metabolism.

KEYWORDS Flibanserin; addyi; pediatric

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30. Variability of international clinical toxicologists recommendations concerning the use of digoxin-specific antibody fragments

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Background: Digoxin is a widely used cardiac glycoside for the treatment of congestive heart failure and atrial fibrillation. Due to its narrow therapeutic index, digoxin toxicity is common. Digoxin-specific antibody fragments (digoxin-Fab) are an effective antidote to treat digoxin toxicity; however, no evidence-based guideline for the use of digoxin-specific antibody fragments exists to date. Digoxin-specific antibody fragments are expensive, possibly over or underused and not always available in every country or settings. Exploring recommendations of clinical toxicologists and poison centers in recommending digoxin-specific antibody fragments would provide a better understanding of the gaps needed to foster studies, promoted the judicious use of this antidote and perhaps reduce practice variation.
Objective: Explore the current practice of international clinical toxicologists regarding their indications and the amount of digoxin-specific antibody fragments used or recommended in acute and chronic digoxin toxicity.
Methods: Following ethics review approval, an online survey was developed and deployed between January 2017 and February 2017 to the members of the Asia Pacific Association of Medical Toxicology (APAMT), the American Association of Poison Control Centers, the European Association of Poisons Centres and Clinical Toxicologists, the Canadian Association of Poison Control Centers, and poison control centers on the World Health Organization directory.
Results: One hundred and eight responses to at least one question were received. Data could be extracted from 82 responders in 23 countries. The majority of responders (67%) were medical toxicologists. Seventy-four responders reported that their affiliated Poison Control Center had established guidelines for dosing and indication of digoxin-Fab, and 74% of those agreed with their poison control center's current guidelines. Two respondents indicated that this antidote is unavailable in their country (India and Lithuania). Recommendations for digoxin-specific antibody fragments were the strongest for significant dysrhythmias (97%), cardiac arrest due to digoxin toxicity (87%), and rapidly progressive signs and symptoms of toxicity (61%). There was noticeable variability for the Potassium(K) concentrations at which digoxin-specific antibody fragments were recommended ($K > 5$ mmol/L 58% versus $K > 6$ mmol/L 27%). Digoxin-Fab was less recommended in cases of altered mental status or elevated serum digoxin concentration (21% and 23%). Equimolar neutralization of digoxin was recommended by 38% of responders in acute toxicity and by 31% in chronic toxicity. Semi-molar neutralization was recommended by 13% responders in acute toxicity and by 18% in chronic toxicity. Thirty-eight percent recommended 50% neutralization when using semi-molar neutralization. Hemodynamic stability was the therapeutic goal in 60% of the responses.
Conclusions: Current practice as indicated by our results offers wide variability of digoxin-Fab use across the 21 countries surveyed. Many medical toxicologists and poison control centers recommend complete neutralization of digoxin serum concentration (12%) in both acute and chronic toxicity even though it might not be necessary. Given that digoxin-Fab is expensive or unavailable in some places, developing clearer recommendations may help to reduce the variability and the overuse of digoxin-Fab.

KEYWORDS Digoxin; digoxin-specific antibody fragments; digoxin-Fab

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31. Venous thrombosis as a complication of rattlesnake envenomation

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Introduction: There are nearly 8000 snakebites in the United States annually. Envenomings can have many acute and delayed complications including allergic reaction, edema, tissue damage, neurotoxicity and hematologic toxicity. To our knowledge, venous thrombosis had not been widely reported as a result of rattlesnake envenomation.
We report three cases of venous thrombosis following a rattlesnake bite.
Methods: We performed a retrospective review of all snakebites documented in Toxicall® at Arizona Poison and Drug Information Center between 1999 and 2016.
Results: Case 1: A 39-year-old with no significant past medical history (PMH) was bitten on her right lower extremity. The initial laboratory results were normal. She had severe pain and progressive swelling which required a total of 30 vials of AV. The labs were repeated after treatment and the only abnormal value was a D-dimer of 160 μ/mL. Due to persistent swelling and pain, ultrasonography was performed on the 6th day of admission and revealed deep venous thrombosis (DVT). Patient was started on Rivaroxaban for DVT and discharged on the nineth day of admission. Case 2**:** A 39-year-old with no significant PMH had a snakebite in her right lower extremity. She had severe pain with swelling and she received a total 16 vials of AV. Her initial lab results were normal, including coagulation profile. Swelling progressed on day 2 after admission. Ultrasonography was obtained, DVT was found in two posterior tibial veins. On day 3, patient was discharged on enoxaparin and warfarin. Three days after discharge, the patient's lab results showed PTT >200 s, fibrinogen <20 mg/dL and INR >18. She was readmitted and given eight more vials of AV. Lab result after treatment with AV showed INR 2.1 and fibrinogen 29 mg/dL. INR further decreased to 1.6 and fibrinogen increased to 91 mg/dL. Patient was discharged. Case3**:** A 52-year-old with no significant PMH had a snakebite to his right lower extremities. He had tenderness and swelling. His initial labs were: PTT 25.3 s, INR 1 and platelet 156 1000/μL. Patient was given 11 vials of AV. Labs were repeated after treatment and showed INR 1.2, fibrinogen 92 mg/dL and platelet 175 1000 μL. On day 3, the patient was discharged with fibrinogen of 50 but no signs of bleeding. Two days after discharge, his labs were normal except for low fibrinogen of 22 mg/dL. Patient's leg remained unchanged. Two weeks after discharge he developed redness and rash in the swollen leg. Ultrasonography revealed occlusive clot within the left great saphenous vein. His labs, including fibrinogen, were normal. Patient was discharged home on enoxaparin.
Conclusions: Venous thrombosis can be a rare complication of rattlesnake envenomation. Liberal use of Doppler ultrasonography may help in reveal the true incidence of this complication.

KEYWORDS Rattlesnake; envenomation; venous thrombosis

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32. "It Got Me Bad", copperhead envenomation resulting in cardiac arrest and disseminated intravascular coagulation

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Background: Copperhead (Agkistrodon contortrix) envenomations are the most common venomous snake exposure in North America. Although encounters are common, they are rarely life or limb threatening. In 2015, 1764 copperhead exposures were reported to US poison centers with 1.8% of those exposures having major outcomes and only one death.
Case report: A 51-year-old male with past medical history of hypertension, diverticulosis, and chronic pain handled a copperhead after drinking alcohol and was bit on his right middle finger. Within minutes, the patient stopped breathing and went into cardiac arrest. Emergency medical services (EMS) was called and chest compressions performed by his father. Cardiopulmonary resuscitation was continued by EMS for an additional minute, without medications, before return of spontaneous circulation. The patient arrived to the emergency department breathing spontaneously and complaining of chest pain. He had respiratory distress, tachycardia to 150 bpm, with oxygen saturations of 79% on nasal cannula. He had cyanosis of his chest wall and face and fang marks on the dorsum of his right index finger but no swelling or ecchymosis. The patient's clinical condition rapidly deteriorated requiring intubation 10 min after arrival. After intubation, he became hypotensive requiring fluids and vasopressors. Initial labs were remarkable for a hemoglobin of 22.5 g/dL, platelets of $26 \times 10^3/\mu L$, an ethanol level of 108 mg/dL, and an arterial blood gas with pH of 7.09, pCO2 of 44, pO2 of 146, and HCO3 of 13. On repeat CBC, hemoglobin was 18.6 g/dL and platelets of $135 \times 10^3/\mu L$. There was bleeding from his orogastric tube (OGT) and foley catheter (red, bloody urine) but not from his IV sites or bite site. A CT angiogram of the chest was negative for pulmonary embolism. He was transferred to a tertiary care facility. Upon tertiary care facility arrival, he was noted to have increased bleeding from his foley and OGT. Coagulation studies from the initial hospital resulted, revealing a prothrombin time >100.1 s and international normalized ratio (INR) >10. The patient was given eight vials of crotalidae polyvalent immune fab due to the severe clinical effects following envenomation. An additional 12 vials were given for persistent shock. In total, he received 20 vials of antivenin. The patient's hospital stay was complicated by severe shock. He also developed renal failure requiring dialysis, *Clostridium difficile* colitis, bowel ischemia requiring multiple major surgical procedures, pulmonary emboli, and sepsis. The patient was discharged directly home approximately 2 months after the envenomation.
Discussion: Copperhead envenomations typically result in local tissue injury. Systemic complications are rarely life threatening, and when they occur are related to coagulopathy, rhabdomyolysis, and allergic reactions. In this case, our patient developed cardiac arrest, coagulopathy, and multiple complications following his envenomation. The rapid onset of cardiac arrest and coagulopathy suggests an intravenous envenomation rather than severe systemic effects from a cutaneous envenomation.
Conclusions: Rapid onset of clinical effects following copperhead envenomation may be related to direct intravenous inoculation of venom. Our case adds to the body of knowledge regarding complicated copperhead envenomations and their management.

KEYWORDS Copperhead; disseminated intravascular coagulation; cardiac arrest

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33. Delayed presentation of intraarterial injection of crushed amfetamine/dextroamfetamine treated with conservative management

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Background: Intraarterial injection of sympathomimetics have been known to cause arteriospasm with resulting limb ischemia. Several treatment modalities have been attempted including both arteriodilators (e.g., phentolamine), venodilators (e.g., nitroglycerin). Delayed presentation to medical attention and supportive care without pharmacologic intervention, in particular with the drug amfetamine/dextroamfetamine, has not been described.
Case report: A 37-year-old female with a history of bipolar disorder and IV drug abuse presented to the emergency department 15 h after an inadvertent intraarterial injection of amfetamine/dextroamfetamine with pain and discoloration in her right upper extremity (RUE). She reports crushing the tablets, mixing them with water, then attempting a right forearm antecubital intravenous injection. She noted an immediate burning sensation and 20 min later reported diffuse arm pain and skin changes distal to the injection site. Her vital signs were normal except for a blood pressure of 139/86 mmHg. Physical examination showed numerous violaceous patches with surrounding areas of blanching and mild diffuse edema distal to the injection site. Capillary refill was 3 s and a RUE arterial and venous duplexes did not show flow limiting stenosis or other abnormalities. Given the delay in presentation as well as unavailability of nitroprusside, the patient was admitted to the hospital for compartment and pulse checks, elevation of her arm, and pain control. She developed rhabdomyolysis with a CPK peak of 3362 units/L; a subsequent CT scan of right forearm and hand was obtained and demonstrated ill-defined evidence of myonecrosis of the flexor and extensor muscles of the forearm and thenar eminence. She continued intravenous fluids, elevation, and pain control and on hospital day 6 was discharged with decreased swelling and resolved rhabdomyolysis. She was seen 1 week later in clinic with continued decreased swelling, decreased pain, and improved appearance of her skin changes. No further interventions were planned.
Case discussion: This case is unique given the delay in presentation and lack of availability of the most appropriate treatment medication due to hospital shortage. Due to normal capillary refill and no flow limiting lesion on vascular ultrasound, drug effect was deemed to be minimal at the time of presentation and conservative management was the best course. Although she experienced pain as well as significant skin changes and evidence of myonecrosis on CT scan, she recovered fully without any pharmacologic or surgical intervention.
Conclusions: Although several treatment modalities have been proposed for intraarterial injection of vasoconstrictive drugs, conservative management with close monitoring may be possible, especially in individuals with delayed presentations without evidence of decreased pulses or abnormal capillary refill.

KEYWORDS Amfetamine/dextroamfetamine; injection; intra-arterial

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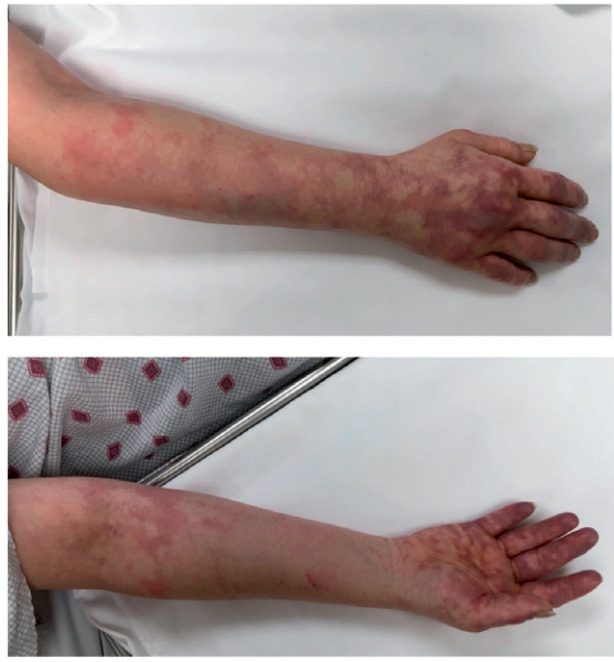

34. Mild tachycardia and hypertension only, after inadvertent parenteral administration of sumatriptan in a young woman

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Background: Sumatriptan is a selective 5-HT1B and 5-HT1D receptor agonist that is used to vasoconstrict cranial arteries to treat migraine headaches. Sumatriptan is administered both in oral tablets and subcutaneous injections. Currently, it is not approved for intravenous use due to a single study that reported increased systemic and pulmonary arterial pressures as well as reduction in coronary artery diameter in humans (Macintyre 1992). We report a case of an individual with an iatrogenic parenteral injection of sumatriptan who suffered no clinical consequences.
Case report: A 35-year-old 54 kg woman with a history of tobacco abuse and migraine headaches presented to an emergency department with a complaint of migraine headache. Inadvertently, the nurse administering the sumatriptan injected it intravenously rather than subcutaneously, as prescribed. The patient received sumatriptan 6 mg (0.11 mg/kg) intravenously. Several minutes after receiving the medication, her pulse was 108 bpm, respiratory rate was 24 bpm, blood pressure was 142/91, oxygen saturation was 100% on room air, and her temperature was 97.8 °F. She reported resolution of her headache. She denied chest pain or shortness of breath. EKG was normal. She was monitored for 4 h at which time she remained asymptomatic. Repeat vital signs demonstrated a pulse of 68 bpm, respiratory rate of 16, blood pressure of 130/82, and oxygen saturation of 95% on room air. The patient was then discharged home.

Case discussion: Sumatriptan is FDA-approved to only be given in oral tablets or subcutaneous injections. In reviewing the literature, there are no reports describing the clinical effects (or lack thereof) of parenteral administration of sumatriptan. Our case demonstrated a mild increase in heart rate and blood pressure that quickly self-resolved without treatment. Although Macintyre et al. reported statistically significant increases in systemic and arterial pressures and a reduction of coronary artery diameter with a dose of 0.48 mcg/kg over 10 min (equivalent to a total dose of 2.59 mg in our patient), it did not appear to of any consequence in our overall healthy 35-year-old woman. A literature search did not yield reports of inadvertent intravenous administration of sumatriptan and the effect in humans. These effects may not be tolerated as well in individuals with a co-morbid history of illnesses that would include poorly controlled hypertension, pulmonary artery hypertension, of coronary artery disease.
Conclusions: Although this only represents one case, no such experiences have been previously reported. In young and fairly healthy individuals, inadvertent intravenous administration of sumatriptan may only cause mild increases in the heart rate and blood pressure without clinically significant effects.

KEYWORDS Sumatriptan; intravenous; iatrogenic

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35. Cyclosporine as a novel treatment for amatoxin-containing mushroom poisoning

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Background: Ingestion of amatoxin-containing mushrooms can lead to fulminant hepatotoxicity and death. Despite the severity of outcomes, there are limited treatment options available for amatoxin-exposed patients. Alpha-amanitin is the principle amatoxin causing human toxicity. Alpha-amanitin enters into hepatocytes via the organic anion transporter polypeptide (OATP) 1B3 transporter protein located on the sinusoidal membrane of hepatocytes. A potential therapeutic approach for management of amatoxin-exposed patients is inhibition of the OATP1B3 transporter, preventing entry of the toxin into hepatocytes. Cyclosporine is a calcineurin inhibitor used in the treatment of organ transplant rejection and autoimmune disorders. Cyclosporine is a potent inhibitor of the OATP1B3 transporter and available in most hospitals. We describe three cases where cyclosporine was used in the treatment of confirmed amatoxin-poisoned patients with full recovery.
Case presentations: Case 1 is a 73-year-old man who presented to hospital with vomiting and diarrhea 12 h after consuming a foraged mushroom, later identified as *Amanita bisperogia*. Transaminases, creatinine and liver function tests were normal on presentation (AST 33 IU, ALT 46 IU, creatinine 108 mmol/L, INR 1.0). He was volume resuscitated, given an octreotide infusion (50 mcg/h) and a cyclosporine infusion (5 mg/kg/24 h) for 48 h. His transaminases peaked at AST 144 and ALT 190 approximately 46 h post-ingestion. Alpha-aminitin was detected in his urine samples 38 h post-ingestion. He had improvement in his symptoms and normalization of liver enzymes 6 d post-ingestion. Cases 2 and 3 are a mother and daughter who presented to hospital 22 h after ingesting a cooked meal made with foraged mushrooms, later identified as *Lepiota spp*. They were symptomatic with vomiting and diarrhea. The 53-year-old mother (Case 2) presented with elevated transaminases (ALT 86 IU), which peaked after 48 h at 950 IU. The 16-year-old daughter (Case 3), despite having severe diarrhea, had normal bloodwork throughout her admission. Alpha-aminitin was detected in urine samples up to 57 h post-ingestion for Case 3. Each patient was treated with intravenous fluids, octreotide (50 mcg/h) and cyclosporine (5 mg/kg/24 h) for 48 h. Both patients had normal liver enzymes and resolution of symptoms by 5 d post-ingestion.
Discussion: We present three patients with confirmed amatoxin-containing mushroom exposures treated with cyclosporine to prevent entry of alpha-aminitin into hepatocytes, and mitigate hepatotoxicity. Other OATP1B3 inhibitors have been previously reported as potential treatment for amatoxin exposures including silibinin. However, purified silbinin derivative is an investigational drug and not readily available in Canada, limiting timely administration. To our knowledge, we are reporting the first case series of patients successfully treated with cyclosporine for confirmed symptomatic amatoxin ingestions. Although two of these patients (Cases 1 and 2) developed a transient rise in transaminases, both had complete clinical recovery and normalization of liver enzymes after several days. There were no adverse effects related to cyclosporine administration in all three cases.
Conclusions: Cyclosporine is a readily available, potent inhibitor of OATP1B3 that may be useful as a treatment to prevent hepatotoxicity in amatoxin-poisoned patients. Further studies are required to confirm the utility of this novel treatment approach.

KEYWORDS Amanita; mushroom; cyclosporine

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36. Poison center characterization of pediatric ropinirole ingestion

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Background: Ropinirole is a non-ergonoline dopamine agonist at central and peripheral dopamine receptors. Immediate and delayed release formulations are available with maximum tablet sizes ranging from 5 mg to 12 mg, respectively. FDA-approved uses in the US are for Parkinson's disease and restless legs syndrome. Ropinirole is not approved for pediatric use; furthermore, there are few reports describing accidental pediatric ingestion of ropinirole. Therefore, the purpose of our study was to retrospectively review and characterize pediatric ropinirole exposures reported to our regional poison center (RPC).
Methods: Prior to case review, a literature search was conducted using the following keywords: ropinirole overdose, ropinirole intoxication, ropinirole pediatric, ropinirole poisoning, and ropinirole toxicity. We queried NPDS for single substance exposures reported to our RPC between the years of 2004–2016 in children aged 0–18 years old and reviewed each case.
Results: About 54 exposures to ropinirole meeting the criteria defined were identified. All were accidental ingestions except for two cases of self-harm. One case was confirmed as non-exposure. Three cases involved therapeutic dispensing errors where risperidone was dispensed instead of ropinirole. Median age was 4.4 years. Estimated amount of ropinirole ingestion ranged from 0.125 mg (asymptomatic) to 12 mg (asymptomatic). Of the cases where weight was provided, doses ingested ranged from 0.018 mg/kg (drowsy) to 0.46 mg/kg (pallor, vomiting). Most exposures were accidental ingestions of 1–2 tablets of ropinirole ranging from total doses of 0.25–4 mg. See Table 1 for medical outcomes. No reported effects occurred in 29 (53.7%) of the exposures. The most commonly reported minor clinical effect was

lethargy/drowsiness, followed by vomiting. Two patients experienced moderate effects (dystonias). There were no deaths or major effects reported. The lowest dose that caused symptoms in children 0–5 years old was 0.25 mg and the highest dose that did not cause symptoms in this same age group was 4 mg. Aside from these two cases, most ingestions over 2 mg caused symptoms. Two children age 14 months and 2 years old had dystonia with an unknown number of ropinirole tablets ingested. Both were evaluated and treated in the emergency department. About 48% of cases involved non-HCF management and 33% were referred to an HCF. Two were admitted to non-critical care units. Ropinirole serum concentrations were not performed.
Conclusions: Pediatric ropinirole ingestion is an infrequent occurrence at our RPC. Most cases involved minor or no clinical effects; no major outcomes or deaths were observed. Moderate outcomes involved dystonic reactions. Current treatment recommendations include home observation for inadvertent ingestion, which is appropriate for the lower tablet strengths. However, if a child ingests a larger strength, there is not enough data from our small case series to safely recommend home observation. More research is needed in this area.

KEYWORDS Ropinirole toxicity; pediatric ropinirole ingestion; ropinirole overdose

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Outcomes	No Effect	Minor	Moderate	Major	Lost to follow-up
# of Cases	29	20	2	0	2

37. Neurocognitive dysfunction in patients with poisoning: is it toxin specific?

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Objectives: To compare the neurocognitive dysfunction in patients with B*ungarus caeruleus* envenomation, organophosphate poisoning (OPC) and Aluminium phosphide poisoning in patients admitted to the emergency at a tertiary care center in North Western India.
Patients and methods: Prospective patients recruited for three different studies carried out in the patients admitted to the medical emergency with neurotoxic snake envenomation, organophosphate compound poisoning and aluminium phosphide poisoning in last 10 years. Detailed history and, clinical evaluation were recorded. All the patients received treatment as per the protocols.They were subjected to a detailed neurocognitive testing before discharge and followed up at 3 months. Trail A, Trail B, PGI memory scale, Bender Visual Motor Gestalt tests were used. The data from the different cohorts was compared.All statistical analysis was done using the SPSS version 15 (SPSS Chicago, IL).
Results: In the snake bite cohort, 48 patients were included in the study. Mean age was 29.67 ± 11.9 years (range = 12-65 years). About 66.7% were male. In the second cohort, 28 patients of acute organophosphate posoning were included.Mean age was 24.61 ± 10.6 years (range = 14–69 years). 64.3% were male. In the third cohort, 23 cases of acute Aluminium phosphide poisoning were included.Mean age was 25.7 ± 12.4 years (range = 13–59 years). 60% were male. At Base line, all the tests were abnormal in all cohorts. At 3 months follow up, there was improvement in all scores but significant dysfunction persisted as compared with normal healthy controls.
Discussion: Both in OPC and in neurotoxic snake envenomation, acetylcholine or its receptor dysfunction may have resulted in cognitive dysfunction. In neuroparalytic snake envenomation hypoxia may have contributed as well. In aluminium phosphide poisoning, although acetylcholine or any other neurotransmitter is not directly affected but hypotension may have resulted in altered blood flow resulting in reversible neurocognitive dysfunction.
Conclusions: Reversible neurocognitive dysfunction seems to be a norm in the studied poisonings. Although dysfunction in cognition is partly reversible, yet return to normality is not seen at 3 months interval.

KEYWORDS Neurocognitive dysfunction; poisoning; self-harm

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38. A drug by any other route would be as toxic? Two cases of treprostinil overdose

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Background: Treprostinil is a synthetic prostacyclin analogue that acts as a vasodilator for the treatment of pulmonary hypertension. The medication, approved in 2002, is available as a subcutaneous injection/continuous infusion (Remodulin®), inhalation (Tyvaso®), or in tablet form (Orenitram®). Although it has a similar mechanism of action to eproprostenol (Flolan®), it has a much longer half-life of approximately 4 h. Experience with overdose is limited. We report two contrasting cases of treprostinil overdose reported to a single poison center.
Case reports: Case 1: A 56-year-old woman with a history of pulmonary artery hypertension who was inadvertently administered 1.2 mg of intravenous treprostinil over 1 h (approximately 286 ng/kg/min; therapeutic dose 8 ng/kg/min) – this represented a 35-fold overdose. She developed severe hypotension, complicated by a period of cardiac arrest (rhythm unknown), and subsequent refractory hypotension. She was administered crystalloid fluids and infusions of norepinephrine, epinephrine, and vasopressin with minimal improvement in blood pressure. A dose of methylene blue was given without significant benefit. Twenty-three hours after the therapeutic error, the patient was declared brain dead. Case 2: A 30-year-old woman with a history of methamfetamine abuse and pulmonary artery hypertension presented 9 h after an intentional overdose of 45 mg of oral treprostinil over approximately 4 h (normal dose 0.25 mg BID). She was initially noted to have flushed skin, and she complained of mild dizziness. Her initial systolic blood pressure was 81/45 mmHg. She was given 1 L of intravenous crystalloid fluid, with improvement of her blood pressure to 102/63 mmHg. She was observed overnight, during which time she maintained a normal blood pressure and had no further complications. She was transferred to mental health the following day.
Discussion: Despite similarly massive overdoses of treprostinil, the two patients reported here had markedly different medical outcomes. The patients both developed hypotension, but the patient who self-administered the oral dose responded to a single fluid bolus and suffered no further effects. The patient who was

inadvertently administered the intravenous overdose suffered profound shock and ultimately succumbed to multi-organ failure despite aggressive interventions. This difference may be due to the bioavailability of the oral formulation, which is reported to be only 18% relative to the intravenous version. The time to peak concentration has been reported to be 4–6 h for the oral formulation – necessitating a period of observation at least that long after an overdose. Both case reports are limited due to the nature of information gathered through the poison center. Further, there were no confirmatory studies to determine the exact quantity of drug administered in either case.
Conclusions: Treprostinil is a vasodilator with the potential to cause significant hemodynamic instability in overdose – although the route of administration (oral versus intravenous) may affect the extent of toxicity.

KEYWORDS Treprostinil; shock; therapeutic error

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39. Hot Tox: one center's experience with drug-induced hyperthermia

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Background: Many patients presenting to an emergency department following an accidental or intentional ingestion are found to be hyperthermic as defined by a body temperature >38 °C. For those patients, there is an increased risk of mortality and morbidity. The mechanism of drug induced hyperthermia has been well studied. There has been little research done evaluating the incidence of drug induced hyperthermia syndromes. We reviewed one poison center's exposure data to determine the frequency at which increased body temperature may be correlated with exposure to specific medications. The objective of this study is to describe the patients that are reported to one poison center with hyperthermia.
Methods: This retrospective observational study utilized data from a single poison center that was entered and stored by the Toxicall data collection system. Inclusion criteria were human exposure, clinical effect of hyperthermia, dates 1/1/2012–12/31/16. All data were de-identified prior to abstraction. Specific data were verified and abstracted from the case notes and stored in an Excel spreadsheet. Abstraction was performed by the three authors. Each author worked off a common set of definitions. Consistency of abstraction was tested by comparing the data abstraction of 20 cases. Cause of hyperthermia was determined by published information and set by the abstracting author. IRB approval of the study was obtained.
Results: About 507 cases meet the inclusion criteria. Of those 507, 299 patients had documented temperatures greater than or equal to 38 °C. Ninety cases were excluded for reported positive serum and/or sputum cultures, or a positive chest X-ray. Additionally, four cases were excluded due to food poisoning, and one excluded due to a documented viral infection. Of the 204 remaining hyperthermic patients, 13 (6.4%) had minor effects only, 127 (62.2%) moderate, 56 (24.4%) major, and there were eight (3.9%) deaths. Thirty-seven of the 204 patients (18.2%) were determined to be hyperthermic due to exposure to serotonergic medications (including 11 dextromethorphan) or serotonin syndrome. Thirty patients (14.7%) were exposed to sympathomimetic medications (including amfetamines), 16 patients (7.8%) due to antihistamines/anticholinergic exposure, six salicylate, five withdrawal, and five synthetic cannabinoids. There were only two hyperthermic patients that were exposed antipsychotic medications and no patient had malignant hyperthermia. Ninety-seven (47.5%) hyperthermic patients had a polydrug ingestion. Twenty-eight (13.7%) exposures were associated with an unknown drug. Sixty-five hyperthermic patients (31.9%) reported utilizing mechanical cooling measures.
Conclusions: Based on our analysis of patients managed by a single poison center, hyperthermia (≥38 °C) is most commonly correlated with exposures to serotonergic medications, sympathomimetics and anticholinergics. Sixty-four of the hyperthermic patients (31.4%) reported a life threatening event or died. This study is limited by its retrospective nature, passive reporting, and reliance on caller information.

KEYWORDS Hyperthermia; serotonin syndrome; poison center

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40. A review of rufinamide exposures as reported to US poison centers

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Background: Rufinamide (Banzel®) is a member of the latest generation of antiepilepsy medications approved in November 2008. Rufinamide is a triazole derivative that is postulated to work on neuronal sodium channels prolonging their inactive state. There are no published studies to date on the toxicity of rufinamide in overdose. The objective of this study is to describe the patient demographics, outcomes, reason for exposure and clinical effects of rufinamide exposures in children and adult patients.
Methods: This retrospective observational study utilized data from the National Poison Data System (NPDS). Inclusion criteria were single substance exposure to rufinamide between 1/1/2008 and 12/31/16. Variables of interest were collected and descriptive statistics were performed. IRB approval was obtained.
Results: About 137 patients with exposure to rufinamide were indentified. The median age was 10 years (range 1–67 years), there were 66 males and 69 females. Eighty-nine of the 137 patients (64.9%) were unintentional-therapeutic error and 35 (25.5%) exposures were unintentional-general. Fifteen of the 137 patients (10.9%) were treated in a health care facility, 3 of which were in an ICU. Of the 137 patients, a subset of 58 were followed to a known outcome, of which 42 (72.4%) remained asymptomatic and had no effect, 12 patients (20.7%) reported minor effects, 4 (6.9%) of the patients had moderate or major effect. There were no deaths. Four patients had a moderate or major outcome. Clinical effects reported by those four include: nausea, vomiting, tremor, seizure (multi/discrete), edema, urinary incontinence and drowsiness/lethargy.
Conclusions: This is the first study examining the effects of rufinamide in overdose. The majority of patients were asymptomatic and only one patient had a life threatening event. No patients died. This study is limited by its retrospective nature, passive reporting and reliance on caller information. Additional research is needed to better characterize the toxic dose, clinical effects and treatment following rufinamide exposure.

KEYWORDS Rufinamide; overdose; National Poison Data System

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41. Should play dough be on your non-toxic list? High salt content of home-made play dough products

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Background: Commercially made Play-Doh® is considered non-toxic and has a sodium chloride content listed as 5.52%. However, there are many recipes available for home-made play dough on the internet and social media. Some recipes call for glitter to make "galactic" play dough, while others add powdered drink mix or spices to make it smell good. Many of these recipes call for large quantities of salt which can change this seemingly non-toxic exposure into a toxic one. Due to the potential increased risk of toxicity with home-made play dough, we wanted to more accurately quantify the salt concentration in these products.
Method: Nine popular play dough recipes were obtained from the internet. Ingredients were purchased from local grocery stores. Each recipe was made in triplicate, with one person making one product for each of the nine recipes; each person's nine products are referred to as a "batch." Exact weight of each component was recorded before being added to the mixing bowl; exact weight of the final product was also recorded. Salt content based on weight of the components was calculated. To more directly measure the sodium content for each of the 27 products made, 25 g from each product was homogenized with 100 mL distilled water. An aliquot of the supernatant was diluted 1:100 and analyzed with a sodium-specific ion electrode connected to a pH meter in mV mode. Each batch was analyzed twice. Commercially made white Play-Doh® was used as the standard for the sodium ion measurements.
Results: The average calculated salt content (weight/weight) of the nine recipes ranged from 16.8% (SD 0.78%) to 34% (SD 3.7%). The final average weights of the three products for each recipe had small standard deviations, with the standard deviations ranging from 1.7% (ave. weight 557.8 ± 9.4 g) to 7.4% (ave. weight 1519 ± 113 g) of the three products' average weight. Direct sodium measurement was complicated by impurities in the supernatant, but still showed good correlation between calculated salt content and sodium ion measurement, with correlations ranging from $r = 0.85$ (batch 3) to $r = 0.92$ (batch 1).
Discussion: The lowest average calculated salt content (16.8%) is more than three times the amount of NaCl reported in commercially produced Play-Doh® (5.52%), while the highest (34%) is more than 6 times that amount. Direct sodium ion measurement confirmed the significantly higher sodium content of home-made play dough compared with commercially produced Play-Doh®. Using an ingestion of 8 mEq (470 mg) NaCl/kg as a threshold for referring a person to medical attention, the amount of home-made play dough that would need to be ingested to reach this threshold would be between 1.38 g/kg (34% NaCl) and 2.79 g/kg (16.8% NaCl).
Conclusions: Poison center specialists need to ask callers to identify the maker of play dough that is ingested given the very high salt content of home-made products.

KEYWORDS Home made play dough; salt; play dough

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42. The effect of caffeine on central apnea induced by organophosphate poisoning in an anesthetized rat model

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Background: Previous research into organophosphate poisoning has revealed that centrally mediated respiratory depression is a component of toxicity although the exact mechanisms of this are not clear. In animal models, this appears to be at least partially mediated by a cholinergic nucleus in the brainstem. Caffeine has a long history of use to stimulate breathing in neonates with incompletely developed respiratory drive, although the exact mechanisms are multifactorial and do not appear to involve cholinergic neural transmission. We hypothesized that treatment with caffeine may reverse some components of centrally mediated apnea in rats treated with a lethal dose of 2,2-dichlorovinyl dimethyl phosphate (dichlorvos).
Experimental design: Male Wistar rats (Charles River Laboratories) were anesthetized with isoflurane to the point of loss of foot pinch reflex. Tracheostomy was performed and respiratory effort was monitored via use of a pneumotach to measure respiratory effort and volume of inspired gas. End tidal CO2 was measured via continuous capnography (Columbus Instruments, Columbus, OH) and continuous pulse oximetry was monitored via continuous pulse oximetry (MouseOx). Anesthesia was maintained via continuous administration of inhaled isoflurane. Intravenous access was obtained via femoral cut and cannulation of the femoral vein. Experimental rats ($n = 8$) were treated with 20 mg/kg of caffeine intravenously at 4 min prior to administration of 100 mg/kg or 3 × the LD 50 of dicholorvos subQ and at 4 min intervals afterwards. Control rats received injections of diH2O ($n = 8$) matched in volume to the administration of caffeine in the experimental group. Apnea was defined as the absence of respiratory effort as measured by pneumotach and an absence of end-tidal CO2 readings. At the conclusion of the experiment, animals were euthanized with 100 mg/kg of sodium phenobarbital.
Results and conclusions: In rats that were pre-treated with caffeine, there was a trend towards an increased time until the onset of central apnea (average in caffeine treated rats 210 seconds versus 166 s in control animals). However, this trend did not reach statistical significance ($p = .56$, two sample T-test). There was much larger standard error in the control group that could partially explain the lack of statistical significance; this may be related to the amount of time animals were maintained under anesthesia which did tend to be longer in the control group and prolonged exposure to isoflurane may enhance the effect of dichlorvos. Some animals did regain spontaneous respiration towards the conclusion of the experiment. This did occur more frequently in the caffeine treated group ($n = 5$ in caffeine group, $n = 2$ in control group). The number of animals this occurred in is not enough to draw statistical conclusions from, however, the effect is intriguing and could be further investigated with a larger number of experimental animals. This research does suggest that caffeine could delay and possibly reverse central apnea mediated by organophosphates, however, no conclusions can be definitively reached based on this data.

KEYWORDS Organophosphate; caffeine; apnea

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43. Pediatric ingestion of cariprazine causing bimodal CNS depression and thrombocytopenia: a case report

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Background: Cariprazine was approved by the FDA in 2015 for the treatment of bipolar and schizophrenia. Reported toxicity has been limited to clinical trials. The risk of toxicity after overdose is currently unknown. We report a case of an accidental pediatric overdose.
Case report: A 3-year-old female with no known past medical history was found by her mother with an open bottle of cariprazine. Five, 3mg pills were missing. She was taken to the emergency department with difficulty swallowing, poor head control, abdominal pain, and lethargy. Vitals were age appropriate and exam was unremarkable other than central nervous system (CNS) depression. A complete blood count revealed a platelet count of $43 \times 10^3/\mu L$. A basic metabolic panel, ethanol, acetaminophen, salicylate, urine drug screen and computed tomography (CT) of her head were unremarkable. She was admitted to the pediatric floor for observation with mild improvement of her CNS depression over the next 24 h. Approximately 36 h post-ingestion, she became obtunded with excessive drooling and no response to painful stimuli. A focused neurologic exam demonstrated normal reflexes, normal pupils, and no clonus. Vitals remained age appropriate. A fasting blood glucose was 133 mg/dL and a repeat stat head CT was negative. Her thrombocytopenia persisted with a platelet count of $50 \times 10^3/\mu L$. She was transferred to the pediatric ICU for closer monitoring. She never required intubation. On hospital day (HD)#3, she became more alert with mild agitation and tremors. Platelets increased to $94 \times 10^3/\mu L$. She was discharged on HD #4 with normal mentation and labs.
Discussion: This is the first reported pediatric overdose of cariprazine. Previously reported adverse effects in adults were typical for second-generation antipsychotics, including akathisia, insomnia, sedation, and extrapyramidal symptoms (EPS). EPS has been reported to cause tremors and drooling in pediatric cases. Typical dosing for adults is 1.5 mg/d to 12 mg/d. A 15mg, acute ingestion is significant for a toddler. Cariprazine is a partial agonist of D_3/D_2 and 5-HT_{1A} receptors, with lower affinity for 5-HT_{2A}, 5-HT_{2C}, histamine H_1, and adrenergic α_1 receptors with mild antagonism at serotonin 5-HT_{2B} receptors. It is unclear if selectivity is lost in overdose. Given the receptors involved, CNS depression was a likely consequence. Recurrent CNS depression along with thrombocytopenia is a previously undescribed toxicity of cariprazine. Cariprazine undergoes hepatic metabolism, mainly through cytochrome P450 (CYP) 3A4, to active metabolites, including didesmethylcariprazine. Didesmethylcariprazine has displayed similar pharmacokinetics to its parent compound with a much longer terminal half-life of 2–3 weeks. Active metabolites may explain the recurrent CNS depression. Thrombocytopenia has been associated with fluctuations in dopamine and serotonin; however, it has not been reported as an adverse effect of cariprazine. Although a temporal association was established, it remains unclear if cariprazine was causative.
Conclusions: Cariprazine toxicity may be unique among atypical antipsychotics. Further cases of toxicity and surveillance are needed to assess potential toxicity.

KEYWORDS Cariprazine; pediatric; antipsychotic

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44. Beta-blockers and hypoglycemia: myth or reality?

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Background: Beta-blockers are a commonly used class of drugs in the treatment of several diseases. While effective in the management of various acute and chronic illness, acute overdoses can be difficult to treat and can be fatal. Included in texts across many specialties is a description of the phenomenon of beta-blocker induced hypoglycemia in the setting of acute overdose. While there are reports of hypoglycemia in children and diabetic adults in beta-blocker overdose, it is very rarely reported in healthy adults. Therefore, the purpose of this study was to determine the prevalence of hypoglycemia in adolescent and adult patients exposed to beta blockers who presented to an emergency department.
Methods: All calls to a large regional poison center for beta-blocker exposure from 1 January 2016 through 31 December 2016 were extracted and analyzed. Inclusion criteria included age greater than 13 years, beta-blocker ingestion, and presentation to an emergency department. Comorbidities and coingestions were not excluded. Specialists in poison information (SPI) recorded the products ingested, signs, symptoms, vital signs, electrolytes, and blood glucose concentrations. Bradycardia and hypotension were defined as a heart rate less than 60 beats per minute (bpm) and a systolic blood pressure less than 90 mm of mercury (mmHg), respectively. Hypoglycemia was defined as a blood glucose less than 70 mg per deciliter (mg/dL). These data were analyzed using descriptive statistics.
Results: Ninety-seven cases met inclusion criteria. The mean patient age was 43.5 years. Thirty-eight (39%) cases were male and 59 (61%) female. Propranolol ($N = 36$; 37%) was involved most frequently followed by metoprolol ($N = 25$; 26%). In 40 cases (41%), a heart rate of less than 60 bpm was documented. Twenty-eight (29%) cases had isolated bradycardia. In eighteen cases (19%) there was a systolic blood pressure of 90 mmHg or less. Among hypotensive patients, none had a heart rate greater than 74 bpm. In 15 cases, there were no documented vital signs. Two cases did not have documented blood pressures but did have documented bradycardia of 52 and 30, respectively. Two (2%) patients were intubated. Most common treatments were parenteral fluids (8; 8%), glucagon (6; 6%), vasopressor therapy (11; 11%), or high-dose insulin and euglycemic therapy (HIE) (7; 7%). Six patients were treated with both vasopressors and HIE, five were treated with only vasopressors and one was treated with only HIE. Two patients (2%) had documented hypoglycemia. One patient was a known diabetic who ingested 400 mg of atenolol. He developed symptoms of hypoglycemia with a blood glucose of 52 mg/dL which improved with enteral juice. The second patient became hypoglycemic only after HIE therapy was initiated in the intensive care unit. No deaths were reported.
Conclusions: In our study, there were no episodes of hypoglycemia in adolescents or adults after beta-blocker overdose unless high dose insulin and euglycemic therapy was administered or the patient had pre-existing diabetes. More prospective research should be performed to determine whether this widely disseminated phenomenon occurs.

KEYWORDS Beta blockers; hypoglycemia; bradycardia

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	Total Cases	Maximum Dose (mg)
Atenolol	15	12000
Carvedilol	15	500
Labetalol	2	400
Metoprolol	25	3000
Nadalol	1	1000
Nebivolol	2	Unknown dose
Propranolol	36	4000
Satenolol	1	10

45. Unintentional pediatric exposures to antidementia medications reported to US poison control centers

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Background: An estimated 5.5 million Americans have Alzheimer's disease, and the prevalence is anticipated to increase. Previous work has characterized unintentional pediatric exposures to antidementia (AD) medications at a regional level. The objective of this study is to describe unintentional pediatric exposures to AD medications reported to the American Association of Poison Control Center's National Poison Data System (NPDS).
Methods: This is a retrospective review of exposures reported to NPDS between 1 January 2005 and 31 December 2014. Unintentional, single-substance human exposures to donepezil, galantamine, memantine and rivastigmine in children ≤6 years were included in the analysis.
Results: About 9977 exposures to AD medications were reported to NPDS during the study period, with 1552 (15.6%) of cases occurring in children ≤6 years. Of the pediatric cases, 946 (61.0%) were followed to a known outcome. The median age was 2 years (range: 3 months–6 years) and males were more commonly exposed (529, 55.9%). Donepezil accounted for 495 (52.3%) exposures, memantine 304 (32.1%), rivastigmine 85 (9.0%), and galantamine 62 (6.6%). Patients were managed on site in 489 (51.7%) cases, and 453 (47.9%) were managed in a health care facility. Patients requiring treatment in a healthcare facility were most often treated/evaluated and released (358, 79.0%). No effect was reported in 745 (78.8%) cases, minor effect in 160 (16.9%), and moderate effect in 41 (4.3%). There were no major effects or deaths reported throughout the duration of the study. Exposure to rivastigmine was associated with the highest incidence of clinical effects, followed by donepezil, memantine and galantamine (table 1). Clinical effects documented in > 1% of cases include: vomiting (101, 10.7%), drowsiness/lethargy (51, 5.4%), "other" (23, 2.4%), diaphoresis (16, 1.7%), nausea (16, 1.7%), agitation/irritability (11, 1.2%), and bradycardia (9, 1.0%).
Conclusions: Pediatric exposures to AD medications were followed to a known outcome in 61.0% of cases. Vomiting and drowsiness were the most common clinical manifestations of unintentional pediatric exposure to AD medications. There were no major effects or deaths reported during the study period.

KEYWORDS Antidementia medications; donepezil; acetylcholinesterase inhibitors

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46. Unintentional pediatric exposures to anti-Parkinson's medications reported to US poison control centers

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Background: Levodopa has been a cornerstone for management of Parkinson's disease since the 1960s. Available coformulated products include carbidopa/levodopa (carb/levo) and carbidopa/levodopa/entacapone (carb/levo/enta). Despite the long history of carb/levo use, the consequences of unintentional pediatric poisoning has yet to be formally characterized.
Methods: This is a retrospective review of exposures reported to the American Association of Poison Control Center's National Poison Data System (NPDS) between 1 January 2005 and 31 December 2014. Unintentional, single-substance exposures to carb/levo and carb/levo/enta in children ≤6 years were included in the analysis.
Results: About 6590 human exposures to carb/levo and carb/levo/enta were reported to NPDS during the study period. Of these, 1944 (29.5%) exposures were reported in children ≤6 years old. About 1163 (59.8%) were followed to a known outcome and included in the final analysis. The median age was 2 years (2 months–6 years). The majority of the population was male (619, 53.2%). Reason for exposure was documented as unintentional-general for 1143 (98.3%) cases. Most exposures (639, 54.9%) were managed on site. No or minor effects were documented in 1142 (98.2%) cases followed to a known outcome. There were no major effects or deaths reported. See table 1 for stratification of medical outcomes by formulation. Clinical effects reported in >1% of exposures included: vomiting (228, 19.6%), drowsiness (89, 7.7%), agitation/irritability (1.89, 1.9%), "other" (20, 1.7%), and tachycardia (11, 1.0%). Clinical effects occurring in <1% of exposures included ataxia, confusion, dystonia, and hallucinations. Hypotension was reported in three patients with a moderate outcome, however, none of these patients required vasopressors. The most common therapies administered to patients in health care facilities included: activated charcoal (120, 23.1%), dilute/irrigate/wash (46, 8.9%), IV fluids (21, 4.0%), cathartics (13, 2.5%), and antiemetics (10, 1.9%).
Conclusions: Exposures to carb/levo and carb/levo/enta were followed to a known outcome in 59.8% of cases. Vomiting was the

Table 1. Medical outcome for patients followed to a known outcome

Medical outcome, n (%)	AD medications, n				
	Donepezil, 495	Galantamine, 62	Memantine, 304	Rivastigmine, 85	Total, 946
No effect	363 (73.3)	55 (88.7)	270 (88.8)	57 (67.1)	745 (78.8)
Minor effect	104 (21.0)	5 (8.1)	30 (9.9)	21 (24.7)	160 (16.9)
Moderate effect	28 (5.7)	2 (3.2)	4 (1.3)	7 (8.2)	41 (4.3)

Table 1. Medical outcome for patients followed to a known outcome

Medical outcome, n (%)	Formulation, n		
	Carb/levo/enta, 192	Carb/levo, 971	Total, 1163
No effect	167 (87.0)	690 (71.0)	857 (73.7)
Minor effect	23 (12.0)	262 (27.0)	285 (24.5)
Moderate effect	2 (1.0)	19 (2.0)	21 (1.8)

most common manifestation of toxicity and there were no major effects or deaths reported during the study period.

KEYWORDS Carbidopa/levodopa; carbidopa/levodopa/entacapone; anti-parkinson's medications

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47. Challenges to SPI-led research

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Background: Specialists in Poison Information (SPIs) have expressed interest in research but have often encountered obstacles. The American Association of Poison Control Centers (AAPCC) SPI Committee developed a research subcommittee to study these barriers. Our objective was to determine interest, gauge perception, identify obstacles, and determine best ways to promote SPI-led research.
Methods: The subcommittee designed a survey consisting of 12 multiple-choice questions on SPI background and education; previous research achievements; identification of needs and perceived obstacles; and self-assessment of desire to participate in research in the coming year. Questions were piloted on seven SPIs and then revised for clarity. A SurveyMonkey® link was sent to US and Canadian SPIs from 60 poison centers on the AAPCC listserv. Participation was voluntary and remained open for 60 d. De-identified data were collected and analyzed using descriptive statistics.
Results: Of 1017 SPIs, 321 responded (31.5%). Respondents were 64% Registered Nurses, 30% Pharmacists, 3% Medical Doctors, 1% PhD, and 2% other (Nurse Practitioner or Paramedics), in which 84% were certified SPIs, 11% non-certified, 4% diplomates, and one board-certified toxicologist. Only 20% were American Academy of Clinical Toxicology members. Regarding years in practice, 33% had $<$ 5 years, and 20% $>$ 20 years. Respondents identified the following barriers to doing research (in order of interest): (47%) designing a study; (45%) navigating publication; (38%) collecting data; (38%) searching literature; (30%) forming a hypothesis; (30%) drafting a manuscript; (30%) working with specific programs; and (28%) finding a co-author. Sixty-nine percent had never published research, 25% had published 1–5 articles, 3.5% 6–10 articles, and 2% more than 10 articles. Twenty-seven percent had published as first or second author in toxicology research. Of all respondents, 37% had presented a poster at a North American Congress of Clinical Toxicology meeting, and 22% of these had more than five posters accepted. Finally, 71% reported they were interested in pursuing a research topic in the next year.
Conclusions: SPIs have demonstrated interest in toxicology research but commonly faced difficulties in starting the process. Common barriers were designing a study, navigating the publication process, collecting data, and searching the literature. In a budget-limited environment, the SPI Research subcommittee can help SPIs engage in research by closely aligning support and implementing measures to address these challenges to SPI-led research.

KEYWORDS Research; specialists in Poison Information; SPI committee

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48. Perception and knowledge assessment of physicians on intravenous lipid emulsion

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Background: Intravenous lipid emulsion (ILE) was initially trialed as a rescue treatment for local anesthetic systemic toxicity (LAST). Since its first use in a human case in 2006, ILE has been used as a therapeutic intervention for over 60 different xenobiotic overdoses. Professional societies have provided guidelines for the use of ILE in a setting of LAST including the International Liaison Committee on Resuscitation. Even so, evidence and consensus on its use remains limited.
Objectives: To assess the perception and knowledge of physicians regarding ILE.
Methods: Between July 2015 and January 2016, an anonymous cross-sectional survey was sent to physicians who opted into an email list from an online resource center, which provides evidence-based management resources for toxicologic emergencies. Four questions established demographic information including specialty, years of practice, volume of the emergency department (ED), and number of past-year overdose-related resuscitations performed. Two questions queried stocking of lipid emulsion in the ED and personal use of ILE. One question was a self-assessment of knowledge regarding LAST, guidelines on ILE, dosing of ILE, efficacy of ILE, and adverse effects of ILE using Likert scales. Three questions assessed likelihood of the physician to administer ILE in xenobiotic overdoses generally acknowledged to be responsive (bupivacaine), possibly responsive (verapamil), and unlikely responsive (ibuprofen toxicity). Descriptive statistics describe group data. Subgroup analysis by specialty performed by Chi-squared.
Results: Of 326 responses, there were anesthesiologists (60%, $n = 197$), emergency physicians (26%, $n = 84$), and intensivists (5%, $n = 17$) with an additional combined 9% as general practitioners, internists, pain specialists, toxicologists, and other unspecified specialties. Other characteristics: 86% practiced his/her specialty for greater than 5 years, 72% performed at least one past-year overdose-related resuscitation, 44% had lipid emulsion available in the ED, but most (67%) had not administered ILE within the last 5 years. Most respondents (21%) who had

administered ILE only used it once or twice, but 2% reported more than 10 administrations. Most (66%) stated he/she was "knowledgeable enough to explain [LAST] to a colleague," but only 46% felt "knowledgeable enough to explain [ILE current guidelines] to a colleague," and only 28% were confident they could explain the evidence behind ILE usage and adverse effects of ILE. For clinical cases, 67% of respondents would administer ILE to a pulseless patient secondary to bupivacaine toxicity as opposed 25% of respondents for a similar verapamil patient. Six percent would administer ILE to an ill patient from ibuprofen toxicity. Anesthesiologists were more likely to administer ILE for bupivacaine than emergency physicians ($p < .05$), whereas emergency physicians were more likely to administer ILE for verapamil ($p < .05$). Both groups were unlikely to administer ILE for ibuprofen with no statistical difference ($p = .3$).
Conclusions: In this survey, physicians have greater confidence in their knowledge of LAST than ILE. Currently, ILE is a recommended first line treatment for bupivacaine systemic toxicity, but as of the survey, only 67% of physicians would have administered the therapy. Greater clinical uncertainty exists for other xenobiotics. Further education regarding ILE including dosage and adverse effects is needed.

KEYWORDS Intravenous lipid emulsion; intralipid; lipid emulsion therapy

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49. Somniferum somnolence: a case of prolonged opioid toxidrome following poppy seed tea ingestion

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Background: Poppy seeds contain the opiates morphine and codeine in varying concentrations and this information is distributed widely on the Internet for various home remedies and do-it-yourself detox and pain treatments. Natural and homemade products are sometimes misconceived as safe, which can lead to homemade products with unknown and possibly high concentrations of opiates. We present a case of respiratory depression requiring repeat doses of naloxone after intentional poppy seed tea ingestion.
Case report: An otherwise healthy 22-year-old man attempted "natural pain control" using a homemade poppy seed tea. He reported boiling store-bought poppy seeds in order to make a tea. He drank approximately 8 ounces of the tea along with 4 beers. Around 8 h after drinking the tea, he was found unresponsive in his home and was described as "blue" so 911 was called. EMS arrived and described the patient as lethargic and cyanotic with pinpoint pupils. Two milligrams of naloxone was administered intranasally followed by 2 mg IV with return of normal mental and respiratory status. He was transported to the Emergency Department where his urine drug screen was positive for opiates and his ethanol concentration was 62 mg/dL. During observation in the Emergency Department, approximately 3 h after arrival and 11 h after the ingestion, he was increasingly lethargic and hypoxemic so 2 mg of IV naloxone was administered with return of normal mental status so he was admitted for observation. His last dose of naloxone was 13 h after the ingestion. This patient received a total of 8mg of naloxone administered in four separate doses at 8 h, 8 h, 11 h and 13 h post-ingestion. He was discharged with normal mental and respiratory status 6 h after his last dose of naloxone and 19 h after the ingestion.
Case discussion: Societal trends toward natural treatments and misconceptions that "natural" or homemade products are safe can lead to unintentional, possibly life threatening exposures. Home remedies are often sought because of their perceived safety. Many online resources are available and provide detailed instructions for preparation as well as exhaustive anecdotes and experiences. Poppy seed tea recipes are described for laypersons to treat various types of pain as well as opioid addiction. The variable concentration of opiates in poppy seeds makes predicting the severity and length of symptomatology difficult in a patient who has prepared their own poppy seed tea.
Conclusions: Toxicologists should be aware that poppy seed tea recipes are available on the internet, that poppy seeds are available by mail or in stores, and that ingestion of these teas may lead to severe and prolonged opioid toxicity.

KEYWORDS Poppy seed; opiates; naloxone

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50. Peripartum acetaminophen overdose with IV *N*-acetylcysteine treatment in neonate

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Background: There is limited published information on the use of IV *N*-acetylcysteine (NAC) to treat potentially toxic exposures of acetaminophen (APAP) in the peripartum period. We report the use of IV NAC to treat a mother and her 7-h old neonate who presented with a history of a repeated supratherapeutic ingestion (RSTI) of APAP.
Case report: A woman in labour, approximately 38 weeks pregnant, presented crowning to an emergency department with a history of ingesting 24 tablets of 500 mg APAP over a 48-h period. Her last dose was reported to be 12 h prior to initial lab draws. Clinically the woman was stable, no nausea or vomiting. Initial lab results were as follows: APAP level 284 umol/L, ALT 17 U/L, AST 27 U/L, INR 1.0, venous blood gas pH 7.24, pO2 45 mmHg. A 3.0 kg child was delivered, experienced some respiratory distress, and was admitted to the neonatal intensive care with Apgar scores of 8, 8, and 7 at 1, 5, and 10, min, respectively. Initial labs on admission, drawn 40 min after the mother's, were Na 133 mmol/L, K 5.0 mmol/L, Cl 111 mmol/L, glucose 4.3 mmol/L, arterial blood gas pH 7.3, pCO2 38 mmHg, pO2 63 mmHg, HCO3 18.1 mmol/L, O2 sat 94.3%, and lactate 2.9 mmol/L. Approximately 3.5 h after admission, 15 h after last exposure to APAP, the neonate was more alert, had no gastrointestinal symptoms, and was being weaned from CPAP. Lab results at that time were APAP 222 umol/L, ALT 16 U/L (reference range <50 U/L), AST 82 U/L (reference range <140 U/L), and INR 1.6 (reference range 0.9–1.2). The mother was started on IV NAC approximately 15 h post last APAP ingestion, and the 7-h old neonate was started on the same treatment approximately 18.5 h post-last APAP exposure. Each patient received a full 21-h course of IV NAC, 150 mg/kg over 1 h, 12.5 mg/kg/h for 4 h, and then 6.25 mg/kg/h for 16 h, with no noted adverse events. At the end of the treatment, the mother's lab results were APAP <66umol/L, ALT 16 U/L, AST 24 U/L, INR 1.0, creatinine 63 mmol/L. The baby's lab results at the end of treatment were APAP <66 umol/L, ALT 13 U/L, AST 43 U/L, and creatinine 50 mmol/L.
Case discussion: The risk of hepatotoxicity from APAP overdose increases as the time increases before the initiation of NAC treatment. Very little evidence exists for APAP overdoses in the peripartum period. The risk of supratherapeutic APAP exposures to fetuses prior to delivery is unknown. Mother and neonate were

treated with a 21-h course of IV NAC and both did well. The neonate is the youngest known person to receive IV NAC for treatment of a RSTI APAP overdose that we could find reported in the literature.
Conclusions: IV NAC can be used in the neonate population to treat potentially toxic APAP exposures.

KEYWORDS Acetaminophen; peripartum; overdose

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51. Accidental administration of oxytocin to neonates: a case series

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Introduction: Oxytocin is often given to postpartum mothers while they are in close proximity to their newborns. Accidental administration of oxytocin alone to the infant has only been previously described one time in literature. Despite advances in medication safety this phenomenon continues to occur. We describe three more cases of neonates being administered oxytocin intramuscularly (IM), mistaken for other neonatal medications.
Case Report 1: A term neonate was accidentally given oxytocin 10 IU IM shortly after birth. The patient was then transferred to a level IV Neonatal Intensive Care Unit (NICU) for observation. There was one episode of supraventricular tachycardia that was brief and self-resolved. Gamma-glutamyl transferase (GGT) was elevated on admission with normal aspartate aminotransferase and alanine aminotransferase. GGT trended down to 243 U/L prior to discharge. A basic metabolic panel was monitored every 12 h and remained within normal limits.
Case Report 2: A 36-week gestational age neonate was inadvertently given oxytocin 5 IU IM 1 h after birth. Heart rate (HR), blood pressure (BP), as well as an electrocardiogram remained within normal limits during close monitoring over the next 24 h. Serial serum sodium concentration [Na] also remained within normal limits with reported values of 138 mEq/L, 137 mEq/L, and 139 mEq/L.
Case Report 3: A reportedly healthy neonate was accidentally given oxytocin 10 IU IM shortly after birth. Approximately 7 h post-exposure, BP was on the low end of normal at 60/35 mmHg, with a HR of 139 beats/min. Twelve hours later BP was 70/37 mmHg. The next morning [Na] was normal at 139 mEq/L. No other symptoms noted.
Discussion: Oxytocin is a hormone that is used immediately postpartum to control uterine bleeding. Its primary action is to stimulate urine contractions. However, high doses have been found to cause adverse effects, such as hypotension and hyponatremia in adults. There is only one case published of neonate oxytocin IM administration. In this case, the child had apnea and bradycardia spells at 2.75 and 7 h post-exposure as well as hyponatremia. Hyponatremia was corrected without additional complications and no further spells occurred. In the three cases presented here, two of the infants developed transient cardiac abnormalities. Despite the previous report of hyponatremia, all [Na] remained within normal limits.
Conclusions: The risk for a medication error is much higher when two patients are in close proximity. In the event that a neonate is administered 5–10 IU oxytocin, serious cardiovascular and metabolic complications may occur. These three cases add to the scant existing literature to aid in determining the incidence of adverse events following such an exposure. Monitoring for cardiac abnormalities, apnea spells, and electrolyte changes, continues to be advised. These parameters would be best monitored in a NICU setting.

KEYWORDS Oxytoxin; medication error; pediatric

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52. High-dose insulin for beta blocker and calcium channel blocker poisoning: 17 years of experience from a single poison center

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Background/objectives: Despite basic science evidence that high dose insulin (HDI) is superior to glucagon and vasopressors for the treatment of beta blocker (BB) and calcium channel blocker (CCB) induced cardiogenic shock, there remains hesitancy to recommend HDI rather than these traditional therapies. Our poison center routinely recommends HDI in preference to vasopressors or glucagon if IV fluids and calcium fail using a certified specialist in poison information (CSPI)-driven clinical guideline recommending HDI starting at 0.5–1 U/kg/h titrated rapidly up to 10 U/kg/h. Medical toxicologists are involved, but often after HDI has been recommended. We describe our experience with this guideline and its clinical outcomes.
Methods: This was a retrospective study from a single poison center. Cases were identified by querying our electronic patient database (Toxicall®) for generic substance codes for "Beta Blockers" and/or "Calcium Antagonists" and the therapy "insulin" for the years 2000-2016. HDI was defined as a minimum infusion of insulin at 0.5 U/kg/h or 25 U/h recorded in the individual case notes. Cases were abstracted by four board-certified medical toxicologists for the following data: specific drug exposures, HDI dosing, dextrose administered, other therapies, clinical effects, and evidence of hypoglycemia or hypokalemia.
Results: A total of 199 subjects met final inclusion criteria. Median age was 48 years (range 14–89); 50% were male. There were 66 patients (33%) poisoned by BBs, 45 (23%) poisoned by CCBs, and 88 (44%) poisoned by both BBs and CCBs. Specific drugs and co-ingestions are displayed in Table 1. Median initial and nadir pulse rates were 62 beats/min (range, 12–128) and 54 beats/min (range 12–121), respectively. Median initial and nadir systolic blood pressures were 80 mmHg (range 40–223) and 70 mmHg (range, 30–167), respectively. Clinical outcomes based on NPDS definitions were as follows: death, $n = 31$ (16%), major effect, $n = 116$ (58%), moderate effect, $n = 49$ (25%), unrelated effect, $n = 3$ (2%). Insulin dosing was reported as weight-based (U/kg/h) unless only unit-based dosing (U/h) was recorded in the case notes. Median weight-based insulin bolus was 1 U/kg (range 0.5–10, $n = 31$), median unit-based bolus was 50 U (range 5–400, $n = 24$). Median starting weight-based insulin infusion was 1 U/kg/h (range 0.22–10, $n = 94$); median starting unit-based infusion was 53 U/h (range 2.5–700, $n = 76$). Median peak weight-based insulin infusion was 8 U/kg/h (range 0.5–18, $n = 117$); median unit-based peak insulin infusion was 84.5 U/h (range, 25–1200, $n = 71$). Median number of days on HDI and dextrose was 2 (range 1–7 for HDI, 1–10 for dextrose). Selected clinical effects, including glucose and potassium results, are reported in Table 2. Selected other therapies are reported in Table 3.
Conclusions: In this large poison center study, a CSPI-driven clinical guideline recommending HDI, dosed at 0.5–1 U/kg/h titrated

up to 10 U/kg/h, appeared feasible. Concomitant vasopressor use routinely occurred. Hypoglycemia was common but easily treatable.

KEYWORDS High-dose insulin; beta blocker; calcium channel blocker

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Table 1: Specific Drugs & Co-ingestions	
Beta Blockers	
Metoprolol*	n = 49 (25%)
Atenolol	n = 32 (16%)
Propranolol*	n = 29 (15%)
Carvedilol	n = 14 (7%)
Labetalol	n = 4 (2%)
Nebivolol	n = 2 (1%)
Sotalol	n = 2 (1%)
Other beta blocker	n = 4 (2%)
Calcium Channel Blockers	
Amlodipine	n = 40 (20%)
Diltiazem*	n = 36 (28%)
Verapamil*	n = 29 (15%)
Nifedipine	n = 5 (2.5%)
Other calcium channel blocker	n = 1 (0.5%)
Co-ingested drugs	
Sedative/Hypnotics	n = 57 (29%)
Antihypertensives (other)	n = 52 (26%)
Ethanol	n = 45 (23%)
Antidepressants (other)	n = 39 (20%)
Bupropion/Citalopram/Venlafaxine	n = 23 (12%)
Opioids	n = 19 (10%)
Antipsychotics	n = 19 (10%)
Antihistamines	n = 13 (7%)
Sympathomimetics	n = 10 (5%)
Acetaminophen	n = 8 (4%)
Antiepileptics	n = 6 (3%)
Amiodarone	n = 4 (2%)
Alpha-2 agonists	n = 4 (2%)
Antidepressants (tricyclic)	n = 3 (1.5%)
Digoxin	n = 3 (1.5%)
* includes both immediate and sustained/extended release formulations	

Table 2: Selected Clinical Effects		
Clinical Effect	**Related**	**Unknown if Related**
Acidosis	n = 66 (33%)	n = 9
Asystole	n = 16 (8%)	n = 0
Bradycardia	n = 129 (65%)	n = 3
Cardiac Arrest	n = 33 (17%)	n = 1
Coma	n = 42 (21%)	n = 3
Conduction Disturbance	n = 49 (25%)	n = 10
Dysrhythmia (V-tach/V-fib)	n = 3 (1.5%)	n = 1
Dysrhythmia (other)	n = 17 (8.5%)	n = 5
Electrolyte Abnormality	n = 54 (27%)	n = 17
Nadir potassium (K) recorded (mEq/L)	n = 74	
K = "normal" or > 3.5	n = 17 (23%)	
K = 3.1 – 3.5	n = 19 (26%)	
K = 2.8 – 3.0	n = 17 (23%)	
K = 2.5 – 2.7	n = 11 (15%)	
K = 2.0 – 2.4	n = 10 (13%)	
K < 2.0	n = 0	
Hypoglycemia	n = 63 (32%)	n = 6
Documented < 70 mg/dL	n = 40 (20%)	
Hypoglycemia that was treated, no value specified	n = 23 (12%)	
Hypotension	n = 187 (94%)	n = 3
Oliguria	n = 32 (16%)	n = 4
Renal Failure	n = 13 (6.5%)	n = 3
Seizures	n = 14 (7%)	n = 1
Tachycardia	n = 21 (10%)	n = 11

Table 3: Selected Other Therapies	
Antiarrhythmic	*n* = 28 (14%)
Atropine	*n* = 39 (20%)
Calcium	*n* = 141 (71%)
CPR	*n* = 18 (9%)
Dextrose	*n* = 184 (92%)
Infusion concentration (when documented)	*n* = 166
D5	*n* = 8 (5%)
D10	*n* = 50 (30%)
D20	*n* = 27 (16%)
D25, 30, or 40	*n* = 3 (3.6%)
D50	*n* = 58 (35%)
D70	*n* = 17 (10%)
Median number dextrose boluses/patient (bolus dosing recorded in only 48 cases)	*n* = 1, (range, 1-10)
ECMO	*n* = 6 (3%)
Glucagon	*n* = 84 (42%)
Hemodialysis	*n* = 21 (10%)
Intra-aortic Balloon Pump	*n* = 7 (3.5%)
Intravenous Fat Emulsion	*n* = 14 (7%)
Intubation	*n* = 133 (67%)
LVAD (percutaneous)	*n* = 1 (0.5%)
Methylene Blue	*n* = 12 (6%)
Pacemaker	*n* = 13 (6.5%)
Vasopressors (and Inotropes)	*n* = 152 (76%)
Norepinephrine	*n* = 116 (58%)
Dopamine	*n* = 86 (43%)
Epinephrine	*n* = 71 (36%)
Vasopressin	*n* = 46 (23%)
Phenylephrine	*n* = 30 (15%)
Dobutamine	*n* = 10 (5%)
Milrinone	*n* = 1 (0.5%)

53. Pediatric ingestions of amfetamine/dextroamfetamine salts

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Background: Adderall (amfetamine and dextroamfetamine salts) was FDA approved for the treatment of attention deficit hyperactivity disorder in 1996. Despite being on the market and in homes with children for over 20 years, no clear triage threshold for out-of-hospital management of unintentional pediatric ingestions has been established. The aim of this study was to report one regional poison center's (RPC) experience with unintentional amfetamine/dextroamfetamine salts exposures in the pediatric population.

Methods: RPC cases with an unintentional ingestion of amfetamine/dextroamfetamine salts in patients age 5 and under for the period 1/1/2011–12/31/2016 were retrospectively reviewed. Cases were excluded if they involved coingestants or were not followed to a known outcome. A mg/kg dose was calculated for cases where a weight and estimated ingested dose were documented.

Results: A total of 227 cases met inclusion criteria. In 204 of these cases, an estimated dose ingested was able to be obtained by history and ranged from a taste (intact tablet recovered from mouth) to 60mg. Fifty-nine cases involved sustained release

Table 1	Average ingestion	Range	95% CI	99% CI
No effect	1 mg/kg	0.2 – 2.8 mg/kg	0.8 – 1.2 mg/kg	0.8 – 1.2 mg/kg
Minor effect	1.4 mg/kg	0.3 – 3.3 mg/kg	1.1 – 1.6 mg/kg	1.0 – 1.7 mg/kg
Moderate effect	2 mg/kg	0.7 – 3.9 mg/kg	1.5 – 2.5 mg/kg	1.3 – 2.7 mg/kg

products; 164 cases involved immediate release products; four were of unknown dosage form. Ages ranged from 8 months to 5 years. 63 patients were managed onsite and 164 were referred to a healthcare facility (HCF); of those evaluated in a HCF, 21 were admitted to non-critical care unit and 8 were admitted to a critical care unit. One hundred and fifty-four ingestions resulted in no effect (average dose 13.2 mg, range 2.5–40 mg); 49 resulted in minor effect (average dose 14.9 mg, range 5–45mg) and 24 resulted in a moderate effect (average dose 25.7mg, range 10–60 mg). No cases had a major effect or death. Symptoms in patients with a minor effect included agitation (35), tachycardia (24), vomiting (10), and other (21). Symptoms in patients with a moderate effect included agitation (26), tachycardia (21), CPK elevation (11), LFT elevation (7), vomiting (5), diaphoresis (4), rhabdomyolysis (3), hallucinations (2), tremor (2), and other (12). A total of 24 patients received activated charcoal (two minor effects; 22 no effect). About 22/24 patients with a moderate effect required treatment with benzodiazepines. A mg/kg dose was calculated for 118 cases where weight was documented and the dose could be estimated (taste ingestions and unknown amount were excluded). Patients with no effect ingested an average of 1 mg/kg (range 0.18–2.84mg/kg 95%CI 0.8–1.2 mg/kg); patients with a minor effect average 1.4 mg/kg (range 0.31–3.33mg/kg, 95%CI 1.1–1.6 mg/kg); patients with a moderate effect average 2 mg/kg (range 0.74–3.85mg/kg 95%CI 1.5–2.5 mg/kg). Higher average doses were associated with an increase in symptom severity, and the dose range associated with each of the different outcomes was wide with overlap in range and confidence intervals (see Table 1).

Conclusions: Unintentional pediatric ingestions of amfetamine/dextroamfetamine salts have the potential to cause significant effects; 10% of patients in this RPC study developed moderate effects. There was wide variability in the doses associated with symptoms and some overlap at 95% confidence intervals. Unintentional pediatric ingestions of 1mg/kg are unlikely to cause significant effects.

KEYWORDS adderall; amfetamine salt; pediatric

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54. Reason of exposure and seasonal clinical effect variation in 17 years of mushrooms exposures reported to a poison center

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Background. Toxicologists and poison centers (PC) currently assess human mushroom exposures using mycotoxicologic categories which describe clinical effects from mushroom species. However, this approach is limited when the mushroom is unidentified. This report instead focuses on how clinical effects from mushrooms vary with the exposure reason and the time of year.

Method: The human mushroom exposures were retrospectively collected from Toxicall® spanning 2000–2016 that originated from the service area. Variables examined were reason for exposure, clinical effects, gender, age and exposure date. When possible, cases were corrected for incomplete or incorrect entries. A new category of "Unintended Adverse Event" was created by combining the similar categories of "Adverse Reaction" and "Unintentional Misuse". Seasonal analysis included the entire data set. Clinical effect analysis included patients managed at health care facilities (HCF).

Results: A total of 6528 individual cases were reported. Of these, 5684 were single person cases and 399 were multiple person events. The vast majority (6266 = 96%) of cases were described by three reasons: Unintended General (the Toddlers), Intended Abuse (the Abusers), and Unintended Adverse Event (the Food-Foragers). Table 1 shows how these three major reason categories differed by age, gender and outcome. Figure 1 shows biphasic seasonal variation with cases peaking in May–June (late spring) and then in September–October (early autumn) followed by a rapid decline in winter. The most common reason for these cases is the "Unintended General' Toddler ($n = 4132$) whose exposure is a function of general exploratory behaviors and of mushroom seasonal growth patterns. Exposure patterns of Food-Foragers and Abusers probably reflect the growth distribution of the desired mushrooms, namely the edible and the psychotropic mushroom, respectively. Call distribution of cases was strongly correlated to county population ($R^2 = 0.97$). Average precipitation and temperature statistics for the most populous city in each of the three most populous counties showed that decreasing rain/increasing temperature (spring) and increasing rain/decreasing temperature (autumn) corresponded to increased reporting (climate data from Office of the State Climatologist). Table 2 shows selected clinical effects in symptomatic cases seen at a HCF by the three major exposure reasons. Approximately 56% of Abuser cases and 34% of Food-Forager cases were symptomatic and managed at HCF. In contrast, the Toddler cases rarely presented with symptoms to HCF (1.8%). The predominant organ systems affected were gastrointestinal, neurological and cardiovascular with neurological symptoms common among the Abusers (77%) and gastrointestinal symptoms common among the Food-Foragers (83%). The Toddler group was afflicted primarily by gastrointestinal effects (81%). Major outcomes and fatalities were rarely reported (Table 1) with no cases in the Unintended General group. However, young children were still at risk when part of Food-Foraging (Unintended Adverse Reaction). Specimen identification was uncommon, but 65 cases were accompanied by digital photos and some with mycologist identification.

Conclusions: Mushroom exposures can be described as a function of intent and of a biphasic mycological season within a poison center's region of service. Of these factors, reason for exposure is most important in determining the clinical effect outcome.

KEYWORDS Mushroom; seasonality; reason

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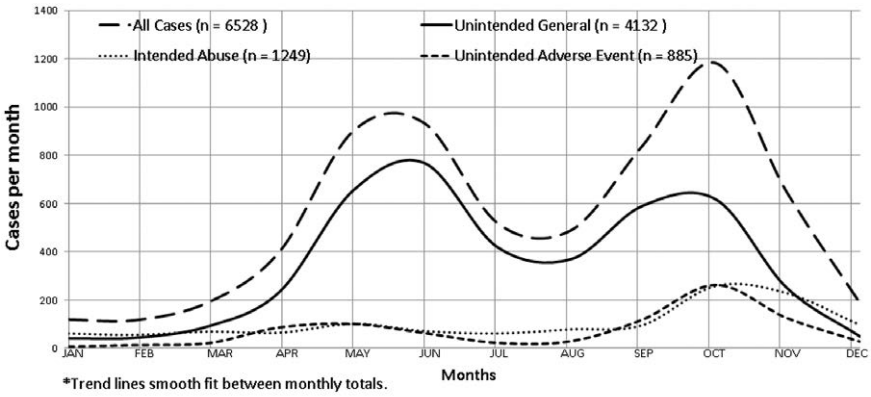

Figure 1. Cumulative 17-year Trends*: Mushroom Exposure Reason and Time of Year

Table 1. Selected Exposure Reasons of Cases (% of 6528)

Main Reasons	Cases (%)	Years (SD)	M:F ratio	HCF (%)	Moderate	Major	Fatality
Unintended General	4132 (63)	3.2 (5.1)	1.1	271 (4.2)	14	0	0
Intended Abuse	1249 (19)	21 (8)	3.9	762 (12)	443	23	3
Unintended Adverse Event*	885 (14)	41 (20)	1	363 (5.6)	80	14	1
Total Included Categories	6266 (96)	12 (17)	1.4	1396 (21)	537	37	4

*Combined Adverse Reaction and Unintended Misuse cases.

Category of Intent (n)	Asystole	Cardiac Arrest	Bradycardia	Tachycardia	V. tach-fib	Dysrhythmia	Hypotension	Hypertension	Vomiting	Diarrhea	Hematemesis	Rectal blood	ast,alt >100-1,000	ast,alt >1,000	DIC	PT prolonged	Agitated, irritable	Lethargy	Coma	Confusion	Hallucinations	Muscle weakness	Muscle Rigidity	Single seizure	Multiple or status	Fasciculation	Tremor	Mydriasis	Miosis	Creatinine	Renal failure	CPK	Rhabdomyolysis	Diaphoresis	Fever
Int. Abuse (696)	3	5	11	120	1	3	11	59	167	24	6	4	11	5	1	4	184	103	34	109	259	13	2	12	8	5	17	114	14	7	2	9	2	34	20
Unint. Adverse Event (302)	0	0	5	7	1	2	14	8	179	70	1	1	11	6	0	4	15	38	7	31	18	6	1	3	1	8	5	9	5	5	2	2	3	23	4
Unint. General (74)	0	0	1	1	0	0	0	1	41	7	0	0	0	0	0	0	5	6	1	3	3	0	0	0	1	1	0	1	0	0	0	0	0	0	2

55. Pediatric methadone exposure: poison center time documentation of dose and clinical effects

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Background: Methadone is a long-acting synthetic opiate with reports of low doses leading to profound and prolonged toxicity in pediatric patients. This poison center (PC) currently recommends a 24-h observation period in a health care facility (HCF) with suspected exposure. However, some hospitals will subsequently transfer pediatric patients requiring prolonged monitoring. This documentation study aims to determine the need for referral or prolonged admission after pediatric methadone exposure.
Methods: The poison center Toxicall® database was queried for all single-substance methadone cases for the years 2006 through 2016. Included were cases of human exposure, ages ≤6 years old, adequate duration of follow-up (at least 4 h), estimable time of exposure, onset with duration of clinical effects and methadone dose. Data were extracted through chart note review by two reviewers with a 3rd reviewer acting to resolve discrepancies. The onset was defined as the interval of time between the exposure and where patients were reported with symptoms. The duration was determined by subtracting the earliest reported onset time from the time of symptom resolution. Maximum values for onset and duration were used to avoid underestimation of time. The duration of followup by the poison center for asymptomatic patients was also noted. The symptomatic (SX) and asymptomatic (ASX) cases were described with descriptive statistic. The mean times with standard deviations (SD) and percentiles were determined for onset and duration of effects.
Results: The query resulted in 154 methadone cases in children ≤6 years old for the defined time-period. A total of 95 patients (62%) were excluded primarily for lack of an adequate follow-up period (<4 h) or no exposure time. Table 1 shows the primary demographics for SX and ASX cases. Both groups were of similar size, age, and gender. The time of first call to the PC was shorter in the ASX than in the SX group, possibly because the former group more often initially called from home. Naloxone was used in 47% of SX cases and the need for mechanical ventilation was uncommon. Methadone dose was often uncertain but the dose was roughly double in the SX versus the ASX groups (median 10 mg versus 5 mg). The cumulative percentile timelines for onset and duration (maximum values) are shown in Figure 1 along with the duration of followup for asymptomatic patients. Many cases had reported symptom onset >4 h, a characteristic partially attributable to the delay in reporting. The correlation of onset time and reporting time can be seen in Figure 2 ($R^2 = 0.53$).
Conclusions: Pediatric methadone exposures in this series resulted in symptoms about 50% of the time and most were followed for prolonged periods whether or not symptoms occurred. The optimal duration of observation time is unclear due to reporting delays leading to conservatively long estimation of symptom onset time. Although many patients had only brief symptoms or not all, patient referral and prolonged observation seem unavoidable.

KEYWORDS Methadone; pediatric; timeline

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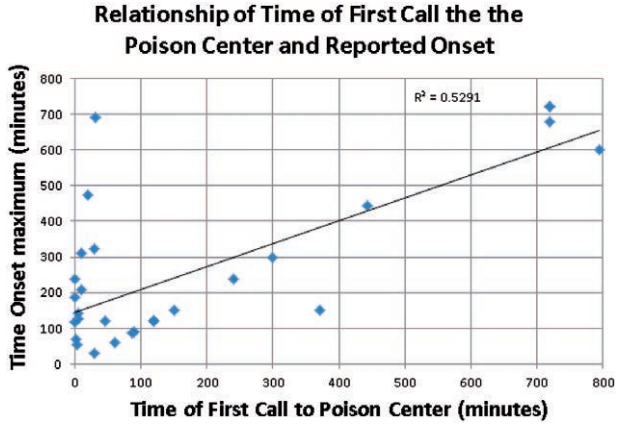

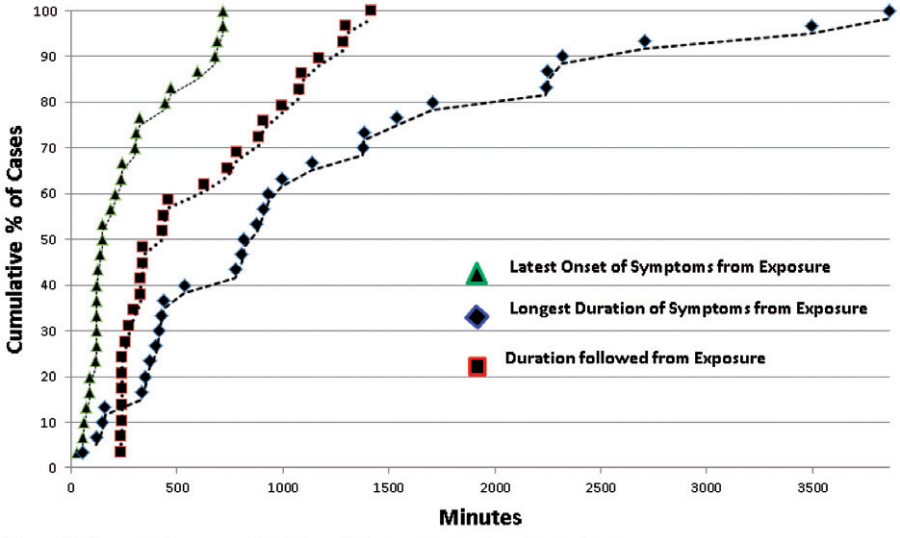

Figure 1. Cumulative percentile Time Data for Methadone Pediatric Exposure Cases, Symptomatic (onset and duration) and Asymptomatic (time followed)

56. Fatality secondary to nivolumab induced hepatitis: a medication error

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Background: Nivolumab is a human monoclonal antibody that is used in a variety of cancer treatments to modulate T cell immune reactivity. Nivolumab-induced hepatitis has been well documented but management of these patients is not clear. Fatalities have been reported in patients in which treatment with corticosteroids was delayed and/or had continued exposure following an initial hepatic injury. We present a case fatality and medication error in a patient who received a second dose of nivolumab despite preexisting signs of hepatitis.
Case report: A 70-year-old male with a history of hypertension, coronary artery disease, diabetes mellitus, and malignant melanoma undergoing immunotherapy, presented to the emergency department for hypotension and fever 4 d after his second nivolumab infusion. His presenting vital signs: HR – 75 bpm, BP – 103/57 mmHg, RR – 20/min, O2 sat – 98%, Temp –97.8 °F orally. His medications included: insulin,metformin, sitagliptin, enoxaparin, oxycodone, lisinopril, aspirin, escitalopram, risperidone, metoprolol, omeprazole, and prednisone. He had an unremarkable physical exam. Initial laboratory analysis revealed a lactate – 7.2mmol/L. The patient was also found to have transaminitis with an AST – 1506 U/L, ALT – 3190 U/L, and total bilirubin 1.0 mg/dL. CT of the abdomen was normal and a right upper quadrant ultrasound and duplex demonstrated diffuse non-specific mild gall bladder wall thickening. The hepatic vasculature was patent. Five hours after admission the patient's AST and ALT rose to 2844U/L and 4388 U/L, respectively. Lipase was 50 U/L. INR was 1.36 with a lactate of 7.2 mmol/L. He continued to deteriorate and his AST/ALT peaked at 5458 and 9400 U/L with an ammonia of 97 umol/L and an INR of 5.93 on hospital day #5. He was treated with intravenous hydrocortisone 100mg every 8 h and N-acetylcysteine (dosed at typical 21-h protocol with continued phase 3 dosing). The patient also received multiple doses of vitamin K as needed for coagulopathy. His sepsis workup and cultures were all negative. He required dobutamine continuous infusion for hypotension. The patient expired on hospital day #6 after he was enrolled in hospice/palliative care. One month prior to presentation the patient experienced transaminitis following his initial infusion of nivolumab. His AST and ALT were 275 U/L and 1138 U/L at their peak and trended back down to 76 U/L and 553 U/L 5 d prior to admission after treatment with prednisone. Oncology recommended discontinuation of the monoclonal antibody to avoid worsening hepatic injury. However, the patient received an additional infusion of the nivolumab in error, 4 d prior to when he presented to the emergency department.
Case discussion: We present a case fatality secondary to nivolumab-induced hepatitis following a medication error. Despite proper treatment with hydrocortisone and additional liver support with *N*-acetylcysteine, our patient died from fulminant hepatic failure.
Conclusions: Patients who suffer from a hepatic injury secondary to treatment with nivolumab need to be closely monitored, treated with corticosteroids, and consideration given to discontinuation of the treatment. Providers need to exercise caution when re-administering nivolumab, and ensure that it is appropriately discontinued after an initial hepatic injury due to this medication.

KEYWORDS Nivolumab; hepatitis; medication error

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Table 1. Pediatric Methadone Exposure Demographics and Time Onset and Duration

	Symptomatic (n = 30)	Asymptomatic (n = 29)
Average age in years (SD)	2.2 (1)	2 (1)
Gender M:F	1.5	1.4
Methadone dose evaluable	21 (70 %)	19 (66%)
Evaluable mean methadone mg dose (SD)	16 (16)	7.3 (9.5)
Evaluable median methadone mg dose	10	5
1st Call to PC = Health Care Facility (HCF)	15 (50%)	8 (28%)
Managed at HCF	27 (90%)	27 (93%)
Any Naloxone	14 (47 %)	0
Multiple dose naloxone	6 (20 %)	0
Naloxone infusion	5 (17 %)	0
Oxygen	3 (10 %)	0
Ventilator	1 (3.3 %)	0
Minutes from Exposure to 1st call	179 (246)	51 (63)
Mean Onset(maximum) in minutes (SD)	260 (216)	X
# Cases with Onset = 8 hours	25 (83%)	X
Mean Duration(maximum) in hours (SD)	19 (16)	X
# Cases with Maximum Durations =8 hours	11 (37%)	X
Hours of PC follow up (SD)	27 (16)	10 (6.5)

57. Women speakers at two national toxicology meetings from 2012 to 2017

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Background/objectives: Women make up almost half of all students entering medical school. However, it seems that when speakers are determined for grand rounds and national Emergency Medicine conference meetings, women are less likely to be represented. This study was to determine the representation of female speakers at two national meetings in toxicology.
Methods: Programs from the North American Congress on Clinical Toxicology (NACCT) and the American College of Medical Toxicology's (ACMT) Annual Scientific Meeting (ASM) were reviewed to categorize the speakers as male or female for the following sessions: ACMT Pre-Meeting, American Academy of Clinical Toxicology, Toxinology Course in 2014, and Main Congress. The Main Congress was divided into the following: Main Congress Speakers, Platform Speakers, Trainees/Fellows-in-Training Platform. For the ASM, the sessions were: Speakers and Platform. *Inclusion*: For NACCT, the pre-meetings and main congress programs were reviewed from 2012 to 2016. For ASM, the main meeting programs were reviewed for 2012 and 2014–2017. *Exclusion*: For NACCT, the ACMT clinicopathologic conference (CPC) was not included as not all speaker information was available. For ASM, the pre-meetings, Fellows-in-Training Open Mic sessions, and Fellows-in-Training Research forums were excluded, as was the 2013 program as it was not available. There were no Platform speakers in 2012. Male versus female speakers were confirmed by review of online biographies associated with the programs, online information from the organizations they work for, and/or by listening or reviewing the introductions made for each speaker.
Results: The overall speakers for NACCT were: M 347 F 210. In each category for NACCT: ACMT Pre-Symposium (M 28, F 13); AACT Pre-Symposium (M 36, F 7); Main Congress Speakers (M 204, F 146); Platform (M 59, F 31), Fellows-in-Training Platform (M 13, F 13). Two programs stood out as having no female speakers: The 2014 NACCT Pre-Meeting Toxinology Course and the AACT Pre-Symposium Meeting in 2016. The overall speakers for ASM were 113 males and 61 females. Eighty-one males and 42 females spoke as a part of the main meeting while 32 males and 19 females were platform speakers. See Tables 1 and 2 for further details.
Conclusions: Women are underrepresented, as speakers, at national toxicology meetings.

KEYWORDS Toxicology; women; speakers

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58. Etizolam toxicity with positive benzodiazepine screening test in a pediatric patient

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Background: Etizolam is a theinodiazepine with GABA A agonist activity. Etizolam is a pharmaceutical in some countries but is not a legal substance in the United States.
Case: A 3-year-old female presents with sedation, ataxia, and slurred speech. The patient's mother had difficulty waking the patient up, noticed "mumbling" speech, and difficulty walking 2 h prior to presentation. 1 h prior to presentation she was given a cold shower. She was taken to an urgent visit center and transferred to a tertiary care facility. The patient was given a 20 mL/kg IV normal saline bolus and started on maintenance IV fluids. The patient had been given melatonin and Nyquil® 17 h prior to presentation. No other known ingestion or exposure. Clonazepam was in the patient's house. *Exam*: T 36.2 C, P 102 bpm, BP 98/56 mmHg, RR 30 br/min, 100% on room air, mild sedation, horizontal nystagmus, slurred speech, truncal ataxia, difficulty with fine motor movements with upper extremities. Otherwise normal exam. *Initial data*: Head CT-normal, Comprehensive metabolic panel-normal, CBC-normal, EKG-normal sinus rhythm QRS-78 ms QTc-437 ms, ASA-negative, APAP-negative, ethanol-negative, UDS(enzyme immunoassay(EIA))-benzodiazepine positive (negative amfetamine, barbiturates, cannabinoids, cocaine, opiates, PCP, oxycodone), serum drug screen (EIA and fluorescent polarization immunoassay)-benzodiazepine positive (negative barbiturates and tricyclic antidepressants). *Hospital course*: The patient was admitted to the hospital. Neurology was consulted and recommended a routine EEG with showed diffuse beta activity consistent with medication effect. Toxicology was consulted and recommended supportive care. Her vital signs remained normal. Her sedation, nystagmus, slurred speech, and ataxia resolved and she was back to baseline within 24 h after admission.
Send out Lab Results: Benzodiazepine urine confirmation (Mayo Medical Laboratories, GC/MS) did not detect benzodiazepines, reported a substance that interfered with detection of alpha OH-triazolam. Urine drug screen-expanded (NMS Labs, EIA, LC-TOF/MS, ELISA) was positive for etizolam (detection limit: 10 ng/mL)
Discussion: Data regarding Etizolam toxicity in the pediatric population is limited. Other case reports of etizolam toxicity describe clinical effects similar to benzodiazepine toxicity, possible positive benzodiazepine testing by EIA, and difficulty in obtaining confirmation with benzodiazepine confirmatory testing.
Conclusions: Etizolam toxicity in this pediatric patient had expected GABA A agonist effects: sedation, ataxia, horizontal nystagmus, and slurred speech. Etizolam toxicity may result in positive benzodiazepine urine or serum EIA tests and negative confirmatory testing by GC/MS. Laboratories with the capability of detecting etizolam should be used when confirmation of this substance is deemed necessary.

KEYWORDS Etizolam; benzodiazepine; drug of abuse

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59. Evaluation of dose and outcomes from pediatric vilazodone ingestions

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Context: Selective serotonin reuptake inhibitor (SSRI) exposures in patients younger than 6 years of age are generally well tolerated. Vilazodone is an SSRI with partial agonism at the 5-HT_{1A} receptor with demonstrated clinical efficacy for depression whose off-label usage is likely to increase. Recent evidence suggests that unintentional ingestion of vilazodone is correlated with more severe clinical effects compared with other SSRIs.
Objective: To evaluate dose and outcomes from pediatric vilazodone ingestions.

Table 1. Medical Outcome Associated with Vilazodone Exposure Among Children Younger than 6 Years, NPDS 2011-2016

	All Cases	Dose Ingested (mg)				Dose Ingested per Body Weight (mg/kg)			
Characteristics	n (%)[a]	n (%)	Mean (SD)	Median	Min	n (%)	Mean (SD)	Median	Min
Medical Outcome									
Major effect	29 (5.0)	18 (4.0)	106.39 (126.23)	50.00	10.00	12 (4.3)	6.79 (9.38)	3.76	0.97
Moderate effect	113 (19.6)	87 (19.3)	81.15 (116.47)	40.00	5.00	52 (18.8)	4.73 (5.77)	3.37	0.02
Minor effect	233 (40.5)	179 (39.7)	52.58 (79.87)	40.00	5.00	110 (39.9)	4.36 (6.86)	2.51	0.27
No effect	201 (34.9)	167 (37.0)	48.29 (66.69)	20.00	1.25	102 (37.0)	3.41 (4.59)	1.52	0.09
Subtotal	***576 (100.0)***	***451 (100.0)***				***276 (100.0)***			

[a] Percentages may not sum to 100.0% due to rounding error.

Methods: A retrospective analysis of single substance exposures associated with vilazodone among children younger than 6-years-old from 2011 to 2016 was conducted using data from the National Poison Data System (NPDS).
Results: During 2011–2016, 753 vilazodone ingestions in children <6-years-old were reported to the US poison control centers. The average dose associated with major outcomes was 106.39 mg (median: 50.00) and 81.15 mg (median 40.00) for moderate outcomes. Half (50.0%) of children with a major effect and 54.0% with a moderate effect ingested ≤40 mg of vilazodone. There was an increasing trend associated with vilazodone dose ingested and the proportions of healthcare facility admissions ($p<.001$) and serious outcomes ($p< .001$). Children ≤2 years have higher odds of being admitted to a healthcare facility (OR: 1.70; 95% CI: 1.10–2.61) or developing a serious outcome (OR: 1.73, 95% CI: 1.07–2.77) compared with children 3–5 years of age. Serious clinical effects, such as coma, seizures, ataxia, and hallucinations/delusions, were observed in children ingesting doses of vilazodone as low as 10 mg.
Conclusions: Exposure to vilazodone poses a unique and potentially serious threat to children <6 years of age. Children in this age group who are exposed to vilazodone should be evaluated promptly in a clinical setting. Off-label use of vilazodone in young children should be discouraged until further research is conducted regarding its safety in this population.

KEYWORDS Selective serotonin reuptake inhibitor; vilazodone; pediatrics

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60. Local effects of Western hognose envenoming (*Heterodon nasicus*)

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Background: Colubrid, or rear-fanged snakes, are generally thought to have little human toxicologic significance. We present a case of envenoming by a Western hognose (*Heterodon nasicus*).
Case: A 25-year-old female presented to health care hours after a bite from her pet Western hognose snake. She picked it up to check on its health when it latched onto the proximal phalanx of her left third digit. Swelling began soon after, and at the first hospital she received an X-ray, intravenous (IV) antibiotics, and hand specialist consultation. Swelling progressed to the level of the elbow overnight. Dissatisfied with her care, the patient signed out of the first hospital and presented to this author's institution. Swelling stopped progressing about 3 h prior to second hospital presentation. She complained of pain and paresthesias to the affected digit. Examination revealed a well-appearing female with swelling and patchy confluent erythema to the left hand and forearm to the level of the elbow, with intact vascular, sensory, and motor function. Laboratory studies revealed normal blood counts, comprehensive metabolic profile, and coagulation parameters. X-ray showed soft tissue swelling only. She received IV ampicillin/clavulanate and analgesia. The following day she had improvement in the paresthesias, swelling, and rash. She was seen by hand surgery and made arrangements for followup. The patient was lost to follow up after discharge on hospital day 2.
Discussion: *H. nasicus* venom is delivered via the complex Duvernoy's apparatus and appears to contain phosphodiesterase and azocaseinase activity. Additionally, saliva from *H. nasicus* has phospholipase A2 and azocaseinase activity. One prior reported Hognose envenoming described self-limited local swelling, erythema, and bullae. These findings were thought to be due to both local tissue effects of these proteins and type-1 hypersensitivity. Fatalities have been reported with envenoming by other Colubrid species. While neurotoxins have been identified in Duvernoy secretions of other Colubrid species, there do not appear to have been any significant neurotoxic effects in this patient. Our patient appears to have sustained local effects similar to other reported cases of *H. nasicus* envenoming without evidence of neurotoxicity, myotoxicity, or hemotoxicity. Treatment is generally supportive. Clinicians are encouraged to take a conservative approach to the evaluation and treatment of patients with Hognose envenoming until evidence supporting the true range effects is further elucidated.

KEYWORDS Western hognose; envenoming; snakebite

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61. Temporary blindness after unintentional ingestion of concentrated hydrogen peroxide

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Background: Hydrogen peroxide is an unstable, oxidizing agent that readily breaks down to water and oxygen. High concentrations of hydrogen peroxide (10–35%), found in health food stores and available on the Internet, are marketed as "food grade" and are claimed to cure cancer, arthritis and other conditions. Ingestion of high concentrations can cause severe corrosive injury and venous or arterial gas emboli. We report a case of ingestion of 35% hydrogen peroxide (H_2O_2) causing immediate bilateral blindness.

Case report: A 73-year-old female presented to Emergency Department 4 h after ingesting 1.5 ounces (oz) of 35% hydrogen peroxide (Oxy Tech) diluted in 1.5 oz of orange juice. Patient purchased this "food grade" H_2O_2 from a health food store as an arthritis treatment. She misunderstood the instructions, which were to dilute nine drops of H_2O_2 in 11 oz of water. Immediately following ingestion, patient vomited once, developed left-sided flaccidity, severe aphasia and complete blindness in both eyes. Patient had pre-existing mild left-sided weakness from a stroke several years earlier but did not have baseline vision deficits. She denied having any of the liquid splash onto her face or into her eyes. No evidence of oropharyngeal burns were noted, and the patient was in no respiratory distress. MRI of the brain showed multiple areas of flow restriction and multiple infarcts throughout, but no gas bubbles. Patient was transferred to a hyperbaric oxygen (HBO) facility. Due to logistic problems with the transport, the first HBO treatment was initiated about 11 h post-ingestion. By day 3, the patient had improvement in all visual fields, and improved strength on her left side. The patient ultimately underwent 10 sessions of hyperbaric oxygen therapy. She fully regained her vision, though she has persistent left-sided neurologic deficits that are worse than at baseline.
Discussion: This is the first reported case of cortical blindness from ingestion of concentrated H_2O_2. Although the mechanism of injury is unclear, cortical blindness after scuba diving is thought to be from retrochiasmal arterial gas embolism or central retinal artery occlusion from gas emboli in the ophthalmic artery. Cerebral gas embolism from ingestion of concentrated H_2O_2 have resulted in permanent neurologic sequelae, such as spastic quadriplegia and hemiparesis. HBO therapy may reduce the size of gas emboli, and dramatic improvement of neurologic deficits after HBO therapy have been reported.
Conclusions: Ingestion of concentrated H_2O_2 can result in cortical blindness. Repeated treatment with HBO may have aided in the satisfactory resolution of this complication.

KEYWORDS Hydrogen peroxide; hyperbaric oxygen; blindness

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62. What could it be, honey? Think outside the (botulism) box

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Background: Botulism is a rare and potentially lethal disease caused by botulinum neurotoxin. There were 161 confirmed cases of botulism reported to the CDC in 2014 with 128 (80%) infant botulism (IB). Review of data from a statewide poison control system revealed 0 cases of IB in the past 5 years. Since confirmatory testing can be delayed, a clinical diagnosis of IB should be considered in the appropriate patient to expedite treatment. We report a case of IB in an unexpected region, without identified etiology, where clinical suspicion resulted in early treatment.
Case report: A 2-month-old previously healthy male presented to an outside hospital for 2–3 d of upper respiratory infection symptoms and coughing. He had a poor gag, weak cry, decreased oral intake, and no bowel movement for 5 d. He saw his PCP who started him on a beta agonist for bronchiolitis. The patient tested positive for RSV. Within 24 h, he was admitted to a local hospital for possible pneumonia. He began to develop weakness and hypotonia and was transferred to a tertiary care center. Within 24 h of transfer (hospital day 1–HD 1), he was intubated for respiratory failure. The remainder of the septic workup was negative (lumbar puncture, blood cultures, and immunologic evidence of Guillain-Barre Syndrome). Despite no history, the diagnosis of IB was considered. The poison center was contacted to assist in acquiring antitoxin, and for information on how to test for botulism. Antitoxin (BabyBIG) was started on HD 2. After 6 d of intubation, he was successfully extubated despite mild stridor. On HD 7, stool was confirmed positive by the CDC. He remained hospitalized for difficulty with latching on and swallowing, requiring NG feedings. He received occupational, physical, and speech/swallow therapy for continued but improving weakness. He was discharged home with close follow-up on HD 20 and continued to improve. Despite an extensive investigation, no source of the botulism was ever identified.
Discussion: The etiology of the botulism in this case is not clear. Although his mother used very small amounts of store-bought honey in her oatmeal, spores are too large to cross via breast milk. The family adamantly denied giving the child any honey, and despite an extensive evaluation, no cause was ever identified. It is unclear if viral illness had any impact on course of illness. While it is unlikely that the initiation of antitoxin changed the ultimate outcome in this case, the data support early initiation to hopefully shorten the course and lessen respiratory failure.
Conclusions: Even in low-risk areas, IB should be considered in an infant with the appropriate clinical picture. It may be reasonable to initiate antitoxin treatment while awaiting confirmatory testing in an infant with hypotonia, poor feeding, and decreased bowel motility of unclear etiology.

KEYWORDS Botulism; honey; infantile

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63. Monoamine oxidase A inhibition by toxic concentrations of metaxalone

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Background: Serotonin toxicity has been reported with overdose of metaxalone in individuals on therapeutic doses of serotonergic drugs such as serotonin reuptake inhibitors. Monoamine oxidase A (MAO-A) inhibition by metaxalone has been proposed as the etiology of this toxicity. We investigated the effect of metaxalone on MAO-A activity using an *in vitro* model with metaxalone concentrations from 6.25 μM to 800 μM. Therapeutic metaxalone concentrations are about 4 μM and those reported with cases of serotonin toxicity have been from 135 to 315 μM.
Methods: Metaxalone at concentrations of 6.25–800 μM with recombinant human MAO-A (Sigma-Aldrich, Chicago, IL) added was incubated for 1 h with a proprietary MAO substrate (MAO-Glo®, Promega Corp., Madison, WI). MAO-A liberates methyl ester luciferin. Luciferase with an esterase is then added, resulting in luminescence that is proportional to MAO-A activity. Clorgyline, a known MAO-A inhibitor was used as a positive control. Luminescence was measured at 40 min using a Biotek Synergy HT microplate reader.
Results: At the lowest concentration of metaxalone tested, inhibition was minimal. At increasing concentrations, significant inhibition of MAO-A was observed (see Figure). Repeated measures analysis of covariance confirms that there is significant dose-related inhibition of MAO-A activity by metaxalone.

Conclusions: With therapeutic use, metaxalone does not inhibit MAO-A. At higher concentrations similar to those reported in cases of serotonin toxicity MAO-A inhibition was observed. This study supports the theory that metaxalone is an important MAO-A inhibitor at toxic concentrations. A limitation of this conclusion is that what we have observed in this *in vitro* model may not translate directly to the impact on MAO-A *in vivo*.

KEYWORDS Serotonin toxicity; metaxalone; monoamine oxidase A

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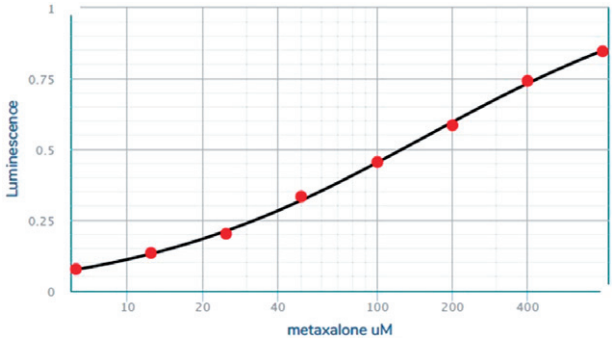

64. Toxicity of inadvertent benzocaine for oral use exposures in the pediatric population

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Background: Unintentional ingestions of oral benzocaine products exceeding the recommended dose are often reported to poison centers. Although there are reports of pediatric toxicity from these products, there are no recommended triage guidelines for referral to a hospital. Our primary aim is to develop a triage strategy based on the minimum dose in a child ≤6 years that resulted in moderate or severe symptoms.
Methods: This IRB approved retrospective chart review of regional poison center (RPC) cases involved children ≤6 years with a single acute ingestion of oral benzocaine from December 1999 to June 2016. Cases with documented historical amounts of benzocaine ingested per weight (mg/kg) and documented outcomes were included.
Results: Out of 481 cases identified, 274 cases met all inclusion criteria; 167 (52%) were male. Ten involved exact known amounts ingested (3.6%), 132 estimated amounts (48.2%), and 132 amounts were described as maximum possible (48.2%). Amounts documented as exact ingestions ranged from 6.3 to 646 mg/kg; amounts documented as max possible were up to 2857 mg/kg. Of the 274 cases, 122 (44.5%) were <2 years old, 110 (40.1%) 2 years old, and the remaining were 3–6 years old. The most common symptoms reported were cough/choke (3.3%, 5.9–225 mg/kg), vomiting (2.6%, 8.8–285 mg/kg), and oral irritation (2.2%, 3.9–62 mg/kg). Two patients received methylene blue for methemoglobin concentrations of 55% and 62% after max possible ingestions of 33 mg/kg and 211 mg/kg, respectively. No effects were reported in 232 (84.7%) cases. Of 274 cases, 137 (50%) were treated at home (mean 34 mg/kg), and 137 (50%) were seen in a hospital (mean 131 mg/kg). Of those treated in a hospital, 29 (10.6%) were given activated charcoal and 2 (0.8%) were given methylene blue. The remaining 106 (77.4%) were observed with no further intervention.
Discussion: Although our study examined oral benzocaine 7.5–20% products, benzocaine 7.5–10% products are typically approved in children. Most oral products state, "Apply a small pea-size amount on gums" up to four times daily. Studies have described "pea-size" to be about 0.25 g. Therefore, a 7.5% product would contain 20 mg per pea-sized application, 10% would contain 26 mg. The recommended maximum daily dose for an average 2-year-old with a 7.5% product would be 6.45 mg/kg, and 8.4 mg/kg with a 10% product.
Conclusions: Pediatric ingestions of <33 mg/kg benzocaine appear unlikely to cause serious toxicity and can be potentially managed outside a hospital setting. Cases with more than minor symptoms should continue to warrant medical evaluation. Continuing assessment of benzocaine ingestions in children ≤6 years will be needed to confirm this triage guideline as safe and reliable.

KEYWORDS Benzocaine; triage; pediatric

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65. A 16-year review of loratadine exposures in the pediatric population

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Background: Unintentional ingestions of loratadine are frequent in children, mostly as tablets or suspensions. Although there are a few case reports of toxicity resulting from loratadine ingestion, there is no consensus dose which would require hospital referral. Our regional poison center (RPC) uses >60 mg as our current triage guideline in children ≤6 years. Our primary aim is to reevaluate our current triage guideline.
Methods: This IRB approved RPC retrospective chart review included children ≤6 years with reports of a single acute ingestion of loratadine from December 1999 to 2015. Cases with documented historical amounts ingested per weight (mg/kg) and documented outcomes were included.
Results: Out of 4368 cases identified, 631 cases met inclusion. There were 319 males (50.6%). 131 (21%) were <2 years, 241 2 years (38.2%), and 259 (41%) were greater than 2 years. Of the 631 cases, 139 involved ingestions with exact amounts (22%), 143 estimated amounts (22.7%), and 349 amounts were described as maximum possible (55.3%). Of the 631 cases, 509 (80.7%) remained asymptomatic, while 122 (19.3%) reported symptoms. The most common symptoms reported were drowsiness (9.5%, 0.4–41.1 mg/kg), tachycardia (5.1%, 1–41.1 mg/kg), hyperactivity (4.1%, 0.3–14.7 mg/kg), and agitation (1.6%, 2.9–32.5 mg/kg). Other noteworthy symptoms included ataxia (0.2%, 0.8 mg/kg), erythema (1.4%, 0.7–33 mg/kg), hyperthermia (0.2%, 16.1 mg/kg), and QTc prolongation (0.3%, 6.7–12.1 mg/kg). Three of the cases were seen by EMS only, while 324 (51.3%) were treated at home (mean 3.1 mg/kg) and 304 (48.2%) were evaluated in a hospital (mean 9.7 mg/kg). Of those treated in a hospital, 104 (34.2%) were given activated charcoal, 5 (1.6%) were given IV fluids, and 1 (0.3%) was given benzodiazepines. Of the 304 treated in a hospital, 236 (77.6%) were asymptomatic and 68 (22.4%) reporting symptoms, of which 41 patients were given no therapies and discharged home after being observed.
Discussion: Of the tachycardic children, only seven out of 32 were reported to also be agitated or hyperactive. Tachycardia may have been missed with patients that were observed at home. Agitation and hyperactivity could be initial signs of anticholinergic toxicity. The lowest reported exact or maximum dose

of a symptom of concern was 0.3 mg/kg (5 mg), with hyperactivity. Symptoms of concern reported at doses lower than loratadine 60 mg, our triage dose, included agitation, ataxia, erythema, hyperactivity, and tachycardia. QTc prolongation with tachycardia was reported at a max dose of 6.7 mg/kg (100 mg) and a max dose of 12.1 mg/kg (170 mg).
Conclusions: Based on this data and our current triage guideline, it is difficult to determine whether symptoms of concern actually warrant referral to a hospital after loratadine exposure. Hyperactivity was seen at a therapeutic dose. However, due to the lack of interventions required after evaluation in a hospital, it may suggest that our initial symptoms of concern post-loratadine overdose may be self-limited.

KEYWORDS Loratadine; triage; pediatric

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66. Incidence of infection in crotalid snake envenoming reported to a regional poison control center

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Background: Envenoming from rattlesnakes often results in extensive cytotoxic effects including edema, ecchymosis, and myonecrosis. These local tissue effects result in erythema, swelling, and tenderness that mimic symptoms of infection. Due to these physical findings, the early treatment guidelines recommended the use of broad-spectrum antibiotics to prevent secondary infection. In contrast, a more recent study of 54 crotalid snake bite victims found a low incidence of bacterial infection (3%), describing one patient with infection as evidenced by purulent material found on incision and drainage. Additionally, other studies have described antibacterial properties of crotalid venom, theorizing that this may contribute to low incidence of bacterial infection. Despite these studies, and current recommendations against prophylactic antibiotic use, the need for antibiotics remains a concern for practitioners. The purpose of this study is to describe the incidence of infection in snakebite victims reported to a regional poison control center.
Methods: The study design was a retrospective observational study of snakebite victims reported to a regional poison control center. Chart review identified patients during the study period of 1999–2016. These cases were then searched for keywords of "infect", "antibiotic", or "pus" to identify cases of possible infection. Data collected included age, sex, use of prophylactic antibiotics, and culture results if known.
Results: Identified cases of rattlesnake bite numbered 2732. A total of 146 cases contained at least one of the key search terms. Of these, 127 received prophylactic antibiotics. Incidence of infection was found to be 0.99%. Approximately 63% of infections were diagnosed at least 5 days post-envenomation. Empiric antibiotic use had an incidence of 5.38%, often despite recommendations against this practice by consulting toxicologists or certified specialists in poison information.
Conclusions: This study demonstrates the low incidence of infection related to crotalid envenoming cases reported to a regional poison control center. More than half of cases of infection occur a minimum of 5 d after initial presentation and thus antibiotics should be reserved for signs of symptoms of infection as they arise. With this information, we hope to add to existing literature supporting the practice of not administering prophylactic antibiotics and avoid overuse of antibiotic therapy in the treatment of crotalid snake envenoming.

KEYWORDS Rattlesnake; envenomation; infection

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67. Chaga tea not good for me

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Background: The natural and/or herbal medicine phenomenon continues to grow in Western cultures as chemophobia and fear of pharmaceutical products grow despite a recent report stating that up to 20% of hepatotoxicity in the United States can be attributed to supplement use. Unfortunately, these products avoid safety and efficacy regulations from the Food and Drug Administration because of their status as supplements. Case Report: A 70-year-old male with a history of atrial fibrillation on warfarin presented to the emergency department following ingestion of 'Chaga tea' made for him by his son to 'enhance his warfarin effects.' The patient denied any additional changes in diet or medications. Laboratory analysis showed the patient's INR to be greater than 10. In addition, the patient had transaminitis with an initial AST of 277 units/L and ALT of 218 units/L. Upon repeat laboratory analysis the following day, the patient had developed worsening liver dysfunction (AST 2,023 units/L, ALT 1,153 units/L, platelet count 174,000, PT 81.3 s, INR >10, total bilirubin 2.8 mg/dL) and the decision was made to initiate treatment with intravenous n-acetylcysteine utilizing the 21-h acetaminophen protocol. The patient also developed an acute kidney injury (maximum BUN 50 mg/dL and maximum serum creatinine of 4.3 mg/dL). The patient's transaminitis and coagulopathy quickly improved over the next 24 h and the patient was discharged on hospital day 7 with a therapeutic INR (2.5). His transaminases at discharge were AST 522 units/L, ALT 942 units/L.
Discussion: A review of the medical literature resulted only one report of toxicity with the use of Chaga fungus in humans. A 72-year-old female was found to have renal tubular atrophy and interstitial fibrosis. No reports of hepatotoxicity were found. Although we cannot ultimately conclude the patient's hepatic and renal toxicity were due to Chaga fungus exposure, we feel there are facts that lend credence to this possibility. The patient was on warfarin therapy, which will elevate the INR, but the rapid rise of INR, and transaminases in one day with subsequent decline the following day are not typical of supratherapeutic warfarin treatment or drug/food interactions. In addition, extensive medical work-up revealed no additional explanation for the patient's presentation. A sample of the fungus was not available for analysis.
Conclusions: We present a case of hepatic and renal toxicity that may be secondary to Chaga fungus exposure. Although we cannot analytically confirm the effect was due to Chaga fungus, temporal relation to use of Chaga-based tea as well as prompt resolution of symptoms upon withdrawal of the product provides convincing evidence. This case should serve as a reminder that the use of alternative/herbal medicine should be considered when investigating hepatotoxicity.

KEYWORDS Chaga; mushroom; hepatotoxicity

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68. When enigmatic pheochromocytoma bites back: metoclopramide-induced pheochromocytoma in a patient with previously undiagnosed adrenal mass

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Background: Pheochromocytoma is a rare catecholamine-producing neuroendocrine tumor. Several classes of medications (e.g., dopamine type 2 receptor antagonists, sympathomimetic agents, b-adrenergic receptor blockers, antidepressants – monoamine oxidase inhibitors and norepinephrine reuptake inhibitors, etc.) have been implicated in precipitating acute pheochromocytoma crisis. We report a case of multi-organ failure due to metoclopramide-induced pheochromocytoma crisis in a previously healthy individual.

Case report: A 36-year-old female presented to the emergency department with a complaint of headache and nausea. Initial vital signs were temperature, afebrile; blood pressure, 134/86 mmHg; pulse, 71 beats per minute; respiratory rate, 16 breaths per minute; and 96% O_2 saturation. Initial laboratory evaluation and CT scan of the brain was unremarkable. Metoclopramide was administered for nausea. One hour later, patient became restless and received diphenhydramine and methylprednisolone for suspected allergic reaction to metoclopramide. Subsequently, blood pressure increased to 223/102 mmHg and she developed diaphoresis, left-sided chest pain, and wide-complex tachycardia (177 beats per minute). Repeat laboratory showed metabolic acidosis with acidemia (pH <6.81) and lactic acidosis (16.4 mmol/L). CT scan of chest/abdomen/pelvis revealed a right adrenal mass and no other abnormalities. The patient experienced multi-organ failure, including acute respiratory distress syndrome requiring mechanical ventilation and extracoporeal membrane oxygenation, cardiogenic shock, myocardial ischemia (troponin: 36.1 ng/mL), acute liver failure (AST/ALT: 13,794/10,569 units/L; INR: 3.3), and acute kidney injury (creatinine 3.08 mg/dL). Serum metanephrine and normetanephrine levels were elevated at 6754 pg/mL and 10,565 pg/mL, respectively. Patient's multi-organ failure improved during prolonged hospitalization with medical management. Pheochromocytoma was confirmed after the right adrenal mass was surgically removed.

Discussion: Drug-induced pheochromocytoma crisis is a rare event. However, metoclopramide, a common antiemetic with dopamine (DA_2)-receptor antagonist property, has been frequently implicated in drug-induced pheochromocytoma crisis. Historically, clinicians performed provocative test using metoclopramide to help diagnose pheochromocytoma. The mechanism is believed to involve presynaptic DA_2 receptors that inhibit the release of catecholamines when stimulated. Thus, blockade of DA_2-receptor accentuates catecholamines release from adrenal tissue. A recent *in vivo* study showed that metoclopramide also stimulates 5-HT_4 receptors and increases catecholamine release in pheochromocytoma cells. Awareness of this rare adverse drug reaction of metoclopramide is important for clinicians to recognize the potentially undiagnosed pheochromocytoma and implement appropriate intervention.

Conclusions: Hypertensive emergency due to undiagnosed pheochromocytoma is a rare but life-threatening adverse drug reaction from therapeutic use of metoclopramide.

KEYWORDS Metoclopramide; pheochromocytoma; adverse drug reaction

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69. Survey of common sodium bicarbonate prescribing for tricyclic antidepressant poisoned patients

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Objective: Although sodium bicarbonate (NaHCO3) is a commonly used antidote for tricyclic antidepressant (TCA) poisoning, there are no controlled or comparative trials showing its efficacy and optimal dosing. This survey aims to identify common NaHCO3 prescribing patterns used by toxicologists.

Methods: An anonymous Internet-based survey, through Survey Monkey®, was distributed to members of the American Academy of Clinical Toxicology which included demographic inquiries and questions regarding the use of NaHCO3 (indications, dose, monitoring parameters, and endpoints). Results were analyzed using descriptive statistics.

Results: Estimated response rate of 31% was attained with 244 professionals participating in this survey including physicians 60%, pharmacists 23%, and toxicology fellows 14%. A total of 191 (78%) surveys were completed. Most respondents (92%) utilize NaHCO3 for management of TCA poisoned patients. Isolated symptoms warranting NaHCO3 include QRS prolongation 99%, acidosis 61%, seizures 55%, and QTc prolongation 12%. Altered mental status (AMS), hypotension (HoTN), and detectable R/R' wave in aVR would not warrant therapy. QRS treatment thresholds varied from 100 ms, 101–119 ms, and 120–159 ms with 29%, 30%, and 28%, respectively; there were no differences for pediatric patients. All providers administer bolus doses with various regimens of 1–2 mEq/kg, 2–3 mEq/kg, or empiric 1–2 amps by 53%, 6%, and 29% respectively. Majority (72%) utilize infusions with a common dose of 150 mEq in 1L of D5W at 1.5–2× patient's maintenance rate, initiated after the bolus if the QRS narrowed. No differences were correlated between prescribing infusions and the toxicologist's practice site. An endpoint that was predominately agreed upon, by 94%, was QRS normalization. QTc normalization would prompt NaHCO3 discontinuation by 11%. Diminished R wave, defined doses/time of therapy, resolution of HoTN/AMS, or serum alkalinization were not considered as endpoints to stop treatment by 60%, 93%, 86%, 57%, 82%, and 50.3% respectively. Treatment failure was defined as a lack of improvement after a set number of boluses (range 1–15), after an alkalotic environment (7.45–7.55) was achieved, or undefined by 38%, 20%, and 25%.

Conclusions: Although a majority of toxicologists utilize NaHCO3 to treat TCA poisoned patients the indications, dosing, endpoints, and definition of treatment failure can vary by practitioner. QRS prolongation and subsequent normalization was illustrated as the only consistent indication and endpoint. A limitation of this study was that respondents were able to skip questions, and all questions may not have had a 100% response rate. Further research is needed to determine if standardizing NaHCO3 dosing regimens would improve patient outcomes.

KEYWORDS Sodium bicarbonate; tricyclic antidepressant; survey

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70. Novel approach to using haloperidol during an active shooter hostage situation

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Background: Law enforcement is frequently involved in dangerous hostage situations. Commonly, perpetrators are subdued by conducted-energy devices (such as stun guns), however, these may cause serious injury or death. Alternatives are being explored that could be used to subdue victims with minimal harm. We report a case of a patient who became tranquilized after oral consumption of water containing sedative medications.
Case report: EMS was dispatched to the scene of a 20-year-old, 66-kg male with a history of depression who was expressing suicidal ideations and was involved in an armed standoff with law enforcement. After several hours, the patient asked for water. With approval from the command supervisor and an ED physician, two 16-ounce water bottles were each instilled with 5mg midazolam and 5mg haloperidol solutions for IV injection. The patient drank both water bottles over the course of 1 h. Soon after finishing the second water bottle (a total of 10 mg midazolam and 10 mg haloperidol) the patient became drowsy and dropped his gun. Law enforcement subdued the patient with a rubber bullet. He became combative as he was being taken into custody, so EMS administered another 5mg of haloperidol and 5mg midazolam, this time via IM injection. The patient arrived to a regional level 1 trauma center with HR 73, BP 137/74, RR 18, temp 36.6 °C, and SpO2 100% on room air. Urine drug screen was positive for benzodiazepines. Three hours after drinking the initial water bottle and 1.5 h post-IM injection, serum haloperidol level resulted at 14 ng/mL [reference range, 5–15 ng/mL]. A midazolam level was also drawn but unfortunately misplaced in transit to the lab.
Discussion: Serum haloperidol concentrations are variable following administration via the oral, IV, IM, or inhalation routes. Based on previous studies, haloperidol levels are expected to be <10 ng/mL 1.5 h after parenteral administration of a 2.5-mg dose, and to fall to <5 ng/mL by 3 h after administration. In other reports, oral doses of 0.03–0.71 mg/kg/day resulted in serum levels of 1.5–33 ng/mL; this patient received a total of 0.23 mg/kg of haloperidol. Our patient had a haloperidol concentration that remained elevated several hours after oral administration of IV solutions and provision of an additional IM dose.
Conclusions: To our knowledge, this is the first case report describing oral administration of IV haloperidol in a hostage situation. This route of delivery produced a therapeutic serum level and the desired clinical effect of sedation. This approach may be a safe and effective alternative to subdue active shooters in similar situations. Additional research in this topic is warranted to further explore the pharmacokinetics and pharmacodynamics of IV sedatives consumed orally.

KEYWORDS Haloperidol; water bottle; hostage

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71. Dragon's Tongue (*Sauropus spatulifolius*)-induced liver injury – a report of two cases

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Background: The leaves of *Sauropus spatulifolius*, commonly known as Dragon's Tongue, are used in traditional Chinese medicine to treat upper respiratory tract infection and bronchitis. Little is known about its ingredient and toxicity. We report two cases of liver injury probably induced by the roots of *S. spatulifolius*.
Case reports: A family of seven consumed a homemade herbal soup and six developed nausea, vomiting, and diarrhoea at around 12 h after consumption. The soup was made by boiling the leaves and roots of *S. spatulifolius* grown by the family (shown in Figure 1) with pork. The family had consumed soup made in a similar manner once before without any problem. Two family members presented to the emergency department (ED) 3 d after ingestion and were admitted to our hospital because of deranged liver function. The clinical details are summarized in Table 1. Both patients were non-drinker with no known underlying liver disease. There was no suspicious food history other than herbal soup consumption or recent change in their usual medication. Extensive workup for both cases, including hepatitis A, B, C, and E serology, cytomegalovirus pp65 antigen, Epstein-Barr virus serology, and ultrasound of the liver were all unremarkable. Urine toxicology screen was unrevealing. Both patients recovered uneventfully with normalisation of liver function within 2 months after consumption. The remaining five family members who were exposed to the herbal soup were called to our ED for blood testing but their liver function was unremarkable. The unconsumed fresh plant specimens were identified to be *S. spatulifolius* by independent botanists. Unfortunately, no herbal soup was left for analytical investigation.
Case discussions: *S. spatulifolius* is regarded as a benign herb in traditional Chinese medicine but the its roots are seldom used to treat ailments. In animal study on mice, the water extract of its roots appeared to have low toxicity with a LD50 152.24 g/kg. However, diarrhoea, anorexia, decrease in activity, and unsteady gait were observed in mice in a dose-dependent manner. In the literature, we could only identify a single case series of human poisoning published in Chinese in 1976, in which seven patients developed gastrointestinal symptoms 5–32 h after drinking soup made by boiling its leaves and roots but hepatotoxicity was not reported. Here, we report two cases of liver injury after drinking soup made by boiling its leaves and roots. Using the Roussel Uclaf Causality Assessment Method (RUCAM), both cases had a hepatocellular pattern of injury and a RUCAM score of 8 for *S. spatulifolius*, indicating that the causal relationship was "probable". Yet, the exact ingredient of *S. spatulifolius* and mechanism that caused liver injury have remained unknown.
Conclusions: *S. spatulifolius* can probably induce liver injury, especially when the roots are consumed. Further studies are warranted to elucidate the ingredient and mechanism responsible for such an injury.

KEYWORDS Medicinal herbs; drug-induced liver injury; *Sauropus spatulifolius*

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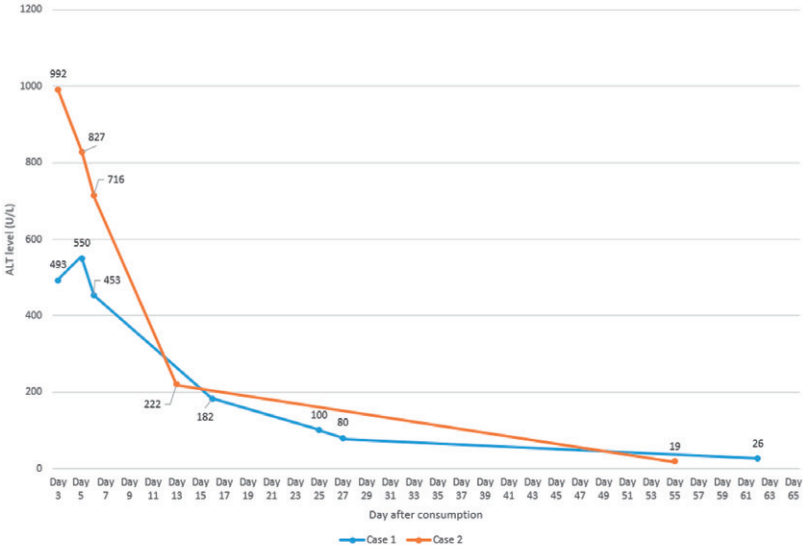
The trend of alanine transferase after consumption of *S. spatulifolius*



	Case 1	Case 2
Age (in years)	70	83
Gender	Female	Male
Symptoms	Fever, epigastric discomfort, diarrhoea at around 12 hours after ingestion	Vomiting, abdominal pain and diarrhoea at around 12 hours after ingestion
Past medical history	Hypertension, diabetes mellitus, hyperlipidaemia and ischaemic heart disease	Hypertension, hyperlipidaemia, and chronic obstructive pulmonary disease
Current medications	Aspirin, atorvastatin, isosorbide mononitrate, losartan and trimetazidine	Nifedipine, theophylline and simvastatin
Alcohol use	Non-drinker	Non-drinker
ALT	493 U/L (ULN 45 U/L)	992 U/L (ULN 58 U/L)
AST	436 U/L (ULN 37 U/L)	607 U/L (ULN 38 U/L)
ALP	51 U/L (ULN 124 U/L)	44 U/L (ULN 110 U/L)
Liver injury pattern	Hepatocellular	Hepatocellular
RUCAM score		
Time to onset	2 (suggestive)	2 (suggestive)
Course	3 (highly suggestive)	3 (highly suggestive)
Risk factors	1 (for age ≥ 55 years)	1 (for age ≥ 55 years)
Concomitant Drug(s)	0 (incompatible time to onset)	0 (incompatible time to onset)
Non-drug causes	2	2
Previous information on hepatotoxicity	0	0
Response to readministration	0 (no rechallenge was done)	0 (no rechallenge was done)
Total score	8	8

Abbreviations: ALT= alanine transferase; AST = aspartate transferase; ALP = alkaline phosphatase; ULN = upper limit of the normal range

72. Apnea in a child following dermal exposure to compounded pain cream

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Background: Topical compounded pain creams are gaining popularity as a treatment for neuropathic pain. Compounding allows the medication to be customized to individual patient's needs. Often individual ingredients are listed as abbreviations on the label, which may lead to confusion and delayed treatment when dealing with unplanned exposures. We present a case of dermal exposure of such a product in a child that resulted in CNS and respiratory depression requiring mechanical ventilation.
Case report: A 2-year-old girl was playing with her mother's compounded topical pain cream and rubbed the cream all over her face. Parents insisted that she did not ingest any and promptly washed her face with soap and water. Poison Control was contacted 20 min post-exposure with the girl already in the ED. At that time she was drowsy. The girl's mother brought the prescription, however, she was unaware of what the abbreviations on the label meant. The label read as c-pgb 2.5/kea 10/gab 8/cl 0.3. It was initially suspected that the cream contained a combination of gabapentin, pregabalin, clonidine, and an NSAID. Initial vital signs: BP 152/97, HR 102, SpO2 90%. Shortly after ED arrival she became apneic and was intubated. Through contacting the compounding pharmacy it was determined that the cream contained ketamine, not an NSAID. The girl was extubated and discharged home within 24 h from the time of exposure.
Discussion: The prescription was confirmed by the compounding pharmacy to contain pregabalin 2.5% (w/v), ketamine 10%, gabapentin 8% and clonidine 0.3%. All these medications have the potential to cause significant CNS depression, though we believe ketamine is the primary culprit as the patient did not experience bradycardia or hypotension. The maximum sedation dose for ketamine is 10 mg/kg, which would be as little as 1 mL of a 10% product for a 10 kg child. Ketamine has a half-life of 2–4 h which explains the relatively short duration of effects. It has a rapid peak plasma level of about 30 min via several routes, although the pharmacokinetics following dermal absorption are not well described. Review of the literature reveals only 1 other case of dermal ketamine absorption causing apnea in a child. Our case had a similar presentation.
Conclusions: Compounded prescription pain creams may contain potent ingredients with the potential to cause rapid onset of apnea requiring airway intervention, even via the dermal route. Non-standard labels may lead to confusion and delayed treatment in unplanned exposures. Dispensing pharmacies should counsel patients regarding safety, and standardized abbreviations of medications would aid poison providers in triage, diagnosis and treatment.

KEYWORDS Dermal; pediatric; ketamine

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73. Rattlesnake envenomation in a patient with Erhlers–Danlos Syndrome

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Background: Ehlers–Danlos Syndrome (EDS) is a heritable connective tissue disorder with multisystem involvement. Easy bruising and bleeding are characteristic of the disorder but coagulation tests are generally normal. EDS type III (hypermobility type) is the least severe type of EDS. Rattlesnake venom in the southwest commonly has hemotoxic and cytotoxic effects; neurotoxic effects are less common. We report here a case of patient with EDS type III with severe envenomation who had neurologic symptoms, hematologic effects, and severe local effects.
Case description: The patient is a 23-year-old female with a history of EDS type III who sustained rattlesnake envenomation to her right (dominant) hand. Initially she had severe swelling, bruising and pallor of the right arm and thrombocytopenia at 8000/μL. Approximately 2.5 h post-envenomation, the patient developed right eye droop and numbness of the right face. She underwent neuroimaging; CT and MRI were normal. She received 36 vials of CroFab during her initial hospitalization due to difficulty with control of arm swelling well as evolving neurologic complaints including R leg numbness and urinary retention. After 6 d in the hospital, she was discharged to a rehabilitation facility. Eight days after envenomation, she had a recurrent thrombocytopenia and received another four vials of CroFab. She had several subsequent presentations for continued nose bleeding, but with no laboratory abnormalities. She had persistent of symptoms of pain, discoloration, numbness, and decreased strength and mobility in her right arm. Two months after the envenomation, MRI showed localized subcutaneous soft tissue fibrosis of the dorsal R hand with underlying diffuse myositis of the first dorsal interosseous muscle. Three months after envenomation, nerve conduction studies were normal but EMG was abnormal suggesting myositis in the extensor carpi radialis longus. Repeat MRI 3.5 months after envenomation was again abnormal. The patient continued with multidisciplinary care with hand surgery, toxicology, rheumatology, occupational therapy, and a geneticist involved. Seven months after her envenomation, she continues to have limitation in the function of her right hand.
Discussion: Both rattlesnake venom and EDS have significant individual variability. It is difficult to determine if this patient's EDS contributed to her complicated clinical course. The tissue fragility and bleeding as well as propensity for chronic musculoskeletal pain associated with EDS may have contributed to the morbidity of this patient's envenomation.
Conclusions: In this case, an underlying collagen vascular disorder may have exacerbated the cyototoxic effects of rattlesnake envenomation.

KEYWORDS Rattlesnake; envenomation; Ehlers–Danlos

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74. Pharmacognosy in 2017: exploring the feasibility of a vitamin K extraction method for management of brodifacoum toxicity

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Background: Brodifacoum is a long-acting anticoagulant rodenticide (LAAR) which causes prolonged morbidity and possible mortality following intentional ingestion. Clinical management of LAAR toxicity requires supportive care including long-term doses of vitamin K_1 (VK) due to rebound coagulopathy after initial

treatment. The oral route is preferred for chronic outpatient VK therapy, although patients must be willing to ingest a large number of pills daily. Other approved routes, such as IV and SQ, are not feasible for outpatient management. Many health insurance plans consider VK a supplement and are unwilling to cover its cost, complicating therapy with financial burden. The amount of vitamin-K rich foods required to supply a therapeutic dose would be extraordinary; an estimated 10–20 lb of kale would have to be consumed daily to meet the VK requirement for a single patient. VK is extremely hydrophobic (logP 9.3) and is therefore extractable with lipophilic solvents. We explored the feasibility of a protocol to prepare a concentrated VK extract from readily-attainable food products for the long-term management of LAAR toxicity.

Methods: A kale and water emulsion was created using a consumer-grade emulsifying blender. To design a potentially patient friendly extraction protocol, constraints were placed on the use of laboratory instruments and kitchen appliances were substituted. Laboratory instruments and techniques were employed only for verification purposes. The emulsion was filtered using unbleached muslin to remove excess liquid while retaining the plant material and VK for further processing. To verify that VK was not lost during filtration, we qualitatively correlated our sample to the external standard, phylloquinone (vitamin K_1), using thin-layer chromatography. We conducted extraction of the plant material with an organic solvent, hexanes, which served as a control substitution for our subsequent transition into edible oils. Evaporation of the organic solvent reduced the size of our sample and allowed us to quantify and verify VK in our sample through High-Performance Liquid Chromatography (HPLC). We compared the HPLC data to the external standard to determine the quantity of VK present in our sample. To validate our method, we used an internal standard, menaquinone (vitamin K_2), which allowed us to determine VK recovery rate in relation to the available literature.

Results: Preliminary results suggest that our protocol can extract 15.5 mcg/g of VK from kale. This coincides with the limited literature on extraction of VK from edible sources conducted via laboratory techniques. In addition, recovery rates of the internal standard have been 80–85%, suggesting that the process is retaining optimal levels of VK. Lastly, HPLC data suggests that the primary extract component found in our samples is VK.

Conclusions: Although further studies are needed to determine the consistency of this method for clinical applicability, initial results support that VK can be extracted and concentrated from kale with consumer kitchen appliances. Hexanes will be replaced with edible oils in subsequent tests. If similar efficiency is observed, this protocol may become a viable option for chronic management of LAAR ingestions.

KEYWORDS Brodifacoum; extraction; antidote

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75. Treating life's bleachable moments: an *ex vivo* examination of ocular damage of splashless versus conventional bleach

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Introduction: Sodium hypochlorite (bleach) exposures are common, especially with low-concentration household products, and are generally considered benign. Among more than 41,000 exposures to bleach reported to Poison Centers in 2015, there were only 31 major outcomes and 3 reported deaths. Accidental splash exposures to the eye are often managed at home with tap water irrigation. Several years ago, a splashless bleach formulation was introduced with a reported concentration of 1–5%. Household bleach was originally sold as a 5–6% sodium hypochlorite solution, but current products are now generally 8.25%. Due to the increased viscosity of the splashless formulation, we propose that despite a lower overall concentration, the inflicted injury could be worse and require more prolonged irrigation than original formulations.

Methods: Three bleach products were compared: "concentrated" 8.25% bleach, "standard" 1–5% bleach, and splashless 1–5% bleach. Sheep eyes were obtained from a local slaughterhouse. Three drops of product were applied to the corneal surface and an initial surface pH was measured. The surface was rinsed with 2 mL tap water every 30 s until the surface pH returned to baseline. A final pH was checked 5 min afterwards and rinsing was re-initiated if pH had increased. Corneal damage was assessed with a Wood's lamp, under both white light and with fluorescein under ultraviolet (UV) light. The primary objective was to determine which bleach product required more rinse cycles. The secondary objective was to compare the extent of corneal damage caused by each product.

Results: Splashless bleach required 4 rinse cycles to return to baseline pH. Concentrated bleach required five rinse cycles and standard bleach required 6 (Table 1). Five minutes following the final rinse, the concentrated and standard products remained at baseline pH, while the splashless product had increased to 6.8, requiring two more rinse cycles to return to baseline. Both standard viscosity products caused limited apparent damage, while the splashless product appeared to cause more diffuse injury to the surface (see photos).

Discussion: We identified several limitations. First, observer bias may have occurred as evaluators were not blinded. Second, pH paper was affected by bleach, rapidly fading to white, and it is unknown to what extent this may have altered results. Third, viscosity differences affected product dispersal on the corneal surface and therefore the measurement of pH was dependent on where the pH paper was placed; the splashless product appeared to spread more evenly across the surface while traditional viscosity products quickly ran down the side of the eye. Finally, *ex vivo* application of fluorescein did not disperse across the surface of the cornea as it does *in vivo* without tear production and blinking to evenly distribute the dye.

Conclusions: This experiment sought to simulate ocular exposures to various bleach products. Although the splashless product had the most rapid initial return to normal pH, it was the only product requiring repeat irrigation, and it also caused the most obvious and diffuse injury to the cornea. Future study is needed to determine the clinical implications of these differences.

KEYWORDS Ocular; bleach; decontamination

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76. A bit too spicy? A fatality associated with intravenous turmeric infusion

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Background: Curcumin, the principal curcuminoid present in turmeric has been touted by the naturopathy community as having

	Splashless Bleach (1-5%) pH 10	Standard Bleach (1-5%) pH 11	Concentrated Bleach (8.25%) pH 9	Control Tap water pH 6
Initial Surface pH	9	11	7.8	6
Rinse 1	8	11	7.6	6.4
Rinse 2	8	9	7.4	6.4
Rinse 3	7	8	7.2	-
Rinse 4	6.2	8	6.4	-
Rinse 5	-	7	6.2	-
Rinse 6	-	6.2	-	-
5 min post	6.8	6.2	6.2	6.4
1	6.2			-
2	6			-
White light	Diffuse haziness	No apparent corneal changes	Patches of haziness	No apparent corneal changes
Fluorescein/ UV light	Diffuse uptake	Small discrete uptake at 2:00	Discrete uptake at 1:00, 3:00, 11:00	No uptake

benefits in the treatment of inflammation and cancer. Due to poor bioavailability, some alternative medicine practitioners have advocated in favor of intravenous administration despite a lack of scientific support. We report the case of a fatality temporally associated with the intravenous administration of turmeric.
Case report: A 30-year-old female with a history of tobacco use, food allergies, and obesity went to her naturopath's office for treatment of her eczema with intravenous turmeric. Minutes after the onset of her infusion, the patient became unresponsive. CPR was initiated by the naturopath, and the patient was given a dose of intramuscular epinephrine. When EMS arrived, the patient was in Pulseless Electrical Activity with a king airway in place. Upon arrival to the emergency department, the patient underwent ACLS and return of spontaneous circulation (ROSC) was obtained. Initial vital signs in the emergency department after ROSC were: temperature 35.8, pulse 130 beats per minute, blood pressure 110/70 mmHg, a respiratory rate 12 breaths per minute, oxygen saturation of 100%. On initial examination, the patient was noted to have dilated pupils, myoclonus, and decerebate posturing. The patient was cooled for 36 h. A CT scan of the patient's brain demonstrated diffuse cerebral edema. After rewarming, the patient had continued decerebate posturing. It was determined the patient would remain in a persistent vegetative state. Care was withdrawn and the patient expired. Antemortem toxicology studies were positive for cannabinoids and diphenhydramine; turmeric or curcumin detection could not be performed. While an investigation by the Food and Drug Administration is ongoing, the cause of death was determined as "severe anoxic injury secondary to cardiac arrest most likely due to turmeric infusion."
Case discussion: While there is evolving *in vivo* data supporting potential health benefits from adjunctive curcumin/turmeric administration, there is currently no published literature demonstrating the safety and efficacy of intravenous infusions of these products in humans. At this time, the exact mechanism of death remains unclear. Given the rapidity of patient decompensation, postulated mechanisms include an anaphyloid reaction, emboli from impurities of turmeric in the intravenous solution, or potential dysrhythmia. The patient's autopsy did not report any evidence of embolic phenomena or anaphylaxis.
Conclusions: Clinicians should be aware of potential health risks from in vogue health practices in the alternative medicine communities. Administering unproven remedies intravenously can expose patients to unnecessary risk and can result in life-threatening effects.

KEYWORDS Turmeric; natural remedies; curcumin

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77. Eye, Ay, Ay! Another laundry detergent pod injury

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Background: Liquid laundry detergent pods (LDP) are small, liquid packets stored in a water-soluble membrane and contain a high concentration of surfactants that effectively remove stains. Since the introduction of LDP's in 2010, exposures in children under 6 years of age continue to rise. Serious adverse sequelae in young children include airway compromise, sedation, seizures, and rarely, death. This study describes ocular exposures involving LDPs among children less than 6 years old.
Methods: Cases were all exposures reported to a statewide poison center system during 2012–2016 involving liquid LDPs in children under 6 years of age. Variables searched included route of exposure, clinical effect, and treatment. Exposures may have involved multiple routes, including oral and ocular exposures. Cases were compared with all substances reported as ocular exposures to the same network. Descriptive statistics were used.
Results: During 2012–2016, there were 5597 total liquid LDP exposures, of which 818 (14.6%) were ocular, and 784 (95.8%) of these had ocular clinical effects reported. During this period, LDP annual ocular exposure cases accounted for 12% in 2012, 13.3% in 2013, 13.5% in 2014, 13.5% in 2015, and 19.1% in 2016. In

comparison, exposures by the ocular route for all substances (not just LDPs) reported to a statewide poison center system constituted 3.2% in 2012, 5.6% in 2013, 7.9% in 2014, 8.3% in 2015, and 11% in 2016. For ocular injuries from all substances, LDP clinical effects represented 4.1% in 2012, 7.4% in 2013, 8.7% in 2014, 9.2% in 2015, and 12.8% in 2016. Accounting for multiple ocular symptoms in the same patient, a total of 1541 ocular clinical effects were reported. Among the most common clinical effects, irritation/pain were 51.2%, red eye 35%, lacrimation 7.3%, corneal abrasion 5%, and ocular burns 1.1%. Treatment was predominantly irrigation (69.4%). There were no reports of globe perforation.
Conclusions: Ocular exposures and associated clinical effects continue to rise yearly despite engineering and advertising efforts by LDP manufacturers. Irritation/pain and eye redness accounted for the majority of symptoms, while corneal abrasions and burns were also seen. Current educational and safety engineering measures are insufficient to prevent these rising ocular exposure cases.

KEYWORDS Ocular injury; laundry detergent pod; cornea

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78. Novel Oral Anticoagulants (NOACs) exposures reported to a poison center network during 2011–2016

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Background: Until 2010, warfarin was the only oral anticoagulant available. NOACs include dabigatran (direct thrombin inhibitor), first introduced in the US in 2010, followed by rivaroxaban, apixaban, and edoxaban (factor Xa inhibitors). The study aim was to characterize NOAC exposures and outcomes reported to a statewide poison center system.
Methods: Cases were all exposures reported to a statewide poison center system during 2011–2016 involving NOACs. Search terms also included four factor prothrombin complex concentrate (PCCC), Kcentra®, idarucizumab, and Praxbind®. Exposures involving NOACs and those followed to a final outcome were included. Cases were compared by selected variables and descriptive analysis.
Results: There were 518 NOAC exposures reported: 336 (64.9%) for rivaroxaban, 179 (34.6%) apixaban, 3 (0.6%) edoxaban, and 0 dabigatran. 15.1% of the exposures were in children less than 5 years, 0.8% 6–12 years, 0.6% unknown age, and 83.6% adults. 56% were females. Exposure reasons included unintentional error 65.6%, unintentional general 18.3%, suspected suicide 8.3%, adverse drug reaction 4.6%, and unknown 3.2%. Exposure site was mostly residential (98.2%). In terms of management, 65.8% were managed on-site, and 33.8% en-route or already at a healthcare facility (HCF). Most patients were treated and released from HCF (45.1%), with 16.6% admitted to a ward, 15.4% to ICU, and 6.3% transferred to psychiatric facility. Most cases (61.7%) were judged as none or minimally toxic and were not followed. Of the 198 followed cases, 64.1% had no effects, 10.1% minor, 20.2% moderate, 3.5% major effects, and 2% death, but unconfirmed if related. Most common clinical effects related to anticoagulation were bleeding miscellaneous 2.5%, PT prolonged 2.3%, coagulopathy 2.3%, hematemesis 0.8%, hematochezia 0.6%, neurological intracranial bleed 0.4%, and ecchymosis 0.2%. Most common treatments performed were oral fluids 13.1%, IV fluids 10.8%, food 8.1%, activated charcoal 7.7%, gastric lavage 0.4%, phytonadione 0.2%. No cases reported using 4-factor PCC, Kcentra, idarucizumab, or Praxbind.
Discussion: The incidence of NOAC exposures continues to rise. Although bleeding is an expected risk, our data suggest that many patients did not have significant clinical effects, and most cases are managed at the exposure site. This may speak to a medication error with 1 or 2 pills or a pediatric exposure with a low dose. Our data are limited by lack of dosing information and lack of treatment specificity.
Conclusions: NOAC exposures are increasingly reported to PCs. Most exposures were managed at home, and even those at HCF had minimal clinical effect and could be discharged home. More information is needed to better determine dosing relationship with clinical effects and outcome.

KEYWORDS Novel oral anticoagulants (NOACs); bleeding; anticoagulants

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79. Severe, early thrombocytopenia with late recurrence following rattlesnake envenomation

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Background: Severe recurrent thrombocytopenia has been reported following rattlesnake envenomations (RSE). The mechanism is not clear, although persistence of venom and immune mediated effects have been hypothesized. Case #1: A 60-year-old man presented 1 h after RSE to his right leg. On arrival, he reported leg numbness progressing centrally. Puncture wounds with localized edema and ataxia were present on examination. Initial laboratory studies revealed platelets 56,000, PT 10.3 s, and fibrinogen 209 mg/dL. He received six vials of CroFab with improvement in the exam. One hour after CroFab, platelets were 148,000 and remained normal for 24 h. About 36 h post-envenomation, platelets down-trended to 100,000. He received two additional vials of CroFab with some improvement in platelets, although fibrinogen fell to 81 mg/dL, prompting additional CroFab. He received a total of 14 vials of CroFab upon discharge. Discharge fibrinogen was 152 mg/dL and platelets were 106,000. About 48 h later, platelets were 7000; PT and fibrinogen were not reportable as the blood never clotted. He denied any bleeding. On re-admission, he received 16 additional vials CroFab and 10 mg intravenous dexamethasone without improvement in thrombocytopenia. His platelets fluctuated between 6 and 25 for the next 6 d (12 d post-envenomation), before slowly improving. Venom levels, targeting *C. atrox* venom, failed to detect any venom during the second admission. Case #2: A 25-year-old man presented 1 h after a RSE to his foot. Edema, ecchymosis, and platelets of 14,000 prompted administration of 4 vials CroFab. Subsequently, platelets were 44,000 and an additional 4 vials were administered. Edema progressed, prompting 6 more vials (platelets 233,000 without coagulopathy). CK initially peaked at 4029 U/L 20 h post-envenomation (platelets 231,000 at that time), then down-trended. 68 h post-envenomation, platelets were 70,000 and CK increased to 8990 IU/L. Platelets continued to down-trend, remaining below 20,000 d 4–10. On day 4, edema and ecchymosis extended into the thorax with a concurrent hemoglobin fall. A foot drop developed, although compartments were soft. CT revealed extensive soft tissue edema but no retroperitoneal hematoma. A leg MRI revealed extensive intramuscular hematoma. PRBCs and platelets were transfused (hemoglobin of

Case #1: : Table summarizing laboratory trends and treatment rendered for case 1

Hours post envenomation	Platelet count (x1000/mL)	PT (seconds)	Fibrinogen (mg/dL)	Antivenom	Miscellaneous treatment
1	56	10.3	209		
3				6 vials	
4	148				
9				2 vials	
10	142				
15	138	11.1	178		
28	148	10.4	185		
42	100	11.4	107		
46	95	11	90		
52				2 vials	
54	105	11.7	81		
58				2 vials	
63	91	11.3	110		
72				2 vials	
74	106	10.1	152		Pt discharged
121	7	No clotting	No clotting		
124	6	No clotting	No clotting	6 vials	
128	12	No clotting	No clotting		
132				6 vials	
134	15	13.7	44		
138	14				
140				4 vials	
143	26	11.3	76		10 mg IV Dexamethasone
161	26	10.8	100		
186	5	10.4	155		
195	12				
209	9	10.3	193		
232	8	9.9	149		
239	16				
256	25	9.9	222		
281	48	10.0	258		
305	74				
430	278	10.6			

Table II: Table summarizing laboratory trends and treatment rendered for case 2

Hours post envenomation	Platelet count (x1000/mL)	Hemoglobin (mg/dL)	Creatinine kinase (U/L)	Antivenom	Miscellaneous treatment
0	14	15.3	157		
1				4 vials	
2	44				
3				4 vials	
5	233	13.2	470	6 vials	
8	235	13.7	1434		
12	237	13.3	3000		
16	247	13.6	3892		
20	231	13.5	4029		
21			3515		
40	175	11.2	3701		
68	70	10.2	8990		
75	27	9.8	9190		
77				6 vials	
80	81	9.2	8990		
83				2 vials	
88	53	8.3	8730		
98	17	7.7	7724		
104	15	7.1	7343		
105				6 vials	
109				4 vials	1 Unit PRBC
112					1 Unit PRBC
116	18	8.1	6705		
118					10 mg IV dexamethasone
121					1 unit plateletpheresis platelets
123					1 unit plateletpheresis platelets
135	11	7.7	2330		
138					1 unit plateletpheresis platelets
162	5	7.5			
165				4 vials	
174	13	7.9			
186	11	7.9			
210	12	8.4			
243	53	10.5			
260	74	9.9			

7.1 [down from initial 15.3] mg/dL with platelets of 15,000). He received 10 mg of dexamethasone on day 5 and platelet transfusion; both failed to significantly improve thrombocytopenia.

Discussion: Severe recurrent thrombocytopenia after RSE remains a perplexing problem. Although several mechanisms have been proposed, the etiology remains unclear. Persistence of venom after clearance of Crofab has been theorized but the lack of response to additional Crofab and the absence of detectable venom levels in case one argue against that mechanism. Immune mediated effects are plausible, however a lack of response to steroids, as seen in both cases, fails to offer support to this theory. More studies are needed.

Conclusions: We present two cases of severe, early recurrent thrombocytopenia. While recurrent thrombocytopenia has been hypothesized to be immune-mediated in neither case did steroids result in a temporal improvement in thrombocytopenia. Case 1 also failed to detect venom during the recurrence.

KEYWORDS Rattlesnake; recurrence; thrombocytopenia

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80. Practice points for prescribing and dispensing colchicine identified from a retrospective review of colchicine calls to a poison control centre

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Objectives: In [location], the number of colchicine prescriptions is increasing. Colchicine has a narrow therapeutic index. Therapeutic errors, drug interactions, and overdose may result in toxicity and death. Calls to the poison control centre were reviewed to determine whether these scenarios affect the morbidity and the mortality of patients in [location], and to reveal important education points for prescribers, pharmacists, and patients.

Methods: A retrospective review of all colchicine exposures reported to the [location] poison control centre from October 2011 to March 2017 was performed. Exposures were classified as

Table 1: Colchicine exposures reported to a regional poison control centre

Scenario Number cases, gender Mean age (range)	Mean dose[1] (range)	Hospitalized	Symptoms[2]/Outcome					
			None[3]	Minor	Mod	Major	Death	Unk[4]
Therapeutic error n = 20, 55% male 65 yr (35-83 yr)	3.41 mg (0.6-10.8 mg)	8 (40%)	2 (10%)	7 (35%)	2 (10%)	3 (15%)	1 (5%)	5 (25%)
Intentional (suicide) n = 12, 33% male 38 yr (12 – 59 yr)	14 mg (1.2 – 34.8 mg) Unknown (n=4)	12 (100%)	4 (33%)		3 (25%)	2 (17%)	2 (17%)	1 (8%)
Unintentional general (pediatric) n = 2, 0% male 20 mo (18-22 mo)	0.6 mg Unknown (n=1)	1 (50%)	1 (50%)					1 (50%)

[1] One time acute dose or dose received in a 24 hour period [2] Symptoms related to colchicine exposure
[3] No symptoms or unrelated symptoms [4] Follow-up not available

Table 2: Colchicine therapeutic errors reported to a regional poison control centre

Scenario Number cases, gender	Mean dose[1] (range)	Hospitalized (%)	Symptoms/Outcome					
			None	Minor	Mod	Major	Death	Unk[2]
Incorrect dose, other[3] n = 9, 56% male	5.5 mg (1.2 – 10.8 mg)	4 (44%)		6 (67%)	2 (22%)	1 (11%)		
Took wrong/others medication n = 4, 0% male	2.85 mg (0.6 – 3.6 mg)	0 (0%)	1 (25%)	1 (25%)				2 (50%)
Took double dose n = 4, 75% male	1.2 mg (1.2 mg)	1[4] (25%)	1[5] (25%)					3 (75%)
Drug interaction n = 3, 100 % male	1.3 mg (1.2 – 1.6 mg)	3 (100%)				2 (67%)	1[6] (33%)	

[1] Daily dose or dose received in a 24 hour period [2] Follow-up not available [3] Prescriber error (n=4); Patient misunderstood instructions (n=5) [4] Referred to hospital because of other medications [5] Unrelated symptoms
[6] Contribution of colchicine to death undetermined

intentional (suicide), unintentional general (pediatric exposure), or therapeutic error. Therapeutic errors were further described to determine recurring scenarios. Outcome was classified as minor, moderate, major, death, or unknown.

Results: There were 35 colchicine exposures (Table 1). One case of adverse drug reaction was excluded. Among intentional overdose patients ($n = 12$), there were two deaths and five patients with moderate or major toxicity; all patients were hospitalized. Among two pediatric exposures, one was hospitalized and remained asymptomatic, the other was managed at home without follow-up. Among therapeutic errors ($n = 20$, Table 2), the scenario with greatest morbidity and mortality was "drug interaction". Two cases of drug interaction with clarithromycin resulted in hospitalization with major symptoms. There was one potential case of drug interaction with tacrolimus, contribution to death undetermined. The scenario "incorrect dose, other" ($n = 9$) resulted in four hospitalizations, two with moderate and one with major symptoms.

Conclusions: Colchicine overdoses and therapeutic errors are associated with significant morbidity and mortality. Intentional overdose with colchicine has a high fatality rate (17%) compared with intentional overdose of any pharmaceutical (0.4%) at our centre. Poison control data can be used to identify practice points for prescribing and dispensing colchicine. An education article was written for the [location] Pharmacy Association journal. Recommendations included

1. Ensure the correct colchicine doses are prescribed based on current lower dosing recommendations, renal/hepatic function and age.
2. Adjust colchicine dosages for drug interactions or choose non-interacting drugs.
3. Ensure the patients understand how to take their colchicine and what their maximum daily dose is.
4. Instruct patients to stop colchicine and call their prescriber or pharmacist if they develop gastrointestinal side effects.
5. Advise patients who take multiple medications to be careful when taking their medications and keep all medications for family members in separate locations.
6. Ensure patients keep all medications out of reach of children.
7. Colchicine should not be readily available to those at risk of suicide.

KEYWORDS Colchicine; interaction; error

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81. Accidental toxicoscordion ingestion by two Native Americans presenting as acute coronary syndrome with QTc prolongation

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Background: Bulbous plants of the genus *Toxicoscordion*, a type of wild onion, can produce emesis, hypotension and bradycardia. Most toxic ingestions are reported in livestock due to the large amount consumed. The plant may be mistaken for edible wild onions by humans. We report two cases of accidental *Toxicoscordion* ingestion. Both presented with chest pain and abnormal electrocardiograms (EKGs), including QTc prolongation, with normal cardiac enzymes.
Case reports: Two patients, a 62 daughter and her 83-year-old mother, ate "wild onions" growing near their home. They both became symptomatic approximately 1 h after ingestion and went to a local emergency department (ED). The younger patient, who had undergone prior coronary artery bypass grafting, presented with nausea, vomiting, left sided-chest pain with radiation to the neck, dyspnea, and lightheadedness. Her initial vital signs revealed a heart rate 57 bpm and blood pressure of 98/47. Her EKG showed a new incomplete right bundle branch block when compared with a prior tracing, a heart rate of 59 bpm, and a prolonged QTc of 522 m. She received aspirin, supplemental oxygen, antiemetics, morphine, and a bolus of IV normal saline. Troponin was negative. Poison Control was contacted and the possibility of *Toxicoscordion* exposure was raised. The patient's family provided a sample of the "wild onions" (see photo). She was transferred to our facility for intensive care. Repeat EKG showed persistent incomplete RBBB; however, the QTc had shortened to 429 with a normal heart rate. Repeat troponin was negative. She was discharged 24 h after the ingestion. The older patient presented with nausea, vomiting, chest pain, headache, neck pain, and abdominal pain. Initial vital signs revealed a heart rate of 55 bpm. EKG demonstrated sinus bradycardia at 47 bpm with diffuse T wave inversions in the inferior, anterior and lateral leads, unchanged from prior studies, and a QTc of 467 ms. She received aspirin, supplemental oxygen, antiemetics, and a bolus of IV normal saline. Troponin was negative. She was transferred to our facility. Repeat EKG was unchanged and troponin remained negative. She was monitored for 48 h from time of ingestion for persistent bradycardia, which progressively became less severe. Both patients responded to IV fluids. Atropine and vasopressors were not needed.
Case discussion: *Toxicoscordion* are highly cardio-toxic plants that can present with signs and symptoms that mimic underlying cardiac pathology and acute coronary syndromes. Thorough history, including plant exposures, may be useful to distinguish plant-induced cardio-toxicity from endogenous cardiac pathology. While QT abnormalities have been reported after ingestion of *Veratrum spp.* which contain veratrum alkaloids, and of *Aconitum* spp., which contain aconite, QT abnormalities have not previously been reported following *Toxicoscordion* ingestions. QT prolongation is likely secondary to the sodium channel activation produced by toxins found in *Toxicoscordion* spp.
Conclusions: It is important for practitioners to be aware of *Toxicoscordion* as a potential mimic for cardiac pathology. QT prolongation is a possible finding, likely secondary to sodium channel effects.

KEYWORDS Toxicoscordion; cardiotoxicity; natural toxins

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82. Protracted QTc interval prolongation resulting in ventricular arrhythmia after administration of intramuscular haloperidol

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Background: QTc prolongation after parenteral administration of antipsychotics has been widely reported and is seen with both typical and atypical antipsychotics. However, limited data exist on the overall duration of the QTc prolongation. We report a patient with a prolonged QTc interval after administration of intramuscular haloperidol who experienced an episode of pulseless polymorphic ventricular tachycardia 23 h after the last dose of haloperidol.
Case report: A 28-year-old male patient with a longstanding history of schizophrenia presented to the emergency department in an agitated state. After attempts at verbal de-escalation failed, he was physically restrained for patient and provider safety and chemically restrained with 10 mg of IM haloperidol and 2 mg of IM lorazepam. Following the administration of haloperidol, the agitation resolved and the patient allowed further examination and assessment including labs and an EKG. The initial EKG showed a heart rate of 81 and a QTc of 474 ms. initial lab work, including electrolytes, glucose, complete blood count, ethanol, creatine kinase, and urine toxicology screening, was negative. Review of the electronic medical record revealed that the patient had previously been on haloperidol depot injection for non-compliance but that his last dose had been greater than 120 d ago. He had presented to the same emergency department 2 d prior with chest pain and had an EKG done then showing a QTc of 459 ms. While he was being observed pending psychiatric consult his telemetry was noted to have changed and on a repeat EKG his QTc was now 528 ms. He was admitted to telemetry, received no further QT prolonging agents, and over the next 16 h had continued QTc prolongation to 610 ms. He developed polymorphic VT and required several rounds of cardioversion, magnesium, and isoproterenol. His QTc ultimately returned to baseline after 36 h. Upon review of his chart, there were no other QT prolonging agents in his medication list, he had normal electrolytes including magnesium, and he had had several prior EKG's in the system, none of which demonstrated QT prolongation.
Discussion: We present the case of a patient with protracted and severe QTc prolongation after receiving IM haloperidol. While we cannot exclude administration of another QT prolonging agent prior to his arrival in our department, his initial QTc was normal. Routine monitoring of cardiac rhythm for a period after administration of a QT-prolonging agent should be considered.

KEYWORDS QTc prolongation; haloperidol; adverse drug event

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83. Digital intoxication by natura products for weight loss: a report of four cases by Thevetia Peruviana

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Introduction: Although herbal products are often considered safe for weight loss, some of them may pose significant health risks. Thevetia Peruviana, known as yellow oleander contain cardiotoxic glycosides (neriifolina, peruvoside, ruvoside, thevetoxin, thevetina A and B) which may cause gastrointestinal and cardiac symptoms such as headache, nausea, vomit, diarrhea, dysrhythmias, and disturbances in the conduction system of the heart as a result of a blockade in the Na+/K+ ATPase pump and inhibition of sympathetic outflow by antiadrenergic effects with an increase in vagal tone. The diagnosis can be obtained by history of intake, clinical and/or electrocardiographic manifestations and serum levels of digoxin. The specific treatment is with antidigoxin Fab fragments. Moreover, atropine, crystalloids, vasoactive amines and multiple doses of activated charcoal may be really effective.
Case reports: (1) A 22-year-old female with a three-week intake of yellow oleander nuts (Thevetia peruviana), who arrived to the hospital with palpitations and anxiety. In the emergency room (ER) she had a heart rate (HR) of 30 bpm, electrocardiogram (EKG) with Mobitz I, 2nd grade AV block and serum concentration of digoxin (SCD) 0.68 ng/mL. She was treated with atropine, intravenous (IV) fluids and gastrointestinal dialysis (GI dialysis). She was admitted for electrocardiographic monitoring until the resolution. (2) A 29-year-old woman, who received yellow oleander nuts for 2 d, presented dyspnea and dizziness. In the ER she had a HR of 40 bpm, BP 90/50, EKG: First degree AV block, (PR 210mseg), ST segment depression and SDC 0.54 ng/mL. She was treated with atropine and GI dialysis. She was monitored until the resolution. (3) A 18-years-old woman arrived to the hospital with a history of ingestion of five portions of yellow oleander nuts. She developed nausea, hypotension (BP 90/50), Bradycardia (HR 40 bpm), and drowsiness. SDC: 1.3 ng/mL. She was treated with atropine, GI dialysis, and IV fluids until resolution. (4) A 30-year-old female swallowed a handful of yellow oleander nuts, developing nausea, vomit, and dizziness. She was transferred 5 h later to the hospital when she lost consciousness, however, when she arrived at the hospital, he presented a cardiac arrest without response to resuscitation maneuvers. SDC were not obtained.
Conclusions: The readily accessibility to dietary supplements for most people, plus no regulation of the usage of supplements and the lack of awareness of the toxic effects may be factors that contribute to this type of poisoning occur.

KEYWORDS Digital intoxication; natural products; cardiotoxic glycosides

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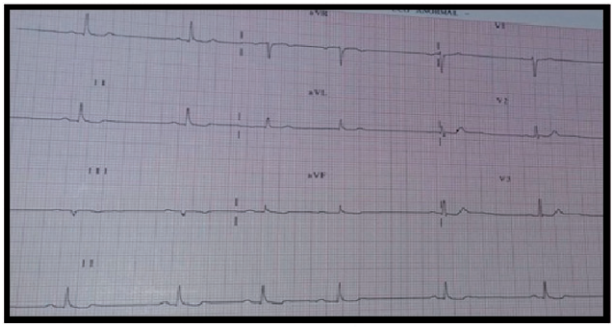

84. Inhibiting apical and basolateral transporters decreases uptake of diglycolic acid in human proximal tubule cells: an *in-vitro* analysis of transport characteristics of the toxic metabolite of diethylene glycol

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Background: Diethylene glycol (DEG) is an industrial solvent and the ingestion of pharmaceutical preparations adulterated with DEG has resulted in mass poisonings worldwide. The hallmark sign of DEG toxicity is acute kidney injury as a result of proximal tubular necrosis. Diglycolic acid (DGA) is one of two primary metabolites of DEG and recent studies have shown that DGA is the metabolite responsible for the proximal tubule damage observed in DEG poisonings. DGA is a dicarboxylic acid, with a similar structure to several TCA cycle intermediates, including succinate. It is possible that DGA is being taken up into the proximal tubule via the same sodium dicarboxylate cotransport (NaDC) mechanism as this TCA cycle substrate, where it then exerts its toxic effects. Therefore, we hypothesize that DGA is taken up into the proximal tubule cells of the kidney via a NaDC mechanism.
Methods: To test this hypothesis, we analyzed the uptake of both succinate and DGA in the presence of apical (NaDC-1) and basolateral (NaDC-3) inhibitors, anthranilic acid (ACA) and 2,3-dimethyl succinate (2,3-DMS), respectively. Primary human proximal tubule cells (HPT) were cultured until confluent, then subcultured onto membrane inserts, allowing for distinct apical and basolateral uptake. Cells were treated with ^{14}C-substrate at increasing subtoxic concentrations from apical and basolateral interfaces, with and without inhibitors. Cells were then rinsed and processed via scintillation counts to measure uptake. We also analyzed the efflux of ^{14}C-succinate and ^{14}C-DGA from pre-loaded HPT cells.
Results: Apical ACA, as well as apical ACA and basolateral 2,3-DMS, significantly decreased uptake of succinate-the primary endogenous substrate of NaDC-1. Similarly, application of bi-directional NaDC inhibitors significantly decreased DGA uptake. Neither DGA nor succinate was significantly effluxed from cells.
Conclusions: These results suggest that DGA is taken up into proximal tubule cells via the sodium dicarboxylate co-transport mechanism, but that very little DGA is effluxed out of these cells. This likely mechanism of uptake gives rise to a potential target area in the effort to develop antidotal therapy.

KEYWORDS Diethylene glycol; renal toxicity; dicarboxylate transporters

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85. To Ingest or Inject? A report of oral ingestion of risperidone long-acting injection

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Background: Risperidone is an atypical antipsychotic that acts as an antagonist at both the D_2 and $5HT_2$ receptors. It has potent

alpha$_1$-adrenergic antagonism and binds to histamine and alpha$_2$ adrenergic receptors with lower affinity. Risperidone long-acting injection (RLAI) with microspheres is a newer depot formulation that is administered every 2–3 weeks intramuscularly (IM). Pharmacokinetics of this new formulation when given by injection are described but it is not clear if and how this formulation would change oral pharmacokinetics. We describe a case of a woman who ingested risperidone long-acting injection with microspheres.
Case report: A 65-year-old woman with a history of depression, insomnia, and schizoaffective disorder recently initiated on risperidone microspheres IM every 2 weeks ingested her 50 mg RLAI dose after experiencing a 2-week delay in her scheduled injection. She reports mixing it with water prior to ingestion. Her home health nurse called the local poison control system who recommended healthcare evaluation. On arrival to the emergency department, the patient endorsed dizziness and weakness. She also noted a 2-d history of diarrhea with one emesis prior to the ingestion. She denied co-ingestion, which was corroborated by prescription medication pill counts. Vital signs were BP 97/65 mmHg (nadir BP 87/49 mmHg), pulse 93, temp 36.3 °C, respiratory rate 16 bpm, and normal oxygen saturation. On physical examination, she appeared tired and nauseous, pupils 2mm, sluggishly reactive without nystagmus, and orientat only to person. No tremor, abnormal tone, or hyper-reflexia was present. Initial laboratory evaluation revealed sodium 126 mEq/L and creatinine 1.56 mg/dL. EKG demonstrated normal QRS and QTc intervals. She received normal saline overnight. Repeat creatinine and sodium were in the normal range the following day and the patient was more alert. Risperidone serum concentration on admission (20 h post-ingestion) was 4.8 ng/mL with 28.3 ng/mL of 9-hydroxy risperidone for a combined total as expected for steady state therapeutic dosing. Nineteen hours later, risperidone combined total was 22.4 ng/mL. She was discharged to home and resumed her home injection schedule one week later.
Case discussion: Risperidone long-acting injection is an extended-release formulation of risperidone encapsulated in polyglactin. Both the parent drug and primary metabolite, 9-hydroxy risperidone, are active. Following injection, there is a small initial release of the drug with increased rate of release at 3 weeks and decrease by week 7. Once the microspheres are broken down, the absorption is presumed to be complete. Microspheres are hydrolyzed in water to lactic and glycolic acid; breakdown is enhanced by acidic environments, such as gastric fluid. When injected every 2 weeks, the trough total risperidone is between 9.9 and 19.2 ng/mL and peak 17.9–45.5 ng/mL. The patient's blood drug concentration should have been closer to trough for her injectable form since she was about 4 weeks out from her last injection, but was therapeutic.
Conclusions: Ingestion of risperidone long acting injection does not lead to supratherapeutic drug concentrations days following exposure.

KEYWORDS Antipsychotic; pharmacokinetics; risperidone

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86. Bradycardia and hypotension post Divya Swasari Ras ingestion

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Background: Divya Swasari Ras (DSR) is a popular Ayurvedic medicine used to treat asthma and bronchitis. As per the package information, over 10 different herbal ingredients are jointly used to alleviate various respiratory symptoms. Suggested dosing is 0.5–1 mg either twice or three times per day. Currently, there is no published clinical toxicology literature on this medicine.
Case report: A 50-year-old male previously known for depression and insomnia, presented to our Emergency Room with a history of feeling weak and dizzy after taking 10g of DSR (over 10 times the recommended dose). He denied suicidality and believed this was the standard dose. His initial blood pressure (BP) was 90/55 mmHg and heart rate (HR) was 52 beats per minute. His respiratory rate, temperature and pulse oximetry were normal. The patient's HR rose to 68 after receiving a dose of Atropine 0.5 mg; however, within 1 h became symptomatic requiring a second dose of Atropine 0.5mg. Despite 3L of normal saline (NS), two doses of Atropine 0.5mg IV and four doses of glycopyrrolate 0.4mg IV given over 18 h, the patient's clinical status remained unchanged. Laboratory values resulted a normal potassium (4.4 nmol/L) and negative serial high sensitivity troponins. A Digoxin concentration measured at 18–20 h post-ingestion of the DSR was 0.4 nmol/L (normal range: 1.0–2.6 nmol/L). The patient denied taking any Digoxin. Two ampules of antidigitalis antibody fragments were administered with complete normalization of BP and HR within 75 min as well as sustained resolution of clinical symptoms. After an additional period of observation of 5 h, the patient was discharged home with no symptoms.
Case discussion: This patient presented with bradycardia and hypotension following an overdose of DSR. We suspect that this compound contains a herbal cardiac glycoside which resulted in classic digoxin toxicity symptoms. Cross reactivity with digoxin assay is possible and was useful in this case to prompt antidotal treatment. Natural occurring cardiac glycosides are well documented; however, there is no previous literature suggesting cardiac glycosides in DSR. A literature search for each of the 15 ingredients contained in DSR could not find any report of toxicity.
Conclusions: Complementary medicine can contain unstudied cardiac glycosides which may produce classic signs of digoxin toxicity. Recognition of the toxicity pattern of cardiac glycosides and use of antidigitalis antibody fragments resulted in prompt clinical improvement and likely prevented further cardiology investigations and admission.

KEYWORDS Anti-digitalic antibodies; antidote; natural cardiac glycoside

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87. Accuracy of estimated amount ingested during accidental unsupervised ingestions involving acetaminophen

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Background: Product safety interventions have been implemented to target pediatric accidental unsupervised ingestions (AUIs) of acetaminophen. A surveillance study was launched to measure the impact of interventions by comparing amounts ingested in the presence or absence of product safety interventions. The objective of this analysis is to understand the accuracy of reported amount ingested of single ingredient acetaminophen using a predictive pharmacokinetic (PK) model as a reference.
Methods: Reported amount ingested was extracted from AUI records involving children aged <12 years reported between 1

August 2013 and 31 January 16 at six participating US poison centers. AUIs were eligible if they involved one single ingredient acetaminophen product, had a known 4-h serum acetaminophen concentration (SAC), and did not receive decontamination (activated charcoal, *n*-acetylcysteine) or vomit prior to the SAC. SACs were compared with predicted values calculated from the Edward's PK model modified for pediatric absorption and elimination rates. The ratio of SAC to predicted values were calculated for liquid and solids separately due to absorption differences. A SAC that is lower than the predicted level (<100%) suggests the amount ingested was overestimated, while a SAC that is greater than the predicted level (>100%) suggests the amount ingested was underestimated. SACs between 80 and 120% (±20%) of the predicted value were considered on target.
Results: Eighty-one AUI cases were evaluable (61 (75%) liquids; 20 (25%) solids). The Figure displays frequency of cases by the ratio of SAC to predicted value by liquids and solids. Six (10%) liquid cases and three (15%) solid cases had an SAC within the target range (within ±20%). About 72% ($n = 44$) of liquid cases involved a SAC that was less than the target range. Of the 11 (18%) cases with a SAC greater than the target range, most ($n = 7$, 64%) were <160% of the predicted value, but four (36%) involved SACs that were >180% of the predicted value. About 70% ($n = 14$) of solid cases had a SAC below the target range and 3 (15%) had a SAC that was greater than the predicted value.
Conclusions: Pediatric exposures to acetaminophen are managed by estimating the amount involved. This study shows that most reported amounts are conservative overestimates, but underestimates occurred in 20–25%. This may be due to inaccurate report of amount ingested or time of ingestion. Poison center exposure information, including amount ingested, provides value in evaluating product and patient safety.
Figure. Distribution of measured to predicted SACs

KEYWORDS Accuracy; acetaminophen reported dose; accidental unsupervised ingestion

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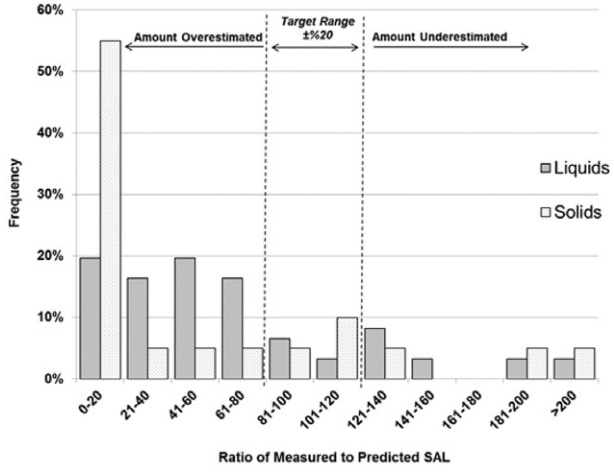

Figure. Distribution of measured to predicted SACs

88. Fatal myocardial infarction after inhalational cannabis use

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Background: Cannabis use has been shown to increase heart rate and cardiac output and precipitate ventricular dysrhythmias, with reported increased risk of myocardial infarction (MI) even in cases of young users with no pre-existing coronary artery disease. We report a case of fatal MI following vaping of concentrated cannabis product.
Case report: A 70-year-old male with no known chronic medical conditions and remote marijuana use (pipe smoking of loose leaf plant material several decades previously) presented to the Emergency Department (ED) in cardiac arrest. The patient had been admitted to the hospital 1 week prior to his arrest with chest pain and exertional dyspnea, and was found to have anemia due to a bleeding duodenal ulcer attributed to non-steroidal anti-inflammatory drug (NSAID) use for headaches. He had a non-ischemic electrocardiogram and negative serial troponin measurements during that admission, with resolution of his dyspnea and chest pain following blood transfusion. The patient was counseled on cessation of NSAID use, so he instead purchased a concentrated cannabis concentrate product (Jack Herer Cannabis Extract, THC 64.75%, CBD 1.24%), which he tried several times following hospital discharge (approximately 1–2 hits each use) for persistent headache. On the day of his ED presentation, the patient took five hits in rapid succession from his vaporizer, as witnessed by his wife. He then had a presyncopal event and lowered himself to the floor; he denied chest pain at that time. The patient's wife called an ambulance, and paramedics found him with agonal respirations and wide-complex tachycardia. The patient received cardiopulmonary resuscitation (CPR), 4 defibrillations, 4–5 doses of epinephrine, one dose of amiodarone, and was intubated. On arrival to the ED, patient was noted to have pulseless electrical cardiac activity (PEA) and received an additional dose of epinephrine with return of spontaneous circulation. An electrocardiogram suggested acute ST-elevation myocardial infarction, although consideration of cardiac catheterization was complicated by the patient's acidemia (venous blood gas 6.9) and prolonged resuscitation. The patient continued to deteriorate throughout his ED course, demonstrating persistent PEA and requiring multiple additional rounds of CPR, epinephrine, dopamine, norepinerphrine, amiodarone, and defibrillation (for one episode of torsades de pointes captured on telemetry). Following discussion with the patient's family, the decision was made to terminate the resuscitation. Autopsy revealed acute myocardial infarction of the anterior left ventricular wall, acute thrombosis of the left anterior descending artery, near complete occlusion of the right coronary artery, and atherosclerotic disease of multiple coronary arteries.
Discussion: Acute cardiovascular and cerebrovascular events following inhalational cannabis use have been reported but remain rare. This patient, with previously unrecognized critical atherosclerotic coronary artery lesions, suffered a fatal MI that was temporally associated with and putatively precipitated by inhalational cannabis use. With the increased number of US states in which medical and recreational cannabis use is allowed, an increased prevalence of such use may be expected. As such, providers should be aware of the cardiovascular risks of inhalational cannabis use and the implications for users who may otherwise be at risk of coronary artery disease.

KEYWORDS Cannabis; fatal; infarction

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89. Almendra Quema Grasa (fat burning almond) cardiac glycoside death from weight loss supplement

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Background: We present a fatal case following weight loss supplement from Mexico, *Almendra Quema Grasa*, translated as "Fat Burning Almond" contains cardiac glycosides from *Thevetia peruviana*.
Case report: A 33-year-old female with negative past medical history presented to emergency department (ED) by ambulance after ingesting a whole single nut of *Almendra Quema Grasa* as a fat loss supplement. She was instructed to only ingest "1/32 of the seed" but unclear as to why took larger dose. On arrival, she was lethargic, pulse 45 bpm, 111/73 mmHg, respiratory rate 18 bpm. Initial EKG showed atrial fibrillation at 36 bpm with QRS 146 ms. Atropine 0.5 mg given with pulse increase 64 but BP declined 92/71 mmgHg. Poison control was contacted and recommended 10 vials digoxin-specific Fab (Digifab). Pharmacy was immediately contacted for Digifab. She lost pulses and CPR began and was intubated. Chemistry showed sodium 134 mEq/L, potassium 8.9 mEq/L, chloride 102 mEq/L, bicarbonate 18 mEq/L, calcium 10 mEq/L, glucose 223 mg/dL, BUN/SCr 7 mg/dL and 1.11 mg/dL. Pharmacy had 3 Digifab vials immediately available. Unfortunately, saline lock infiltrated with initial vial. Subsequent, two vials successfully administered through different saline lock. She showed no improvement following Digifab and CPR continued. Epinephrine 1 mg, calcium chloride 1 g, sodium bicarbonate 50 mEq, D50W and 10 units of regular insulin given intravenously with return of spontaneous circulation (ROSC), QRS narrowed with organized bradycardiac rhythm. A technician went to another hospital for more Digifab. One hour after Digifab she lost pulses, CPR was resumed. Epinephrine 1 mg and calcium chloride 1 g given without any benefit. 35 min after loss of pulses two more vials of Digifab arrived from outside hospital and were given with ROSC. Although palpable pulses present, blood pressure could not be measured and norepinephrine infusion started. About 55 min after repeat Digifab patient again lost pulses. At that time 5 more vials Digifab just arrived from other outside hospital and given with CPR and additional doses of epinephrine. Patient could not be resuscitated and expired 3 h after arrival to ED.
Case discussion: Yellow oleander (*Thevetia peruviana*) is a common ornamental tree in various parts of the world. There have been large numbers of unintentional and intentional deaths in parts of Asia from ingestion of the seeds. In North America, the use of *Almendra Quema Grasa* seeds as a weight loss supplement has been a cause of toxicity. Clinicallypresents similarly to other cardiac glycoside poisoning including digoxin. Though this patient had measurable serum digoxin concentration this does not correlate with interpretable levels. This patient had aggressive resuscitation efforts and ultimately received nine total Digifab vials over 3 h. It is unknown how effective standard doses of Digifab are for *Almendra Quema Grasa* poisoning as affinity would not be expected to same as for digoxin. This patient had severely elevated potassium concentration on arrival signifying severe poisoning.
Conclusions: Clinicians should be aware of *Almendra Quema Grasa* availability including the Internet, and treat as cardiac glycoside poisoning with Digifab along with supportive measures.

KEYWORDS Cardiac glycoside; Almendra Quema Grasa; Thevetia peruviana

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90. Adverse events observed in patients treated for acetaminophen ingestion with the one-bag method of *N*-acetylcysteine

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Background: *N*-Acetylcysteine (NAC) is the antidote for Acetaminophen ingestion. The labeled instructions include a complex three-bag method for loading and maintenance dosing. Its complexity leads to frequent confusion and incorrect dosing. For over a decade, we have used a simplified one-bag approach: 150 mg/kg loading dose followed by 12.5 mg/kg/h maintenance infusion with a uniform concentration of 30 mg/mL.
Objectives: This retrospective chart review evaluates the frequency of adverse events of the one-bag NAC dosing.
Methods: We reviewed all charts of adult patients presenting with a potentially toxic Acetaminophen ingestion treated with NAC from 1/12/2005 through 6/20/2016. Patients received NAC at the discretion of the treating physician or the toxicology service. We used pharmacy records to identify patients receiving NAC. We excluded patients receiving NAC for reason other than acetaminophen ingestions and patients less than 18 years of age. We reviewed pharmacy records, nursing notes, and progress notes and extracted data for adverse events, including nausea, anaphylactoid reactions, and anaphylaxis.
Results: We identified 196 patients who received NAC. We excluded 37 who had NAC started at an outside hospital or were not treated for Acetaminophen ingestion, leaving 159 patients. Out of 159 patients, 52 had an adverse event (32.7%, 95% CI 25.6–40.65%). Forty-five patients reported nausea (28.3%, 95% CI 21.59–36.08%). Excluding nausea, only seven patients experienced adverse events (4.4%, 95% CI 1.94–9.21). Of these seven, five developed a rash (3.14%, 95% CI 1.16–7.56), one of whom also reported pruritus and another reported shortness of breath. The patient with rash and shortness of breath received diphenhydramine, epinephrine, albuterol and steroids. His repeat Acetaminophen concentration was undetectable, his NAC was stopped, and he had complete resolution of symptoms. One additional patient reported only pruritus (1.26%, 95% CI 0.22–4.94), and one additional patient reported nausea and shortness of breath (1.26%, 95% CI 0.22–4.94). NAC was stopped or decreased in five patients (3.14%, 95% CI 1.16–7.56).
Conclusions: The one-bag method was safe and well tolerated by patients, and resulted in relatively few adverse events when compared with published data for the three-bag and two-bag method.

KEYWORDS Acetylcysteine; adverse events; acetaminophen

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91. A case in point: serum ethanol concentration is an ideal surrogate for methanol concentration when co-ingested in a fixed ratio

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Background: Methanol is a well-known toxic alcohol used in many household and industrial solutions. Human metabolism of methanol produces formic acid resulting in metabolic acidosis, neurotoxicity, blindness, and death in poisoning. Small doses easily achieved with accidental ingestions are potentially toxic and require timely evaluation and treatment. Weight-based calculations of dosage and predicted serum concentration are more readily available than analytic measure of serum methanol at most institutions and in the home setting. Direct measure of acid base status, calculation of anion gap, serum osmolality are readily available but imperfect surrogates for toxicity. This is a case of accidental ingestion of a fixed solution of ethanol and methanol where the use of ethanol as a surrogate for serum methanol concentration proved accurate and useful.
Case report: A 76-year-old female called the poison center after accidentally ingesting Sunnyside™ marine stove fuel by accident. She reported drinking approximately 30 mL of the solution, which had been placed in a glass in preparation for refueling a lamp. She called the poison center and was referred immediately to the nearest emergency department. She reported spontaneous emesis en route. Upon arrival to the emergency department, 30 min post-ingestion, she was asymptomatic and had normal vitals. The product was available and manufacturer's specifications showed a 49% ethanol and 50% methanol concentration. She was given 15 mg/kg of fomepizole and a volatile screen was sent to an outside laboratory. Then toxicology was consulted and recommended a serum ethanol concentration, which resulted at 15 mg/dL (drawn 1 h post-ingestion). Concentration = (specific gravity × bioavailability × dose)/(volume of distribution × weight) describes the relationship between ingested dosage and resulting concentration. A predicted ingestion was approximately 5 g or 6.4 ml of ethanol, making a total ingestion of 12.9 mL of solution and 6.5 mL of methanol. A serum methanol concentration of approximately 15.5 mg/dL was predicted. The patient was discharged with telephone follow up. Serum methanol resulted 24 h later at 16 mg/dL consistent with the predicted value.
Discussion: Patient management and disposition is often limited by the availability of toxic alcohol concentrations; however, in cases where a fixed solution is ingested, alternate analytes may prove useful. Given the similar pharmacokinetics of ethanol and methanol in absorption, bioavailability, and physical properties, ethanol is an ideal surrogate marker when co-ingested in a known ratio.
Conclusions: Ethanol is not uncommonly found in solutions with other alcohols and should be considered as a surrogate marker for calculating other potentially toxic alcohol concentrations whenever possible.

KEYWORDS Methanol; surrogate markers; toxic alcohols

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92. This redneck is dangerous: case report of African red spitting cobra envenomation in the US

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Background: The World Health Organization has estimated that, globally, 5 million people are bitten by snakes, 300,000 are permanently disabled, and 100,000 die each year. Snake hobbyists and collectors bring a large number of hazardous non-native, venomous snakes into the US. Healthcare providers may be uncomfortable with proper care of exotic snake envenomation and may be unaware of availability of antivenom resources. We provide a report of a teenager bitten by an African red spitting cobra.
Case report: A 16-year-old amateur herpetologist, keeping snakes including the Gaboon viper, desert horned viper, long-nosed viper, western diamondback rattlesnake, and cottonmouth water moccasin, was bitten on the fifth digit of his left hand by his African red spitting cobra (*Naja pallida*) while cleaning its cage. Over the next few hours he developed progressive erythema, edema, and pain. He denied systemic symptoms, and his initial hematological tests were unremarkable. Due to progressive edema and the tense-confined space of his digit, as well as the progressive proximal spread, he was treated with three vials of SAIMR polyvalent antivenom obtained on emergency loan from the local zoo. Over the ensuing 12 h his prothrombin time rose from 14.4s to 18.3s, his serum D-dimer rose from <0.27 to 3.63 mcg/mL FEU, his blood platelet count dropped from 176 to 102 K/mcL, and his serum albumin declined. He was given an additional two vials of antivenom, envenomation control was achieved, and he was discharged on hospital day #3. He recovered to nearly full function by 3 weeks from envenomation. No complications of antivenom therapy were noted.
Case discussion: Recent analyses of U.S. poison center data find that approximately 2% of reported pediatric snake envenomation victims are bitten by non-native, exotic snakes. African red spitting cobra bites are rarely encountered within the US. The venom of this snake has been described as primarily cytotoxic and can cause dramatic soft tissue injury with "skip lesions." Coagulopathic hemotoxicity, post-synaptic paralytic toxicity, and cardiotoxicity have also been described. This patient demonstrated significant local tissue injury and mild coagulopathy. He was treated with a foreign-made antivenom, not evaluated by the US FDA, and he recovered. His envenomation care was provided by a collaborative team approach that included zoo experts, poison control center specialists, and several medical consultants.
Conclusions: This case report adds to the collective clinical experience of *Naja pallida* envenomation and may help to inform future determinations of prognosis and care. It also adds to US experience with use of the SAIMR polyvalent antivenom. The value of the collaborative team model of snakebite care is emphasized, as is the importance of zoo – poison center partnerships in delivery of exotic antivenom.

KEYWORDS Envenomation; cobra; antivenom

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93. Invokana loving the numbers

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Background: There are many new oral agents available to improve glycemic control in adults with type 2 diabetes mellitus (T2D). These anti-diabetic medications encompass a variety of mechanisms of action. A newer medication, Invokana® (canagliflozin), inhibits the sodium-glucose cotransporter 2 (SGLT2) in the proximal renal tubules. This mechanism is responsible for most renal reabsorption of filtered glucose. Inhibition of SGLT2 decreases reabsorption of filtered glucose and lowers the renal threshold for glucose; thus urinary glucose excretion is increased. The package insert warns of dehydration, renal impairment and

hypoglycemia when used in combination with insulin or an insulin secretagogue. The maximum recommended therapeutic dose is 300 mg. Overdose has not been reported. We report a case of 1500 mg ingestion with no adverse effects. Elimination half-life is dependent on dose and reported to range from 10 to 13 h.

Case report: A 63-year-old female with T2D, with maintained renal function (plasma creatinine of 0.62 mg/dL one month earlier), accidentally took four Canaglifllozin 300 mg about 4am, thinking that she was taking her nighttime dose of Metformin 500mg tablets. Pt had correctly taken one other Canaglifllozin 300mg tablet the morning before, making her 24 h total intake of Canaglifllozin 1500 mg. Patient's prescriptions included: Canaglifllozin 300mg Qam, Sitagliptin phosphate 100mg Qam, Metformin 2000mg Qpm, Glimepiride 2mg Qpm, as well as aspirin 81 mg Qday, Simvastatin 40 mg Qday, Probiotic, Calcium supplement, and eye drops (Brinzolamide, Timolol, Bimatoprost). Her fingerstick glucose was 113 and 160 mg/dL over a 1-h period at the time of the PC call. She was cautioned to monitor her urine output, maintain hydration, and montior her blood glucose every 4–6 h. She was asked to hold her Glimepiride dose that evening, and decrease the evening's Metformin dose by half as a precautionary step should she develop renal dysfunction. In follow-up, we learned that the patient's endocrinologist held her Canaglifllozin for the next three days; the patient chose to hold her Sitagliptin for one day as well. Forty-eight hour follow up revealed that the patient was able to maintain a blood glucose level between 99 and 254 mg/dL (four measurements). The patient did not note any increase in urine output; studies from the day after ingestion showed normal renal function. Pt remained asymptomatic.

Case discussion: This patient was very involved in her own care and diabetic management. While the risk for this drug is related to dehydration from osmotic diuresis and secondary renal dysfunction, that risk is highly dependent on circulating glucose concentrations, oral intake, and renal function. Monitoring of urine output, adjustment of fluid replacement, and close monitoring of capillary glucose is indicated. Complicating features in this case include the concurrent use of insulin secretogogues and biguanides, as well as eye drops containing beta-blockers, prostaglandins, and carbonic anhydrase inhibitors.

Conclusions: An accidental ingestion of four times the maximum recommended daily dose of Canaglifllozin, in the presence of three other oral hypoglycemic agents, produced no adverse clinical effects in a diabetic patient with good renal function.

KEYWORDS Invokana; oral hypoglycemic; therapeutic error

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94. Patterns and correlates of antidote use reported to the poison centers, 2011–2016

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Background: Numerous antidotes are used to treat poisonings. The poison center role in the decision to administer specific antidotes is unclear. The objective of this study is to delineate the epidemiology of antidotes that are being reported to the Poison Centers (PCs) across the US and to determine which antidotes are being administered with and without poison center recommendations.

Methods: The National Poison Data System (NPDS) is the national surveillance database collecting data from PCs across the US. All closed, human exposure cases reported to the NPDS for the use of the common antidotes were retrospectively collected from 1 January 2011 to 31 December 2016. Trends in the reports of these antidotes were examined using the Annual Percent Change (APC) for the study period. The proportions of calls where the individual antidotes were recommended, performed, or both recommended and performed were compared during the study period. Demographic and clinical characteristics including age, gender and medical outcomes were descriptively assessed.

Results: During the study period, there were 367,375 reports of the 25 antidotes analyzed. Among these antidotes, 14 antidotes demonstrated a significant decrease in reports, while 11 demonstrated an increase. The greatest decrease in reports from 2011 to 2016 was observed for EDTA (58 versus 23 reports, APC $= -12.1\%$), followed by amyl nitrite (9 versus 4, APC $= -11.1\%$) and oral *n*-acetyl cysteine (8902 versus 4292, APC $= -10.4\%$). The use of physostigmine (298 versus 566, APC $= 17.9\%$), 2-PAM (94 to 166, APC $= 15.3\%$), and hydroxocobalamin (79 versus 136, APC $= 14.4\%$) demonstrated significant increases during the study period. Among total calls for the individual antidotes, the highest proportion of "performed, not recommended" reports were flumazenil ($n = 9942$, 85.9%) and naloxone ($n = 106{,}125$, 77.4%). In contrast, nalmefene ($n = 20$, 14.8%) and physostigmine ($n = 243$, 9.7%) demonstrated the highest rates of "recommended, known not performed" reports among the total calls for each antidote. Antidotes that were most commonly "recommended and performed", included fomepizole ($n = 8365$, 60.6%) and EDTA ($n = 146$, 55.7%). Antidotes were reported most commonly in females (56.9%), children and young people under 19 years of age (21.5%). In the majority of cases where the antidotes under consideration were used, the exposure site was noted as residence (90.3%) and the patient was admitted to the critical care unit (50.8%). Overall, moderate clinical effects (44.8%) were usually associated with the reports of these antidotes, while death was relatively uncommon (1.5%). A high percentage of cases were intentional exposures (78.5%) with ingestion being the most common route of exposure (88.4%).

Conclusions: This study demonstrated significant differences in the patterns of the antidotes that are being reported to PCs, with some therapies being mainly performed without poison center recommendation, others are being recommended but not performed, and some are consistently being recommended and performed.

KEYWORDS Antidotes; trends; epidemiology

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95. Analytically confirmed severe albenzadole overdose presenting with alopecia and pancytopenia

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Background: Internet-facilitated self-diagnosis and treatment is becoming more prevalent. When individuals acquire drugs without medical oversight they risk adverse events or toxicity.

We report a patient with delusional parasitosis who purchased veterinary albendazole on the internet leading to pancytopenia and alopecia.

Case: A 53-year-old man was sent to the emergency department (ED) by his gastroenterologist due to abnormal lab results. He had known cirrhosis of the liver and used opioids, cocaine and alcohol. His only prescribed medication was buprenorphine/naltrexone. The patient stated he has chronic abdominal pain and has had multiple investigations all reported as normal. He believed he was infected with parasites years ago when he was a sewer worker. He researched treatment options for parasitic infections and subsequently purchased two bottles (500 mL each) of veterinary grade albendazole (56.8 g/500 mL) on the internet. Over the three weeks prior to his ED visit he consumed 113.6g of albendazole (5.4 g/day); a typical therapeutic dose is 400 mg BID. Five days prior to admission he began to notice hair loss and a rash on his face. Presentation vital signs were: BP, 112/72 mmHg; HR, 82/min; RR 18/min; O_2 saturation 100%; temperature 98.3 °F. His examination was notable for significant scalp hair loss and hyperpigmentation along the jaw line. Laboratory studies were remarkable for: WBC 0.4×10^3 cells/mm^3, Hb 7.3 g/dL, Plts 100×10^3 cells/mm^3, absolute neutrophil count (ANC) 0×10^3 cells/mm^3, AST 268, ALT 89, INR 1.3. Additional testing was negative for hepatitis, human immunodeficiency virus, and stool ova and parasites. He was admitted to the hospital, developed a fever to (39.4 °C) 103 °F in the setting of severe neutropenia, and was diagnosed with a *Clostridium difficile* infection. His treatment included cefepime, oral vancomycin, intravenous metronidazole, filgrastim, rifaximin, lactulose, and thiamine. Over the course of 1 week his hepatic transaminases normalized and his ANC increased to 3000×10^3 cells/mm^3. Serial albendazole and albendazole sulphoxide (metabolite) concentrations were measured in serum and urine by liquid chromatography-quadruple time-of-flight mass spectrometry (LC-QTOF/MS) and are shown in Table 1.

Discussion: Albendazole is a broad spectrum anti-parasitic approved for the treatment of echinococcosis and neurocysticercosis. Its reported adverse effects with therapeutic use include elevated liver function tests, abdominal pain, nausea, vomiting, and reversible alopecia. Pancytopenia is a rare effect that occurs more commonly in patients with pre-existing liver disease. Death is occasionally reported after therapeutic albendazole use due to pancytopenia and subsequent septic shock. To our knowledge this is the first case report of albendazole toxicity due to supratherapeutic ingestion with confirmed serum albendazole and albendazole-sulfoxide concentrations.

Conclusions: This case highlights the dangers of delusional self-diagnosis and unregulated pharmaceutical sales on the internet.

KEYWORDS Albendazole; alopecia; pancytopenia

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Hospital Day	Time (24hr)	Specimen	Albendazole* (ng/mL)	Albendazole** Sulphoxide (ng/mL)
1	No specimen available	No specimen available	No specimen available	No specimen available
2	0420	Serum	20.7	4257.7
3	0420	Serum	14.1	1625.2
4	0420	Serum	<LLOQ***	505.4
5	0815	Serum	<LLOQ	86.2
4	2120	Urine	<LLOQ	4233.7
5	0225	Urine	<LLOQ	3638.1
	* no published reference range for albendazole in serum ** reference range for albendazole sulphoxide is 500-1500 ng/mL in serum ***Lower limit of quantification (LLOQ)Q = 1.0 ng/mL			

96. *Sophora secundiflora* ingestions reported to poison centers

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Background: *Sophora secundiflora*, commonly known as Texas mountain laurel, is native to Texas and New Mexico in the United States (US) and Mexico and is used as a landscape plant in various states. *Sophora secundiflora* seeds are purported to be hallucinogenic, and ingestion of *S. secundiflora* seeds has been reported to cause serious adverse effects and death. The objective of this investigation was to characterize *S. secundiflora* ingestions in Texas.

Methods: Cases were *S. secundiflora* ingestions reported to Texas poison centers during 2000–2016. The distribution of cases was determined for various factors related to patient demographics, exposure circumstances, management, and outcome.

Results: Of 672 total *S. secundiflora* ingestions, 573 (85.3%) involved the seed or pod. There was a seasonal pattern with 323 (48.1%) reported during March-June. The patients were male in 385 (57.3%) of the cases; 470 (69.9%) of the patients were age 5 years less, 81 (12.1%) 6–12 years, 58 (8.6%) 13–19 years, and 59 (8.8%) 20 years or older. Most ($n = 598$, 89.0%) of the exposures were unintentional, 44 (6.5%) were intentional misuse/abuse, 10 (1.5%) suspected attempted suicide, and 20 (3.0%) for other/unknown reasons. The most common exposure sites were the patient's own residence ($n = 585$, 87.1%), school ($n = 29$, 4.3%), public area ($n = 26$, 3.9%), and other residence ($n = 20$, 3.0%). Patients were managed outside of a healthcare facility in 537 (79.9%) of the cases; 52 (7.7%) had potentially serious outcomes and there were no deaths. The most frequently reported clinical effects were vomiting ($n = 92$, 13.7%), nausea ($n = 47$, 7.0%), and abdominal pain ($n = 26$, 3.9%); hallucinations were reported on one case. The most common treatments were dilution ($n = 395$, 58.8%) and food/snack ($n = 88$, 13.1%).

Discussion: *Sophora secundiflora* ingestions reported to Texas poison centers tended to involve the plant's seeds. The patients usually were young children. The ingestions often occurred in March-June. In spite of the reported potential for serious affects and even death, the ingestions usually were managed outside of a healthcare facility and did not result in serious outcomes. The most common clinical effects were gastrointestinal in nature.

KEYWORDS Texas Mountain Laurel; *Sophora secundiflora*; plant

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97. Geographic distribution of Texas mountain laurel (*Sophora secundiflora*): reported location versus Texas Poison Center exposures

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Background: Texas mountain laurel (*Sophora secundiflora*) seeds contain the alkaloid cytisine. Ingestion of the seeds may result nausea, vomiting, headaches, vertigo, confusion, fever, excessive thirst, cold sweat, respiratory problems, convulsions, and death. *S. secundiflora* is is reported to be native to 40 Texas counties, according to the United States Department of Agriculture (USDA), and 48 Texas counties, according to the Biota of North America Program (BONAP).
Objective/hypothesis: This study compares the location of *S. secundiflora* according to the USDA and BONAP to where exposures to poison centers were reported from.
Methods: Cases were *S. secundiflora* exposures reported to Texas poison centers during 2000–2016. The distribution of cases was determined for caller county and compared with those counties reported by the USDA and BONAP.
Results: In total, 656 *S. secundiflora* exposures were reported from 59 Texas counties. Eighty-three percent of the exposures were reported from counties were the plant is reported to be found, according to the USDA, and 88% from counties were the plant is reported to be found, according to BONAP. Thirty of the counties where the *S. secundiflora* exposures were reported from were not counties where the USDA/BONAP reported the plant to be found. However, 18 of these 30 counties were adjacent to those counties reported by the USDA/BONAP.
Discussion: Although the majority of *S. secundiflora* exposures were reported from counties where the plant is reported to be found, 12% were from other counties. It may be that the list of USDA and BONAP counties where *S. secundiflora* is supposed to be found is incomplete, in which case, poison center information may be useful for providing a more complete description of the plant's range. Alternately, it may be that some of the plants reported to Texas poison centers as *S. secundiflora* were misidentified.

KEYWORDS Texas Mountain Laurel; location; *Sophora secundiflora*

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98. Analysis of remaining atropine in pre-Strategic National Stockpile antiquated autoinjectors

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Background: Medical Countermeasures (MCM) for chemical warfare agent (CWA) and organophosphorus, ester-based insecticide toxicity include atropine, oxime acetylcholinesterase (AchE) reactivators, and anticonvulsant agents. Community preparedness for chemical incidents involving mass human exposure to nerve agents (NA) depends on the availability of adequate MCM resources. Current MCM capabilities for NA poisoning are limited to community-deployed Chempacks, a strategic national stockpile (SNS) resource. Chempack atropine and oxime contents are maintained past expiration date through a shelf-life extension program (SLEP) based on threshold remaining drug potency. Replacement of Chempack pharmaceuticals is currently hampered by delays in vendor delivery of atropine/oxime dual chambered autoinjectors and atropine mono-chamber autoinjectors. Adequate MCM treatment of NA toxicity is based on a clinical endpoint rather than a fixed dose of MCM; sources of atropine with lower residual activity are still useful and may only require more frequent dosing.
Methods: We obtained older chemical defense sources of atropine (civil defense, Department of Defense/War Department, foreign stock) through online auction, military surplus vendors, and militaria and collectors' items. Autoinjectors, syrettes and dosing cartridges from 1942 (11), 1959 (2), 1986 (1), 1999(1), and 2000 (1) were analyzed using liquid chromatography tandem mass spectrometry (LC-MS/MS) for atropine (and, where applicable, accompanying oxime) concentrations. Concentration and percent of packaged active dose (recovery) are reported.
Results: Drug concentration(s), original packaged dose (source volume, mL), residual potency (%), and date/source and provenance, are presented. Atropine concentrations decreased with age of the source; however, active atropine was present in chemical defense products up to 75 years old.
Conclusion: In light of anticipated shortages of NA MCMs due to interruptions in vendor supply, expired sources – even those whose active drug concentration exceeds the threshold for replacement – may be useful as MCMs for treatment of NA poisoning which is based on a clinical endpoint rather than a specific dose administered.

KEYWORDS Atropine; autoinjector; countermeasure

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99. Incidence of medication errors in acetaminophen overdose patients treated with IV acetylcysteine

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Background: Acetaminophen (APAP) toxicity is one of the most common causes of poisoning; in the 2015 National Poison Data System (NPDS) 20,298 patients were treated with intravenous (IV) acetylcysteine (NAC). Previous research has shown that the complex IV 3-bag NAC dosing regimen is associated with medication errors (33% of cases, including some cases with multiple errors), and that dosing instructions or other communication provided verbally over the telephone by poison centers can be unclear or misinterpreted (22% of cases in one study). The goal of this study is to identify the number and types of medication errors in a cohort of patients receiving IV NAC, for whom verbal instructions on NAC administration were received from the poison center.
Methods: A retrospective chart review of our poison center database was performed on patients treated with IV NAC from 1/1/2015 to 6/1/2016. Medication errors were defined as: delayed initiation of therapy, unnecessary treatment, incorrect dose, incorrect infusion rate, therapy inappropriately ended, and interruptions of therapy $>$ 1 h. Medical outcomes were collected and coded based on AAPCC guidelines. Each chart was reviewed by a single investigator, and treatment was compared with poison center guidelines.

Results: About 454 patients treated with IV NAC were identified during the study period. Sixteen cases were discarded due to incomplete information, resulting in a final sample of 436 cases. A total of 222 medication errors occurred in 178 cases. About 41% of patients treated experienced at least one error, with a range of 1–4 errors per patient. Of these errors, 20% (86 of 436) experienced a >1 h interruption in therapy (range 1–15.5 h), 11% (47 of 436) received the antidote unnecessarily, and 18% (29 of the 163 who presented within 10 h) experienced a delay in initiation of therapy. Other errors included incorrect dose in seven (2%) cases, incorrect infusion rate in 10 (3%) cases, and treatment was discontinued prematurely in 34 (8%) of 436 cases. In addition, the initiation of NAC therapy was delayed by > 1 (range 1–17) h in nine (2%) cases once treatment was recommended. For cases coded as major outcome or death, there were 55 errors in 95 cases, with four different errors in one case (range 1–4 errors).
Conclusions: Medication errors in patients who receive intravenous NAC and poison center verbal consultation are common. Verbal instructions (alone) may be insufficient to provide adequate recommendations on the appropriate dosing of IV NAC. Provision of written information in addition to verbal instructions may significantly reduce the incidence of medication errors associated with intravenous NAC.

KEYWORDS Medication errors; acetaminophen; acetylcysteine

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Table: Most Frequent Errors in IV NAC Administration

Total Cases	Type of Error	Errors	%
436	Interruption in therapy	86	20%
163	Delay in initiation of therapy	29	17%
436	Unnecesary treatment	47	11%

100. Naloxone reversal of clonidine toxicity in pediatric patients

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Background: Naloxone has been administered to reverse clonidine-induced decrease in sensorium, hypotension, and respiratory depression, but the majority of authors conclude that naloxone was not efficacious in this reversal. Many times naloxone is not even administered due to the assumption that it does not work. However, in most of the reported cases, low-dose naloxone (2 mg or less) was administered. Following clonidine administration to rats or human volunteers, naloxone reverses clonidine-induced bradycardia, hypotension, plasma renin activity, and plasma catecholamines in a subgroup (responders) that have baseline elevated resting sympathetic tone (defined as increased heart rate and blood pressure) compared with those that do not respond to naloxone (non-responders). The reversal may be mediated by naloxone's antagonism of β-endorphin, an endogenous opioid peptide that is released after central α2-adrenergic receptor stimulation. The objective of this study was to investigate the efficacy and potential adverse effects of naloxone administered to pediatric patients following clonidine overdose.
Methods: We performed a retrospective review of hospital toxicology records from 2010 to 2014 (IRB-approved) for pediatric patients with a history of clonidine exposure who received naloxone. Demographics, history, clinical course, and interventions were obtained from electronic medical records.
Results: There were 52 patients with clonidine exposure (ages 6 months–16 years) of which 11 (21%) potentially ingested other medications. The most common clinical findings included sedation ($n = 51$), bradycardia ($n = 44$), and hypotension ($n = 11$). Mental status improvement (defined as "not awake" to "awake") occurred in 40 patients; 35 (88%) of the clonidine-only group and five (45%) of the polypharmacy group. The dose of naloxone varied among patients. One patient did not respond to an initial 5mg but woke with a second 5mg dose. Five patients experienced recurrent sedation which resolved with a repeat bolus of the initial naloxone dose. Twenty one patients (40%) received 10mg naloxone via intravenous bolus. Eleven of these 21 patients were less than 2 years old. One patient was awake. Of the 20 not awake patients who received 10mg naloxone, 13 awoke. Of the seven patients that did not awaken, four were intubated and three of these four patients had coingestions. In five patients, heart rates in the 50–60s increased to greater than 80 bpm. Of the remaining 31 patients who received variable doses of naloxone, 22 awoke following administration of 6mg or less of naloxone; one awoke following 18.4mg and another following 13 mg. In the entire group of 52 patients, 10 patients were endotracheally intubated. Four of these patients were awake following naloxone administration, but were subsequently chemically sedated and intubated for transport. There were no adverse events following the administration of any dose of naloxone.
Conclusions: Administration of naloxone to pediatric patients with clonidine toxicity awoke the majority of patients, and resulted in a modest increase in heart rate and blood pressure. There were no adverse effects in any patient including the 21 patients who received 10mg naloxone as an intravenous bolus.

KEYWORDS Naloxone; clonidine; pediatric

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101. Unintentional ingestion of black henbane: two case reports

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Background: Black henbane (*Hyoscyamus niger*), a nightshade, is a species naturalized to Canada, native to Europe and Northern Africa, and grows worldwide. The plant contains tropane alkaloids with antimuscarinic effects, including hyoscyamine, scopolamine, and atropine. We present two cases of poisoning from unintentional black henbane ingestion.
Case reports: A 65-year-old woman and her 71-year-old husband presented to the emergency department (ED) with hallucinations, agitation, mydriasis, urinary retention, dizziness, and warm and dry skin within 4 h of eating a "parsnip" from their garden. Their daughter, a provincial parks worker, identified samples as black henbane. The woman presented with one episode of vomiting, GCS 15, and vitals: temperature (*T*) 36.9 °C, heart rate (HR) 104 beats/min, blood pressure (BP) 125/79 mmHg, respiratory rate (RR) 20 breaths/min, and oxygen saturation (O_2 Sat) of 100%. Her initial electrocardiogram (ECG) showed tachycardia, bigeminy, and non-specific ST changes. The man presented similarly, with GCS 9 and vitals: T 37.4 °C, HR 131 beats/min, BP 157/80 mmHg, RR 24 breaths/min, and O2 Sat of 95%. His initial ECG showed sinus tachycardia. Labs included complete blood counts, electrolytes, venous blood gases, liver function tests, and toxicology screening (ethanol, acetaminophen, and salicylates); all were normal. Both patients were admitted to treat their toxidromes with IV fluids and lorazepam for agitation. The man required physical restraints for agitation for 16h and was discharged once his symptoms

resolved 36 h post-ingestion. The woman had three normal ECGs with sinus tachycardia but, developed a wide QRS and an asymptomatic left bundle branch block (LBBB) 28.5 h post-ingestion. She received D5W and sodium bicarbonate with potassium chloride supplementation for 24 h afterwards; however the QRS remained wide. The toxicology team referred her to cardiology, who found no signs of ischemia. Her toxidrome improved 48 h post-ingestion and she was discharged to outpatient cardiology. Upon follow up, her LBBB remained present, though still asymptomatic. She also had a normal echocardiogram and myocardial perfusion imaging.
Case discussion: Cardiac effects of black henbane are not well reported. In this case, no other causes for the LBBB could be identified, though the authors have been unable to find any reported sodium channel activity with any constituents of black henbane thus far.
Conclusions: These cases show the antimuscarinic effects of black henbane poisoning consistent with previous descriptions in the literature. This is the first report describing a new LBBB in the context of black henbane poisoning, although the connection, if any, is unclear. Increased information is needed to educate the public on recognizing these ubiquitous mimic plants, even in private gardens.

KEYWORDS Ingestion; black henbane; plant

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102. Xa inhibitor adverse events

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Background: Rivaroxaban and apixaban are part of a group of oral anticoagulants targeting factor Xa approved by the FDA in 2011 and 2012. These oral anticoagulants are given at fixed daily doses without the need for laboratory guided adjustments. There is limited data available on supra-therapeutic doses or overdose of the oral Xa inhibitors
Method: A prospective study collected data from 12 regional poison centers covering 4 states. Inclusion criteria included exposure to Xarelto, rivaroxaban, Eliquis or apixaban, managed in a healthcare facility. Exclusion criteria were cases managed on-site (non-HCF) or cases not followed to known outcome. Data for the study were collected by individual chart review including case narratives and compiled into a single dataset after PHI had been removed.
Results: There were 60 patients of which: 36 (60%) were female, mean age was 39.8 and 7 (12%) were children <6 years. 51 patients ingested rivaroxaban (85%) and 9 ingested apixaban (15%). Dose was reported in 40 rivaroxaban patients with a mean dose of 348 mg (range 40–1800 mg) and in seven apixaban patients with a mean dose of 115 mg (range 5–300 mg). Bleeding was reported in 10 rivaroxiban patients (20%) and 0 apixaban patients. The site of bleeding was epistaxis/nose (2) urine (3), GI/stool (2), excessive bleeding/hematoma after venipuncture (2) hemoptysis after extubation (1), and subdural (1). The subdural bleed occurred in a 71-year-old male and was an adverse drug event (chronic daily dose), with coingestants of metoprolol, metformin and lisonopril. The reason for exposure for cases with bleeding: suicide (5), therapeutic error (4), and ADR (1). Coag tests were elevated in a majority of patients with bleeding: INR nine of 10 (90%), PT 7 of eight (88%), and PTT 3 of six (50%). Prothrombin Complex Concentrate was used in two patients and was successful. Dose was not predictive of risk of bleeding or elevated PT, INR or PTT ($p > .05$). Older age, elevated INR or PT was predictive of risk of Bleed ($p < .05$). No bleeding occurred in children but two presented with brief elevations of PT and INR (19.4, 31.8, and 2.8). AST was >100 in three patients (5%) and >1000 in one (1%). The two serious outcomes were with chronic dosing (ADR and therapeutic error); one subdural bleed and one AST/ALT >5000. CoAg labs returned to normal by 24 h (63%) or 48 h (95%). One Pt had sustained elevation of PT/INR for 6 d.
Conclusions: Older age and elevated INR/PT suggest increased risk of bleeding after Xa inhibitor ingestion. Single exploratory ingestion by children did not result in significant toxicity. Adverse events (bleed, hepatic injury) are rare but can result in significant injury

KEYWORDS Xa inhibitor; adverse event; bleeding risk

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103. Gluteal and paraspinal compartment syndrome after overdose

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Background: Physicians are very familiar with classic complications of opioid overdose such as mental status and respiratory depression. More uncommon complications, including severe rhabdomyolysis and compartment syndrome, particularly in uncommon areas of the gluteal and paraspinal muscles, are less familiar to clinicians. This difficulty of this diagnosis can be compounded by non-specific presentations and the inability of an overdose patient to give a history or participate in the physical exam.
Case report: A 58-year-old woman with chronic low back pain and schizophrenia, on oxycodone, alprazolam and quetiapine, presented to the ED complaining of right leg weakness. The previous night, she passed out on the couch after taking an extra oxycodone and woke up on the floor at 3:00 am. At that time, she called EMS and was helped into bed. At 6:00 pm, she was still unable to move and again called EMS. In the ED, she complained of lower back and leg pain, and an inability to move her right leg. She also reported numbness in bilateral legs, right greater than left, below the knee. She had no urinary incontinence or retention. Vital signs were HR 113 bpm, BP 100/78 mm Hg, RR 22 bpm, O2 sat 96%, T 37 C. Heart, lung, and abdominal exams were otherwise unremarkable. She had no cervical or thoracic spinal tenderness, but had diffuse lumbar tenderness, right worse than left. Blisters were present on her right lower leg. See Table 1 for neurologic exam. DP pulses were +1 bilaterally. Intravenous fluids were administered. CT and MRI of the lumbar spine were negative for fracture and cord compression, respectively. On repeat examination, paraspinal muscles were tender and very firm to palpation. Bilateral gluteal muscles were also tender and very firm to palpation. Surgery was consulted. Compartment pressures are reported in Table 2. In the OR, right gluteal and bilateral lumbar compartments were found to bulging and were opened. The muscle was viable. Creatine kinase resulted while the patient was in the OR at 160,200 U/L. She underwent hemodialysis for severe rhabdomyolysis with acute kidney injury and refractory hyperkalemia.
Discussion: Compartment syndrome is a rare condition, even more uncommon when occurring in the gluteal and paraspinal muscles. This diagnosis can be difficult to make, in part due to its non-specific presentation. Involvement of the sciatic nerve (tibial and common femoral branches), however, is typical of a gluteal compartment syndrome, and explains the motor and sensory findings in this case. Careful examination of all muscle

compartments, not just the large muscle groups of the extremities, is essential to make this diagnosis. In an overdose patient, extremity pain with neurologic findings in the setting of rhabdomyolysis should prompt consideration of compartment syndrome. Awareness of this condition is paramount as prompt diagnosis and treatment with fasciotomy can prevent permanent neurologic damage and muscle loss.
Conclusions: Gluteal and paraspinal compartment syndrome is a rare complication of overdose. Awareness of the condition and a careful physical exam can help make the diagnosis.

KEYWORDS Compartment syndrome; opioid; overdose

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Table 1: Neurologic exam

	Motor	Sensory
Cranial Nerves II-XII	Intact	Intact
LUE	5/5 throughout	SLTI
RUE	5/5 throughout	SLTI
LLE	4/5 throughout	SLTI
RLE	3/5 HF, HE 1/5 KF, KE, PF, DF, EHL	Decreased; only sensing strong painful stimuli

Table 2: Lower extremity compartment pressures

	Compartment Pressure
Right gluteal muscle	38 mm Hg
Left gluteal muscle	10 mm Hg
Right lumbar paraspinal muscle	35 mm Hg
Left lumbar paraspinal muscle	31 mm Hg

104. Psilocybin mushroom exposures reported to poison control centers: an NPDS study

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Background: Psilocybin is a tryptamine alkaloid found in some hallucinogenic mushrooms which can cause intense psychedelic experiences. Psilocybin is being reexamined as a potential therapeutic agent for various conditions. The risk and the range of toxicity from intentional and unintentional psilocybin exposures are unknown. One report in the literature from 1962 describes a fatal case of pediatric convulsions and cerebral edema. Other reports describe myocardial infarction, arrhythmia, acute, and persistent psychosis or hallucinations, as well as traumatic injuries. Few studies have examined modern use and effects on humans in a large population. National Poison Data System (NPDS) data were analyzed to assess the effects reported with psilocybin exposures to characterize potentially serious adverse outcomes.
Methods: A retrospective analysis was performed of psilocybin exposures as a single agent or in conjunction with cannabis from 1/1/2000 to 12/31/2015 reported to United States poison centers using the NPDS database. Cases were excluded if exposure to other agents was reported including synthetic and unconventional cannabis use. A separate NPDS request of all fatality reports with psilocybin as a substance was assessed by an independent review by both authors to determine the role of psilocybin in contributing to the cause of death. Cases were excluded (from both sets when applicable) if there was no clear evidence of psilocybin exposure or if significant concurrent exposures were reported. Data trends were examined to determine monthly and yearly exposures with normalization for the varying number of NPDS yearly human exposures. In cases with known outcome, we compared the number of pediatric (<13 years) unintentional exposures versus adult (>19 years) intentional exposures for major outcome versus the grouped outcome of no effect, minor, or moderate. We determined the number of cases with reports of seizures (all types) in the adult and pediatric populations. Groups were compared using Fisher's exact test to assess for significance ($p<.05$).
Results: There were 9015 exposures that met inclusion criteria; all deaths were excluded by unanimous agreement. From 2000 to 2004, psilocybin-containing mushroom exposures trended upward but have declined steadily since. Reported exposures peaked in June and October. The average pediatric exposure age was 3.4 years of age, and the average adult age was 26.4 years. Major outcomes were significantly more likely to occur ($p=.005$) in adults with intentional exposure (54/2062) than with unintentional pediatric exposures (1/321). There were no seizures reported among all 562 pediatric exposures compared with 1.4% (51/3680) of all adult exposures ($p=.002$).
Conclusions: There appears to be seasonality associated with psilocybin exposures. Adult intentional exposures were more likely to experience major outcomes than pediatric unintentional exposures. Seizures were rarely reported in the adult population. Potential explanations for these clinical findings include unreported coingestants, intrinsic lower toxicity in pediatric patients, or lower amount of psilocybin exposure in unintentional ingestions. There were no deaths that could be attributed to psilocybin exposure alone. Our results suggest psilocybin has less toxicity than previously suggested in isolated case reports.

KEYWORDS Psilocybin; mushroom; hallucinogen

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105. Bupropion release rates in water versus polyethylene glycol solution: an *in vitro* pilot study

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Objectives: Bupropion XL is a commonly prescribed antidepressant and smoking cessation drug. However, it is highly toxic in overdose and can lead to serious adverse events including seizure, cardiac dysrhythmias, and death. Since there is currently no antidote for bupropion XL overdose, any method of mitigating toxicity would be clinically useful. Whole bowel irrigation (WBI) with polyethylene glycol (PEG) is commonly used to treat acute overdoses of sustained release drugs like bupropion XL (e.g., verapamil SR). This intervention theoretically can reduce the drug burden by enhancing GI transit. Given the non-absorptive properties and high osmolality of PEG, it is unknown how it will affect the drug delivery system (DDS) of bupropion XL. This study aims to examine whether PEG affects the release of bupropion XL

when compared with a water. We hypothesize that PEG will inhibit the DDS and reduce the release of bupropion XL.

Methods: This was an *in vitro* experiment performed at room temperature with two arms; a control group (500 mL of double-distilled, deionized water in a 1L glass beaker) and an experimental group (500mL of double-distilled deioninzed water with 34 g polyethylene glycol 3350 dissolved in a 1L glass beaker). The PEG dose is equivalent to commonly prescribed dosages for WBI. At time zero, a single 300 mg bupropion XL tablet was added to each beaker and the solutions were continuously stirred at room temperature throughout the experiment. The concentration of bupropion was measured every hour for 8 h by removing 1 mL of solution from each beaker and filtering to remove any particulate matter. The study was repeated three times. The change in bupropion XL concentration over the 8 h were compared between the two groups by looking at the slope over time of the mean concentrations and the area under the curve (AUC), a common measure of drug exposure.

Results: At all time points, bupropion concentrations were consistently higher in the control group compared with the PEG group (Figure 1 and Table 1) and the concentration of bupropion in the control group increased at a faster rate compared with the PEG solution (control, $m = 22.57$ (mg/mL)*h^{-1}, group 2, $m = 6.51$ (mg/mL)*h^{-1}). Furthermore, there was a 67% decrease in the AUC for the PEG group compared with the control group (AUC_{PEG} = 255.5 mg/mL*h versus $AUC_{Control}$ = 774.4 mg/mL*h).

Conclusions: These data show decreased concentrations of bupropion XL in PEG + water compared with water alone. The reasons for this are unclear. It suggests that PEG may inhibit the release kinetics of bupropion XL. Further studies with a larger sample size and mimicking physiological conditions need be done in order to better understand if this study is reproducible and of clinical significance.

KEYWORDS Bupropion; overdose; drug release

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106. Takotsubo cardiomyopathy associated with buprenorphine precipitated withdrawal

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Introduction: Spontaneous opioid withdrawal has been reported to be a stress-inducing trigger in cases of Takotsubo cardiomyopathy.

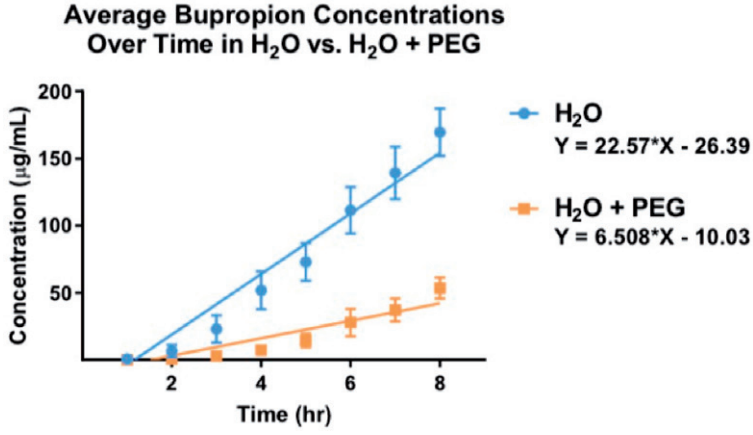

Figure 1: The Average Concentrations of Bupropion XL in "H_2O + PEG" and "H_2O"

Table 1: Summary of Average Concentrations of Bupropion in "H_2O + PEG" and "H_2O"

Time	Average Conc. Bupropion XL H_2O (ng/ml)	St. Dev. H_2O	Average Conc. Bupropion XL H_2O + P EG (ng/ml)	St. Dev H_2O + PEG
0	72	22	58	24
1	599	416	122	54
2	6431	4612	662	141
3	22960	10152	2967	645
4	51668	14059	7303	1729
5	72987	14033	14472	5056
6	111473	17429	27826	10260
7	139258	19440	37133	8606
8	169626	17705	53463	7877

Precipitated opioid withdrawal is more severe and rapid than spontaneous opioid withdrawal, potentially increasing the risk of Takotsubo cardiomyopathy. We report a case of Takotsubo cardiomyopathy associated with precipitated opioid withdrawal caused by buprenorphine administration.
Case report: A 34-year-old female with a one-year history of intravenous heroin use was admitted to a drug rehabilitation facility. She had no relevant past medical history and was taking no prescription medications. She denied other illicit drug use. The last time she used heroin was unknown. She was noted to have mild withdrawal symptoms with a Clinical Opiate Withdrawal Scale of 6. She was given 4mg of sublingual buprenorphine and within 1 h became agitated, tachycardic, tachypneic, and diaphoretic. She was given an additional 2mg of buprenorphine 2 h later followed by another 2mg 4 h later. Nurses noted she appeared to have worsening withdrawal symptoms throughout the day. Approximately 1 h after her last buprenorphine administration, she was noted to be diaphoretic and cyanotic with an oxygen saturation of 80%. She was transferred to the emergency department where her vital signs were BP 124/86, P 140, RR 25, O2 98% on a non-rebreather. Chest radiograph showed diffuse pulmonary edema and an EKG demonstrated sinus tachycardia with anterolateral ST segment depression. She was intubated and admitted to the intensive care unit. Initial echocardiography displayed global hypokinesis of the left ventricle with an ejection fraction (EF) of 10%. Serum troponin levels peaked at 8.7 ng/mL. Left and right cardiac catheterization were normal. The patient clinically improved over the following days. On hospital day 7, a repeat echocardiograph demonstrated return of normal left ventricular function with an EF of 65%. She was discharged on hospital day 10.
Case discussion: Buprenorphine is an opioid partial agonist used to treat opioid addiction. Precipitated withdrawal may occur if insufficient time has lapsed since last opioid use or the patient is not experiencing adequate withdrawal symptoms prior to induction. Our patient may not have disclosed recent use of a long-acting opioid as to not delay her buprenorphine administration. Late recognition and subsequent treatment of the patient's severe opioid withdrawal most likely contributed to the severe cardiac effects.
Conclusions: We report, what we believe, to be the first case of Takotsubo cardiomyopathy associated with precipitated opioid withdrawal secondary to buprenorphine administration. It is important to be aware of this potentially fatal cardiac complication in precipitated opioid withdrawal.

KEYWORDS Buprenorphine; cardiomyopathy; withdrawal

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107. Mathematical modeling of the effect of different intravenous acetylcysteine regimens on hepatic glutathione regeneration and hepatocyte death following simulated acetaminophen overdose

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Objectives: Although acetylcysteine is very effective at preventing acetaminophen-induced hepatotoxicity, the original 3-bag intravenous regimen is associated with adverse reactions. Several intravenous acetylcysteine regimens have been proposed but their comparative efficacy is unproven [1].
Methods: A mathematical model integrating a model of paracetamol transport and metabolism with a model of glutathione metabolism [2] was used to model the effect of several intravenous acetylcysteine regimens following a simulated 20 g acetaminophen overdose with acetylcysteine rescue started at 4 h post-ingestion: (1) current UK 21h acetylcysteine regimen (150 mg/kg over 1h, 50 mg/kg over 4 h then 100 mg/kg over 16 h, total 300 mg/kg over 21 h), (2) Australian 2 bag regimen (200 mg/kg over 4 h then 100mg/kg over 16 h, total 300 mg/kg over 20h), (3) high-dose regimen (150 mg/kg over 1 h, 14 mg/kg/h over 20 h, total 430 mg/kg over 21 h), (4) 12 h SNAP regimen (100 mg/kg over 2 h then 200 mg/kg over 10 h, total 300 mg/kg over 12 h), and (5) extended high dose SNAP regimen (100 mg/kg over 2 h then 400 mg/kg over 20 h, total 500 mg/kg over 22 h).
Results: Following a 20 g acetaminophen overdose, there was no difference in hepatic glutathione regeneration and nadir of functional hepatocytes between the five regimens.
Conclusions: All of the proposed acetylcysteine regimens appear to be equally effective at preventing acetaminophen-induced hepatotoxicity when started early following overdose.

KEYWORDS Acetylcysteine; acetaminophen; mathematical model

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108. Mathematical modeling of the effect of late administration of a novel acetylcysteine regimen based on the SNAP trial on hepatic glutathione regeneration and hepatocyte death following simulated acetaminophen overdose

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Objectives: Although a novel 12h acetylcysteine ("SNAP") regimen has been shown to be associated with a reduction in adverse reactions in the SNAP trial [1], the efficacy of this regimen after delayed administration is unproven. We aimed to model the effect on hepatic glutathione regeneration and hepatocyte death of this novel regimen following simulated acetaminophen overdose.
Methods: A published mathematical model integrating a model of paracetamol transport and metabolism with a model of glutathione metabolism [2] was used to model the effect of two intravenous acetylcysteine regimens following simulated acetaminophen overdose of 8g, 16g, 20g and 24g with acetylcysteine rescue started at 8h and 16h post-ingestion: (1) current UK 21h acetylcysteine regimen (150 mg/kg over 1 h, 50 mg/kg over 4 h then 100 mg/kg over 16h, total 300 mg/kg over 21 h), (2) 12h

SNAP regimen (100 mg/kg over 2 h then 200 mg/kg over 10h, total 300 mg/kg over 12 h).
Results: Both acetylcysteine regimens appear to be equally effective at restoring glutathione and preventing hepatocyte death after acetylcysteine rescue 8h post-ingestion following acetaminophen doses of up to 20 g. When acetylcysteine rescue is delayed to 16h post-ingestion, both acetylcysteine regimens are equally effective at restoring glutathione but both are less effective at preventing hepatocyte death compared with rescue at 8 h.
Conclusions: The model suggests that most patients will be treated as effectively by the 12h SNAP regimen compared with the 21h regimen. Patients with more substantial overdose may require prolonged acetylcysteine therapy beyond 12h e.g., those with persisting plasma paracetamol concentrations or evolving liver function abnormalities after the initial 12h regimen. Further clinical studies are required to evaluate the clinical efficacy of this approach.

KEYWORDS Acetylcysteine; acetaminophen; mathematical model

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109. Bad stickers: pediatric transdermal drug delivery systems exposures reported to the NPDS

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Background: Transdermal drug delivery systems (TDDS) offer a unique method of administration for medications. These products may pose a particular risk to pediatrics patients due to the large amount of drug they contain even when used and tendency to be viewed as "stickers" by children. We sought to characterize pediatric exposures to TDDS reported to the National Poison Data System (NPDS).
Methods: This was a cross sectional study consisting of NPDS data collection utilizing both qualitative and quantitative data for the time period of 1/1/2006–1/1/2016. A qualitative analysis of NPDS fatality abstracts was conducted to characterize pediatric (<19 year of age) exposures to TDDS (recorded as "patch"). A quantitative search in NPDS was conducted for all closed, pediatric human exposure cases to TDDS. All data entered into NPDS was collected and analyzed using Microsoft Excel (*Microsoft Corp., Redmond, Washington*, 2010).
Results: A total of 1990 cases were identified. The average age was 6.7 years (range 3 d–19 years, SD 5.6) and 55% of cases were male ($n = 1104$). Ninety-one percent ($n = 1805$) of cases involved exposure to a single TDDS. The highest number of cases were reported in 2007 ($n = 267$). Since 2011 cases have declined yearly to 135 in 2015. Unintentional exposures, including therapeutic errors, accounted for 73% ($n = 1453$) of cases. Ingestion of the TDDS was reported in 827 (46%) of the single substance exposure. Methylphenidate ($n = 617$) was the most common substance involved, accounting for 32% ($n = 617$) of exposures. Table 1 lists the five most common substances reported. Eighty-eight percent ($N = 1760$) of exposures occurred at the caller's residence and 64% ($n = 1270$) of calls originated from caller's residence. Fifty-eight percent ($n = 1161$) of cases were managed in a non-health care facility. Of the 785 cases referred/treated at a health care facility, a majority ($n = 415$) were treated/evaluated and released. In the 1070 cases that were followed to a known medical outcome there were three deaths, 46 major outcomes, and 326 moderate outcomes. Two of the three deaths involved fentanyl.
Conclusions: Pediatric TDDS exposures reported to the NPDS decreased over the duration of this study. Methylphenidate was the most common substance involved. Major medical outcomes and deaths were rare.

KEYWORDS Transdermal; methylphenidate; Poison control

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Substance	Number of cases
Methylphenidate	617
Fentanyl	311
Lidocaine	248
Nicotine	192
Clonidine	184

110. Iatrogenic bismuth-associated encephalopathy treated with dimercaptosuccinic acid

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Background: Bismuth is a heavy metal historically used for medical purposes. While elemental bismuth is generally non-toxic, bismuth salts can cause significant neurological and renal toxicity despite their therapeutic purpose. We report a case of iatrogenic toxicity following topical bismuth therapy in a burn patient.
Case report: A 76-year-old man sustained 20% TBSA full thickness burns to his legs. Following excisional debridement and grafting procedures, a compounded ointment (containing bismuth subnitrate, iodoform powder, and white petrolatum) and 3% bismuth tribromophenate impregnated dressings (Xeroform®) were used topically to prevent desiccation of exposed tendons. Four days after starting the topical bismuth therapy, the patient developed delirium. By hospital day 27, he had expressive aphasia, inability to follow commands, and inability to eat. All known deliriogenic medications were stopped. Neurologic workup included a brain MRI and basic laboratory studies, including renal function, which were normal. An EEG demonstrated severe generalized slowing. Serum and urine bismuth levels were sent and returned elevated. (Table 1). Despite discontinuation of topical bismuth, the patient's mental status did not improve over 7 d. On hospital day 37, chelation with dimercaptosuccinic acid (DMSA) was started at a dose of 10 mg/kg every 8 h for 5 d, followed by 10 mg/kg every 12 h for 14 d. The patient's mental status improved. At completion of DMSA treatment, the patient's neurological exam was

Table 1

Hospital Day	Days Post-DMSA Initiation	*Urine Bismuth (ng/mL)	*Serum Bismuth (ng/mL)
31	-6	1745	18.9
43	6	1717	109.8
52	15	617.5	34
56	19	308.8	25.2
*Reference range—urine: <200 ng/mL, plasma: <10 ng/mL			

grossly normal, and his mental status returned to baseline. He was discharged from the hospital on day 100.

Case discussion: Published reports of bismuth-induced toxicity usually occur following large, intentional ingestions of over-the-counter bismuth-containing anti-acids. In our case, systemic toxicity likely occurred following significant dermal absorption of topical bismuth in a patient with extensive burns. After identification of bismuth toxicity, supportive care and removal of bismuth exposure are the standards of treatment for this toxicity. The patient's mental status did not improve following cessation of exposure and supportive care, leading to chelation therapy. Due to lack of data, endogenous bismuth elimination rate could not be compared with DMSA-augmented elimination rates. The use of chelating agents is controversial, although DMSA has been shown in case reports and animal studies to cause few adverse effects and potentially limit the complications of toxicity in severely poisoned patients.

Conclusions: Bismuth-containing medications are commonly used and readily available over-the-counter. This case highlights the potential for significant systemic absorption of topical bismuth, leading to severe encephalopathy.

KEYWORDS Bismuth; dimercaptosuccinic acid; encephalopathy

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111. Plant and fungi exposures reported to the Toxicology Investigators Consortium (ToxIC)

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Background: Plant and fungi represent a heterogeneous group of agents, with a wide range of clinical effects. Little has been published regarding the epidemiology or management of plant and fungi ingestions.

Research question: To describe the prevalence of plant and fungi ingestions, including prevalence for specific agents, and review adverse outcomes and specific management strategies associated with specific agents.

Methods: The Toxicology Investigators Consortium (ToxIC) Registry records all clinical consults by an international network of medical toxicologists in a standardized fashion. ToxIC was queried for all cases of exposures categorized as "Plant and Fungi." These exposures were categorized using descriptive statistics.

Results: About 427 Plant and Fungi exposures were reported to ToxIC between 2010 and 2016. Of these exposures, 178 (41.7%) were classified as mold exposure, 176 of which occurred in an outpatient clinic. Of the remaining 249 exposures, there were 64 unique agents reported. Intentional ingestions numbered 146 (58.6%), unintentional ingestions numbered 69 (27.7%), while in 26 the intent was unknown (10.4%). The five most common named exposures were psilocybin mushrooms (20, 8.0%), Datura species (16, 6.4%), Mitragyna speciosa or "kratom" (15, 6.0%), cyclopeptide-containing mushrooms (14, 5.6%), and Nerium oleander (11, 4.4%). There were 78 unknown/other mushroom exposures (31.3%). Other notable exposures include four castor bean exposures, three strychnine exposures, and three solanine exposures. Two deaths were reported, in a case of kratom exposure and in a case of cyclopeptide mushroom exposure. Toxicological antidotes were given in 61 cases (24.5%); the most common antidotes used were *N*-acetylcysteine (26), physostigmine (10), fab for digoxin (8), sodium bicarb (6), atropine (5), and naloxone (5). Seven of 16 Datura sp. poisonings received physostigmine, seven of 11 Nerium oleander poisonings received fab for digoxin, and 20 of 109 mushroom poisonings received *N*-acetylcysteine. Vasopressors were used in two patients, activated charcoal was given to 15 patients, and nine patients were intubated.

Discussion: Plant and fungi exposures reported to ToxIC between 2010 and 2016 were highly heterogeneous. Management strategies and clinical outcomes were variable given the disparate types of ingestions.

Conclusions: In cases recorded in the ToxIC registry, a wide variety of plant and fungi ingestions were reported although fatal outcomes were rare. ToxIC may be a viable tool for studying select rare plant and fungi exposures, including mushrooms, Datura, and Kratom.

KEYWORDS Plants and fungi; natural products; toxic

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112. Myocarditis from Chinese herbal remedies for infertility treatment

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Background: There are multiple reports in the literature of adverse effects secondary to Chinese herbal preparations. These can be from inadvertent contamination, purposeful adulteration with pharmaceuticals, and from drug herbal interactions. We present a case of myocarditis in a young man from pharmaceutical inclusion of digoxin-like compounds, mycophenolic acid and amfetamines in a Chinese herbal tea prescribed and dispensed for the treatment of male infertility. To our knowledge, this is the first case of the addition of mycophenolic acid to an herbal preparation.

Case: A previously healthy male with a history of bipolar disorder for which he took lithium, sought care from a traditional Chinese practitioner for male infertility. He was prescribed and dispensed 13 packages of dehydrated herbs imported from China. He was to add the contents of all 13 packages to two cups of boiling water, allow it to steep for 1–5 min and drink the tea once daily. After 14 d of this therapy, his Western doctor discouraged the practice and the patient stopped consuming the tea. Six days after his last tea treatment he was admitted to hospital with heart failure and complete heart block. Further history revealed symptoms of an upper respiratory tract infection for two weeks prior to hospitalization. As part of his initial cardiac work-up, a digoxin level was measured at 0.4 nmol/L, despite no history of taking therapeutic digoxin. Given the history of herbal tea consumption, the Poison center was consulted for treatment recommendations. Digoxin immune fragment was not recommended as a subsequent digoxin level was undetectable. Analysis of the herbal tea specimens revealed mycophenolic acid, digoxin, and phenethylamine which has aphrodisiac properties. The patient had a prolonged hospital admission, requiring a pacemaker, cardiac catheterization (showing normal coronary arteries and 30% LVEF), before his eventual discharge to cardiac rehabilitation. The final diagnosis was myocarditis complicated by digoxin toxicity. An investigation is ongoing to determine whether an herbal contaminant was the source of the digoxin or whether all three pharmaceuticals were purposeful adulterants of the tea packages. Health authorities are continuing to track prescribers and follow-up on other exposed patients.
Discussion: Toxic drug-induced myocarditis can be caused by any xenobiotic, but has classically been associated with amfetamines, antipsychotics, and anthracycline chemotherapeutics. In this patient, it is theorized that myocarditis was related to the contaminants in the herbal teas: viral myocarditis as a consequence of the immunosuppressive properties of mycophenolic acid or related to the phenethylamine. While, third degree heart block is not a common complication of myocarditis, it is postulated that this aspect of the clinical presentation was related to concomitant digoxin toxicity.
Conclusions: We present the first reported case of mycophenolic acid in a Chinese herbal product that may have contributed to the development of a hemodynamically significant myocarditis. The presence of digoxin-like compounds in the same product may have been responsible for the associated complete heart block.

KEYWORDS Chinese herbals; mycophenolate; myocarditis

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113. A review of lacosamide exposures as reported to US poison centers

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Introduction: Lacosamide (Vimpat®) is an anticonvulsant that is used as monotherapy or with other medications to treat partial-onset seizures for patients 17 and older. Though exact mechanism is unknown, lacosamide acts as a neuronal membrane stabilizer by enhancing slow inactivation of voltage-sensitive sodium channels. Although it was FDA approved in October 2008, little is known about the characteristics and outcomes of patients exposed to lacosamide. The objective of this study was to characterize exposures to lacosamide as reported to United States Poison Centers with regard to patient demographics, clinical effects, and outcomes.
Methods: This retrospective observational study queried the National Poison Data System (NPDS) for human single substance lacosamide exposures from 1/2008 to 12/2016. Variables of interest included age, gender, medical outcome, management site, level of health care facility, reason for exposure, and overall effect. Descriptive statistics were performed. IRB approval was granted.
Results: A total of 1124 patients with an exposure to lacosamide were identified ranging from ages 2 months to 99 years (mean 30 years, SD 22 years). Females outnumbered males 622–500. About 82% of outcomes were either identified as having no toxic effect or minimal effect and did not require treatment. About 10% of exposures were judged to have moderate clinical effects. Life-threatening exposures or those resulting in significant residual disability or disfigurement as defined by the NPDS numbered 2.5%. There was one death related to lacosamide exposure. About 49% of cases did not require a healthcare facility for the management, while 48% were either referred to a hospital or already at the hospital at the time of evaluation and treatment. Among those treated at a healthcare facility, 51% were evaluated, treated, and released without admission. 6% were admitted to a psychiatric care facility, 13% to a non-critical care unit, and 17% to a critical care unit. Patients exposed due to therapeutic error numbered 56%. Suicide accounted for 14% of exposures. Among patients aged 0–6 years that developed major clinical effects, the most common symptoms were coma, respiratory distress, and vomiting. For patients greater than 6 years in age, tachycardia, coma and drowsiness were the most common symptoms in patients categorized as having a major effect.
Conclusions: This is the first large study examining the effects of lacosamide in overdose. In this study population, unintentional exposures are rarely associated with death or disability; however, some patients did require critical care management and one patient died. This study is limited by its retrospective nature, passive reporting, and reliance on caller information. Continued research on lacosamide exposures, toxic effects and treatment is needed.

KEYWORDS Lacosamide; National Poison Data System; overdose

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114. Xyrem® (Sodium oxybate/ pharmaceutical gamma hydroxybutyrate) exposures in NPDS from 2002 to 2015: use, abuse, and adverse effects, with a focus on pediatric exposures

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Background: Xyrem® (sodium oxybate) is a pharmaceutical formulation of gamma hydroxybutyrate (GHB). GHB is a central nervous system (CNS) depressant and a potentially lethal drug of abuse. Xyrem® was FDA approved in 2002 for treatment of narcolepsy with cataplexy. Dispensing is limited to a central pharmacy operated with a risk management program. Published data on Xyrem®-associated adverse effects is limited to clinical trial reports, scattered case reports, and post-marketing data collected in 15 countries from July 2002 to March 2008 through a "spontaneous adverse event" reporting system, which documented

10 cases worldwide meeting DSM-IV abuse criteria and eight overdoses with suicidal intent. Beyond several case reports, there are no published data on Xyrem® use, abuse, and adverse effects among children. We sought to analyze Xyrem® exposures reported to the AAPCC National Poison Data System (NPDS), with special focus on pediatric cases.

Methods: A retrospective review was conducted of de-identified NPDS data on exposures involving any/all GHB analogs and formulations, including Xyrem®, from 2002 to 2015. Data included demographics, co-ingestants, clinical effects, and therapies. Statistics are descriptive.

Results: There were 973 Xyrem® exposure calls to 60 Poison Centers in 50 states and Washington DC. Calls/year were the following: 1/2002; 14/2003; 33/2004; 50/2005;57/2006; 46/2007; 73/2008; 82/2009; 93/2010; 93/2011; 81/2012; 109/2013; 125/2014; and 116/2015. Of 973 exposures, ages 8 months–86 years (634 female, 65%), 915 (94%) listed Xyrem® first in order of relative contribution to clinical effects. About 762(78%) had no co-ingestants (Xyrem®-only); 112(11.5%) had one co-ingestant; 47(5%) had two co-ingestants; 24(2%) had three co-ingestants, and 28(3%) had four or more co-ingestants including recreational drugs (i.e., marijuana, methamfetamine, cocaine) and pharmaceuticals (i.e., benzodiazepines, diphenhydramine, morphine). Alcohol was co-ingested in 38(4%) cases, ± other drugs. Of 973 cases, reasons for exposure were 320(33%) Unintentional-Therapeutic Error; 216 (22%) Intentional-Suspected Suicide, including 45 from 7/2002 to 3/2008 (post-marketing report period); 108 (11%) Adverse Reaction-Drug; 81 (8%) Intentional-Abuse, including 17 from 7/2002 to 3/2008; 69 (7%) Intentional-Unknown; 65 (7%) Unintentional-General; 54 (5.5%) Intentional-Misuse, 43 (4.5%) Unknown Reason; six (0.5%) Other-Withdrawal; five (0.5%) Unintentional-Unknown; four (0.5%) Unintentional-Misuse; and one Other-Malicious. Outcomes included one death (29 year-old female, Xyrem®-only, Intentional-Suspected Suicide); 97 (10%) Major Effect; 291 (30%) Moderate Effect; 250 (26%) Minor Effect; 90 (9%) No Effect; and 244 (25%) in Not Followed/Unable to Follow/Unrelated Effect categories combined. Of 973 total exposures, 72 (7%) were pediatric cases (ages 8 months–17 years), including 66 Xyrem®-only. Of 72 pediatric cases, reasons for exposure were the following: 31(43%) Unintentional-General; 21(29%) Unintentional-Therapeutic Error (ages 8 months–17 years, including 10 children ≤12 years); eight (11%) Adverse Reaction-Drug; six (8.5%) Intentional-Abuse (ages 9–16 years); three (4%) Intentional-Suspected Suicide (ages 15–17 years); two (3%) Unknown; and one (1.5%) Intentional-Misuse. Three children ≤3 years exhibited Major Effects including bradycardia (1), respiratory depression (2), vomiting (2), coma (2), and two were intubated and ventilated.

Conclusions: NPDS data document exposures involving recreational and therapeutic use of Xyrem® concurrent with CNS depressant pharmaceuticals and recreational drugs including alcohol, despite warnings to patients and physician prescribers. Frequency of Xyrem®-associated adverse effects, abuse, potential suicidal actions may exceed previously reported safety post-marketing safety data. There were clinically significant Xyrem® exposures resulting in adverse effects in children.

KEYWORDS Xyrem; GHB; sodium oxybate

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115. A pinhead dose brings the death bed close

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A 19-year-old healthy woman was brought to the emergency department (ED) by ambulance with respiratory distress. That evening she had been drinking alcohol and insufflating a white powder named "White China" that she had purchased as "fentanyl." She insufflated a "pin head" sized amount then rapidly became unresponsive prompting a call to EMS and chest compressions. On EMS arrival, she was unresponsive, normotensive, and bradypneic but breathing spontaneously. She received supplemental oxygen and a total of 3mg of intravenous naloxone without improvement in mental status. In the ED, she was awake but lethargic and minimally responsive. She was in acute respiratory distress. Physical examination revealed mild hypertension (149/112 mmHg), tachycardia (pulse rate 143 beats/min), hypoxemia (80%), normal temperature, and respiratory rate of 13 breaths/min. Her pupils were equally round and reactive to light, and she had normal muscle tone. Her chest examination revealed coarse breath sounds bilaterally. Pulse oximetry improved to 100% with bag valve mask support, and she was urgently intubated. An electrocardiogram demonstrated sinus tachycardia with normal QRS interval (76 ms) and a QTc interval (439ms), without ischemia. Laboratory analysis was significant for serum ethanol concentration of 261 mg/dL. Her urine drug immunoassay was negative for amfetamines, barbiturates, cannabinoids, cocaine, methadone, oxycodone, and opiates. She received IV fluids and antibiotics in accordance with the ED's sepsis protocol, and was admitted to the intensive care unit(ICU). In the ICU, she developed features of acute respiratory distress syndrome. She was initially sedated with fentanyl and midazolam but remained tachycardic (pulse rate 130–140 beats/min). The toxicology consultation service evaluated the patient and recommended discontinuing fentanyl and avoiding other serotoninergic medications. The patient was transitioned to propofol, with improved heart rate to 90 beats/min. Her ventilator requirements quickly improved and she was extubated after 30 h. Her neurologic status also rapidly improved without evidence of serotonin toxicity.The patient's serum, urine, and the product of abuse were analyzed for designer drugs in a comprehensive drug screen using liquid chromatography- quadrupole time-of-flight mass spectrometry (LC-QTOF/MS). A database of 660 target drugs including 370 designer drugs was used. The non-targeted data acquisition facilitated by LC-QTOF/MS allowed the suspect screening of 54 opioid analogs for which the laboratory had no reference standards. Furanylfentanyl was identified in the product, serum and urine using non-targeted analysis. Its confirmation and quantitation followed after a reference standard of the drug was purchased. The product contained 109 mg furanylfentanyl/g powder while the patient's serum and urine contained 3.6 and 17.6 ng/mL, respectively. A plasma sample obtained 8 h after presentation had no detectable furanylfentanyl. In our case furanylfentanyl was detected at a serum concentration of 3.6 ng/mL and a urine concentration of 17.6 mg/mL, via non-targeted testing. Plasma concentration was undetectable 8hrs after initial labs suggesting rapid metabolism similar to what is seen with fentanyl. This case illustrates the utility of non-targeted testing in detecting novel drugs of abuse, as well as the relative potency of furanylfentanyl.

KEYWORDS Furanylfentanyl; designer drugs; drug testing

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116. Acute ischemic strokes in an adolescent after a suicidal warfarin overdose

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Background: Warfarin overdoses can be complicated by supratherapeutic international normalized ratios (INR) and bleeding. In 2015, National Poison Data Systems reported a total of 1660 exposures to warfarin with twelve major outcomes and one death. Although there is an increase in thromboembolic events (TES) after initiation of warfarin without use of "bridging heparin", there have been no case reports describing TES in acute overdoses. We report a case of an intentional warfarin overdose presenting with acute ischemic strokes.
Case report: A 17-year-old otherwise healthy female presented to the emergency department (ED) with vomiting and somnolence. She ingested unknown amounts of warfarin, metoprolol, acetaminophen, and ibuprofen in a suicide attempt. In the ED, she was drowsy, confused, had left sided hand weakness, a persistent facial twitch, and slurred speech. Her pulse was 82, blood pressure 78/54, blood glucose 107 mg/dL. An EKG was normal. Labs included a prothrombin time (PT) 17.3 s, INR 1.37. A urine drug screen was positive for opiates. Head CT showed infarcts in the right frontal lobe, bilateral parietal lobes, and bilateral cerebellar hemispheres. At the tertiary facility, magnetic resonance imaging confirmed subacute infarcts of simultaneous onset. No vascular abnormalities or venous sinuses thrombi were present. The echocardiogram including a bubble study was normal. PT was 22.7 s, INR 2.3, partial thromboplastin time (PTT) 22.4 s, fibrinogen 431 mg/dL, and d-dimer 22.97 mg/L (normal <0.59). Twenty-two hours after admission laboratory assays did not reveal sickle cell anemia, autoimmune disorders, or an inherited coagulopathy. The protein C activity was 44% (70–180) and protein S 33% (60–140). Left upper extremity weakness and incoordination persisted until discharge,12 d later.
Discussion: Initiation of warfarin in patients with atrial fibrillation is associated with an increased risk of TES in the first 30 d; warfarin naïve patients seem to be at greater risk. A decrease in protein C and S activities is thought to be the mechanism behind warfarin's pro-coagulant effects. Although TES have not been reported in acute overdose, the distribution of ischemia, MRI changes, decreased protein C and S activity, and the elevated INR are indicative of warfarin induced thrombosis in our patient.
Conclusions: Our case highlights an unexpected complication from warfarin overdose that can pose a diagnostic and therapeutic dilemma.

KEYWORDS Warfarin; overdose; ischemia

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117. Electroencephalographic (EEG) seizure activity after an intentional strychnine ingestion

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Background: Strychnine is a plant alkaloid derived from the Strychnos species. It inhibits glycine receptors clinically causing violent awake seizures, respiratory insufficiency, and death. In 2015, a total of 54 strychnine exposures were reported to poison centers in the United States. Of these exposures, 24 were managed in healthcare facilities with one death. Although seizures and tonic-clonic activity is frequently reported in strychnine cases, demonstration of EEG proven seizure activity has not been previously reported. To our knowledge, we present the first case of EEG proven seizures in the setting of strychnine toxicity.
Case: A 17-year-old female with a history of depression and anxiety presented to the emergency department (ED) 1 h after drinking an unknown amount of Humco® strychnine sulfate in a suicide attempt. On arrival to ED, she was described as "jumpy" and had noise induced myoclonic activity. Vital signs were normal and her physical exam was unremarkable. Two hours after presentation, she had a generalized tonic-clonic seizure that lasted two and a half minutes. She was given 10mg diazepam, which stopped the seizure activity; however, she became apneic and was intubated. After intubation, she required an additional 7 mg of diazepam and was loaded with 15mg/kg phenobarbital for seizure activity before being transferred for further management. After transfer, she continued to have seizure like activity and was started on midazolam and fentanyl infusions and placed on continuous EEG monitoring. The patient's EEG was consistent with generalized tonic-clonic seizures. She continued to have intermittent seizures on EEG until approximately 34 h post-ingestion despite having a negative CT head. The patient's hospital stay was complicated by development of ventilator associated pneumonia, rhabdomyolysis, and decreased urine output. However, she fully recovered with supportive treatment and was discharged to a psychiatric facility 9 d after presentation.
Discussion: Strychnine is known to cause glycine antagonism; it binds to the α subunit of post-synaptic glycine receptors, preventing glycine induced chloride influx. This leads to neuronal excitation which causes violent generalized myoclonic activity clinically, but central epileptiform activity is usually not expected. To our knowledge, strychnine does not induce EEG changes in animals and human case reports have not demonstrated EEG changes. However, EEGs in previous case reports were often performed after resolution of apparent tonic clonic activity.
Conclusions: Our case provides the first reported EEG confirmed seizure activity following a strychnine ingestion. It adds to the body of knowledge regarding the clinical presentation of strychnine toxicity.

KEYWORDS Strychnine; seizures; EEG

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118. The continuing threat of chemical weapons: a need for toxicological preparedness

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Background: The Syrian Government has committed atrocities against civilians using chemical weapons, and has violated international treaties such as the Geneva Gas Protocol, Chemical Weapons Convention (CWC), Organization for the Prohibition of Chemical Weapons (OPCW), and International Humanitarian Law (IHL). These violations highlight the unique position served by toxicologists, and Poison Control Centers (PCCs), in national and international syndromic surveillance, recognition, treatment and humanitarian advocacy against such sentinel events.

Methods: A systematic review of the existing medical literature was conducted to look for recent toxicologic sources discussing chemical agents, and violations of laws prohibiting their production, stockpiling or use. The literature was also reviewed for emergency toxicological preparedness methods for chemical events, in North America, including the role of PCC's. Peer-reviewed publications were reviewed for relevancy in databases PubMed, CINAHL, Web of Science, and Google Scholar. Search terms included chemical weapons, chemical warfare, vesicants, pulmonary agents, nerve agents, Geneva Gas Protocol, Chemical Weapons Convention, poison control centers.
Results: In light of horrific events in WWI, the Geneva Gas Protocol of 1925 banned the use of chemical weapons in warfare, but overlooked prohibition of development or stockpiling of chemical weapons. The Cold War saw the proliferation of manufacturing and stockpiling of chemical weapons, in 25 countries. Chemical warfare was seen in a number of conflicts, most notably in the Iran-Iraq war. The CWC was the first disarmament agreement negotiated between countries and enforced in 1997. With the CWC, the OPCW was established to help organize procedures and infrastructure for disarmament of member countries. Syria first signed the CWC, in 2013, after the use of sarin gas was confirmed in two separate chemical weapon attacks on civilians, by Syrian government forces. Since signing the CWC, multiple chemical weapons attacks have occurred in Syria. At least eight uses were confirmed during the battle of Aleppo (2016), alone. The terrorist group, Islamic State of Iraq and Syria (ISIS), has conducted numerous chemical attacks, reportedly at least 52 times, in Iraq and Syria. Violations of IHL also continue, where hospitals are commonly targeted with airstrikes before, or after such chemical attacks, in an attempt to obstruct medical treatment and the existing healthcare system. Physicians for Human Rights documented 454 attacks on 310 separate facilities, and deaths of 796 medical personnel, as of October 2016, in Syria.
Conclusions: Toxicologists should remain vigilant, aware of chemical toxidromes, and the global political climate. Presence of stockpiled chemical agents, and associated munitions, in unstable parts of the world allow for terrorist acquisition of these materials for weaponization. Domestic preparedness in the U.S. involves collaborative efforts between the AAPCC and toxicologists of the CDC to help detect chemical exposure events using the National Poisoning Data System, allowing effective response. Preparedness components such as the CDC's strategic national stockpile and the CHEMPACK program exist for recognition, and rapid mobilization, of antidotes for mass casualty incidents. Existing literature supports the need for improved disaster readiness of PCCs, domestically, for mass casualty chemical warfare events, syndromic surveillance, and public health communication and preparedness.

KEYWORDS Chemical weapons; chemical weapons convention; preparedness

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119. Sex differences in pediatric exploratory exposures from 2007 to 2016: a retrospective review of National Poison Data System (NPDS) exposures 2007–2016

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Background: Children develop by exploring their environment, thus placing them at risk for unintentional toxicologic exposures. Little is known about sex differences among pediatric exploratory ingestions.
Methods: National Poison Data System (NPDS) data were extracted for all unintentional exposures (single or multiple substances) for children age 0–5 years, for all exposures categorized as more serious (outcome = moderate, major, or death), between 1 January 2007 and 31 December 2016. Descriptive statistics, graphical displays, linear regression, and multivariate analysis of variance were performed for exposure year and sex (male versus female) using SAS JMP version 12.0.1 (SAS Inc., Cary, NC).
Results: For 2007–2016, NPDS reported 113,128 exposures with more serious outcomes among those age 0–5 years, including 49,932 females, 62,929 males, and 267 of unknown sex. Of the males and females, 9240 were unintentional-general or unintentional-unknown, of which 99.6% were general, and 0.38% unknown. Exploratory exposures showed no consistent changes over time for this decade ($p < .05$) for either sex or total (males + females). From the multivariate analysis, R^2 was 0.967, LogWorth for sex was 13.2 and year 0.131 (ns) with a male:female ratio of 1.24.
Conclusions: Among patients age 0–5 years, unintentional exposures with more severe (outcome = moderate, major, or death), occurred in more males than females. These results may guide both provider awareness, and parental education in preventing serious pediatric exploratory ingestion. More research is needed into the underlying cause of the male predominance in unintentional poisonings.

KEYWORDS Pediatric; National Poison Data System; unintentional exposures

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All Exposures	ADEs	Slope and 95% Confidence Interval			
over time	Mean/year	%/year	#/year	95% CI	Rsquare
Females	4,137	0.36%	15.1	[-5.31, 35.4]	0.267
Males	5,140	-0.40%	-20.4	[-44.6, 3.71]	0.322
Males+Females	9,276	-0.06%	-5.35	[-44.7, 34.0]	0.012

120. Intermittent haemodialysis in lamotrigine poisoning

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Background: Lamotrigine poisoning is usually benign causing only mild to moderate neurological or cardiovascular effects. However, there have been case reports of lamotrigine poisoning leading to seizures, sudden cardiovascular collapse and death. It has not been clear if haemodialysis can effectively remove lamotrigine. We provide pharmacokinetic data on a large lamotrigine overdose that was managed with intermittent haemodialysis.
Case details: A 23-year-old (90 kg) female presented to hospital 2 h post-ingestion of 17.8 g of lamotrigine and 9 g of quetiapine. On presentation GCS 12, heart rate 150bpm, blood pressure 136/90 mmHg. She was intubated 3.5 h post-ingestion and given 50g of activated charcoal. She received three further doses of activated charcoal over the next 12 h. Her initial electrocardiogram (ECG) showed a sinus tachycardia with a rate of 126bpm, QRS 96 ms, absolute QT 330ms with a prominent R wave of 5mm. Her lamotrigine concentration 3 h post-ingestion was 21.5 mg/L ($N = 3$–13mg/L). Her ECG subsequently developed a right bundle branch block pattern with progressive QRS widening (max 120ms) and ST depression in anterior leads with T wave inversion. She was commenced on continuous veno-venous heamodiafiltration therapy (CVVHDF) but the circuit clotted on three occasions. Eleven hours post-ingestion she still had ongoing ECG changes despite a bolus of 100 mmol of sodium bicarbonate. Hence, she was commenced on intermittent haemodialysis (IHD) 16 h post-ingestion (blood flow rate = 250mL/min, dialysate flow rate 500mL/min). During IHD multiple lamotrigine concentrations were collected. Using the A–V pair method, the mean extraction ratio of lamotrigine during IHD was 0.4 with a mean clearance of 78 mL/min. The half-life of lamotrigine was significantly shorter during IHD, 4.1 h versus 30.4 h post-IHD. She was extubated 42 h post-ingestion and made a full recovery. On extubation she acknowledged taking only 9 g of lamotrigine.
Case discussion: How to best predict which patients with lamotrigine overdose will deteriorate is unknown. There also not appear to be a dose related effect with case reports of deterioration at variable doses. In this case, ECG changes suggestive of sodium channel blockade were used to trigger the need for haemodialysis. This patient did not develop severe toxicity and it is difficult to determine if IHD altered her clinical course. However, this case provides very useful information regarding how dialyzable lamotrigine is in an acute overdose. The extraction ratio, clearance, and half-life of lamotrigine, while the patient was receiving IHD were calculated, which has not been previously reported. The calculated clearance using the A–V pair method was 78 mL/min and mean extraction ratio 0.4. In this patient the half-life was substantially reduced to 4.1h during IHD compared with 30.4h post-IHD.
Conclusions: This case demonstrates that intermittent haemodialysis is very effective in removing lamotrigine in acute overdose. IHD resulted in a significantly shorter half-life and should be considered as a treatment option for large lamotrigine poisoning.

KEYWORDS Lamotrigine; intermittent hemodialysis; poisoning

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121. Comparing intentional exposure rates between stimulants in the RADARS® system poison center data

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Background: Stimulant prescriptions have continued to increase over the past two decades. An increase in prescriptions dispensed also brings concerns about non-medical use of stimulants according to the National Institutes of Health. Stimulants have the ability to treat a variety of symptoms, including Attention Deficit Hyperactivity Disorder, narcolepsy, and obesity; however, they also have an appeal for abuse and misuse. This study was interested in how the prescriptions dispensed have changed over time and in the changes in intentional exposure calls rates.
Methods: Data from the Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System Poison Center Program collected from July 2010 through December 2016 as well as estimated prescriptions dispensed data from QuintilesIMS™ were analyzed. QuintilesIMS™ Government Solutions, Inc., a subsidiary of QuintilesIMS™ Health Inc. Intentional exposure calls (suspected suicide, abuse, misuse, and intentional unknown) involving amfetamines and methylphenidate were examined. Analysis was restricted to individuals 6 years of age and older. A generalized estimating equation Poisson regression was used to model the prescriptions dispensed rates as a function of drug group, time, and a drug group by time interaction. The individual poison centers were treated as subjects for the repeated measures as intentional exposure counts are likely correlated within centers over time.
Results: Intentional exposure calls for amfetamines and methylphenidate changed by +37% and +8%, respectively. The number of prescriptions dispensed in the same time period for amfetamines and methylphenidate changed by +80% and +28%, respectively. When accounting for the number of prescriptions dispensed, the rate of intentional abuse exposures to amfetamines and methylphenidate both decreased over time, with amfetamine exposures starting at a significantly higher rate in 2010Q3 ($p < .001$) yet decreasing at a significantly faster rate ($p = .023$) than methylphenidate exposures. However, exposure rates for both amfetamines and methylphenidate are significantly decreasing over time ($p < .001$ and $p = .009$).
Conclusions: While amfetamine calls have increased by 37%, methylphenidate calls have remained fairly constant since July 2010. When adjusting for the number of prescriptions dispensed, the intentional exposure call rate is decreasing for both drugs, with exposure calls for amfetamines decreasing at a faster rate than methylphenidate. Doctors should keep patients informed about the risk factors associated with stimulants along with medication adherence when prescribing these products.

KEYWORDS Stimulants; exposures; domestic poison centers

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122. One pill can kill: a literature review of propafenone

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Background: Propafenone, a class 1c antiarrhythmic, has FDA indications for recurrent paroxysmal atrial fibrillation and flutter (PAF), paroxysmal supraventricular tachycardia (PSVT), and life-threatening ventricular arrhythmias. It is frequently administered off label. Koppel et al. reported a 22.5% mean mortality in overdose with class 1c antiarrhythmics in 1990. By inhibiting Na channels, weakly blocking beta adrenergic receptors, and inhibiting L-type Ca + channels, propafenone has the potential to cause major morbidity and death in pediatric and adult patients. As there are no guidelines for the management of propafenone overdose, the risk and expected clinical effects are an important part of the risk communication performed by all poison specialists.
Objectives: To describe the reported cases of propafenone overdose and symptomatic exposure in pediatric and adult medicine.
Methods: We utilized PubMed MeSH terms and searched for all articles containing the following: (''Propafenone''[Mesh]) AND ''toxicity'' [Subheading], (''Drug Overdose''[Mesh]) AND ''Propafenone''[Mesh], (''Poisoning''[Mesh] AND ''poisoning'' [Subheading]) AND ''Propafenone''[Mesh], (''Propafenone''[Mesh]) AND ''Pediatrics''[Mesh], (''Anti-Arrhythmia Agents''[Mesh]) AND ''Pediatrics''[Mesh]. After excluding articles that did not have English as a primary language, 64 patients were identified from a variety of case reports and case series.
Results: Of 64 total cases, 42% ($n = 27$) were pediatric cases less than 18 years of age. Death occurred in 12.5% ($n = 8$) of total cases. Clinical effects reported included nausea, vomiting, loss of consciousness, cardiorespiratory arrest, seizure, QRS widening, QTc prolongation, bradycardia, hypotension, and dysrhythmias. Doses of propafenone acutely ingested ranged from 300mg to 9000mg with the onset of symptoms in as little as 15 min. The majority of symptoms occurred between 1 and 4 h post-ingestion. Two young children, 3yo M and 2yo M, ingested 15mg/kg and 133mg/kg of propafenone, respectively. Both children suffered seizure, cardiac arrest, dysrhythmias, bradycardia, and hypotension. With good supportive cardiorespiratory care both children survived. The majority of patients included in this review recovered without any expected long-term sequelae.
Conclusions: One tablet of propafenone can be a life-threatening ingestion to a small child. Clinical signs and symptoms of exposure include seizures as well as life-threatening cardiac abnormalities that require good, supportive medical intervention. Antiarrhythmics, propafenone specifically, are inconsistently included on ''one pill can kill'' lists. Poison specialists and clinical toxicologists should remain cautious when managing pediatric and adult patients exposed to any non-therapeutic amount of this drug.

KEYWORDS Propafenone; antiarrhythmics; dysrhythmias

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123. To cool or not to cool: a case of loperamide induced ventricular dysrhythmia

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Background: The use of high-dose loperamide is increasing for management of opioid withdrawal. Ventricular arrhythmias have been previously described, however, the effects of core temperature on toxin-induced bradycardia is less understood.
Case report: A 26-year-old male was found unresponsive at a sober house with miotic pupils. On EMS arrival, the patient was in ventricular fibrillation and defibrillated once with return of spontaneous circulation. At the outside hospital, he had seizure-like activity, underwent endotracheal intubation, and was started on continuous sedation. After transfer to a tertiary care center, the patient's electrocardiogram showed a heart rate of 102 bpm, QRS interval of 121 ms and QT interval of 455 ms. He was started on a sodium bicarbonate infusion for treatment of presumed sodium channel blockade. Therapeutic hypothermia protocol was initiated. Several hours later, he developed persistent bradycardia with a heart rate in the 40–50 bpm range. Rewarming of the patient was initiated for concern of toxin-induced bradycardia. He subsequently developed torsades de pointe that resolved with precordial thump. Hours later, he developed monomorphic ventricular tachycardia which resolved without intervention. He was then given 4 g of magnesium sulfate and 150 mg of amiodarone intravenously. Electrocardiogram prior to the episode of ventricular tachycardia demonstrated a QRS interval of 110 ms and a calculated QT interval of 745 ms. Electrocardiogram 20 min after the episode showed a QRS of 116 ms and a calculated QT of 629 ms. Overnight, the patient had premature ventricular contractions, which became less frequent over time. Electrocardiogram in the morning demonstrated a normal QT interval. The patient was extubated later in the day and stated he had been taking loperamide 20mg TID for the last month for management of opioid withdrawal symptoms. He had complete neurologic recovery. Serum concentrations of loperamide were non-detectable, but the loperamide metabolite desmethylloperamide concentration was 44 ng/mL, which is above the upper limit of 20 ng/mL seen with therapeutic dosing.
Case discussion: This is a case report of a patient taking daily high-dose loperamide causing malignant ventricular dysrhythmia with confirmatory serum concentrations. In this case, therapeutic hypothermia for neurologic protection likely worsened the toxin-induced bradycardia leading to ventricular dysrhythmia. We suggest therapeutic hypothermia be cautiously used in patients with toxin-induced bradycardia and cardiac arrest. More data need to be collected to determine the relationship between heart rate, temperature, and neurologic outcome in critically poisoned patients.
Conclusions: We present a case of a patient with daily high dose loperamide use causing malignant ventricular dysrhythmia that recovered with good neurologic outcome without therapeutic hypothermia.

Table 1. Temperature and heart rate over time

Time	13:22	16:34	18:14	19:51*	21:36	23:00	0:00**	2:00	4:00
Heart rate	88	102	55		46	63		58	66
Temp (C)	36.2	35.1	35.4	35.7	36.4	37.1	36.8	37.2	37.2

*Torsades de pointe
**Monomorphic ventricular tachycardia

KEYWORDS Loperamide; therapeutic hypothermia; dysrhythmia

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124. Serotonin syndrome after intentional ingestion of citalopram in a patient with a deep brain stimulator for Parkinson's disease

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Background: Serotonin syndrome is a well described toxicity in those who are exposed to selective serotonin reuptake inhibitors(SSRI's). We describe a case of serotonin syndrome in a patient being treated for Parkinson's disease with a deep brain stimulator. To our knowledge, this is only the second case of serotonin syndrome reported in a patient with a deep brain stimulator.
Case report: A 49-year-old male presented to the emergency department after a suicide attempt. The patient's wife reported that he ingested approximately 80 citalopram 10mg tablets about 3–4 h prior to arrival. The patient was awake, delirious and profoundly diaphoretic. The patients presenting vital signs were the following: temp: 99.3 F, oral pulse: 114, resp: 18, weight: 90 kg, BP: 155/101 mmHg, pulse ox: 94% on room air. The patient had a past medical history significant for Parkinson's disease treated with a deep brain stimulator and hypertension. He had recently been started on citalopram for worsening depression. Upon physical exam he had grasp strength 5/5 bilaterally, 4+ brachial, brachioradialis reflexes bilaterally and 5+ patellar and ankle jerk reflexes, with the sustained clonus being most apparent on his lower extremities bilaterally. In consultation with poison control the patient was treated with IV normal saline, activated charcoal and cyproheptadine, with dramatic improvement in his symptoms and resolution of his clonus in 24–28 h. During his admission, he had multiple episodes of mania versus delirium that improved with the initiation of valproic acid and quetiapine. The patient's initial presentation was also notable for tangential speech and urinary retention. The patient was eventually discharged home after a prolonged (18 d) inpatient course, with the initial day being spent in the ICU. There was no alteration of the patient's DBS as per the consulting Neurology and Neurosurgery teams.
Case discussion: Serotonin syndrome is diagnosed based on a combination of mental-status changes, autonomic hyperactivity, and neuromuscular abnormalities. The syndrome can present in variable severity; from mild symptoms of tremors and diarrhea, to life threatening delirium, neuromuscular rigidity, and hyperthermia. Parkinson's disease patients, in particular, may prove difficult to accurately assess changes in their examinations as they often have neuropsychiatric symptoms in addition to baseline tremors and muscular rigidity. Patients treated with deep brain stimulation for Parkinson's disease provide additional complexity as they typically have advanced disease and the DBS acts to decrease serotonin release from the subthalamic nucleus as well as decrease some of their neuromuscular symptoms. However, in our case, a high-dose ingestion of a selective serotonin reuptake inhibitor, it appears that the overdose overwhelmed any protective effect of the patient's underlying condition and DBS.
Conclusions: In patients with movement disorders such as Parkinson's disease, the clonus or tremor typical of serotonin syndrome may go unnoticed, be diminished in the presences of a deep brain stimulator, or be confused with the underlying physical exam. Notable, when examining patients with a deep brain stimulator, the stimulator can be switched off, and an exam in the on and off state can be obtained.

KEYWORDS Serotonin syndrome; Parkinson's disease; deep brain stimulator

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125. Diphenhydramine use disorder and withdrawal on hospital admission

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Background: Diphenhydramine is a first-generation antihistamine that antagonizes muscarinic receptors and fast sodium channels. It is commonly employed to treat allergies, insomnia, pruritis, and extrapyramidal symptoms. Inexpensive and readily available over-the-counter, diphenhydramine is also misused for its hallucinogenic and anxiolytic properties. Dependence and tolerance have been published previously. We describe the case of a woman with well-documented diphenhydramine use disorder presenting with cholinergic excess due to acute diphenhydramine withdrawal during psychiatric hospitalization.
Case report: A 31-year-old woman with schizoaffective disorder, antisocial personality disorder, and mental retardation was brought to the emergency department (ED) for altered mental status and several days of decreased appetite. She was well-known to the ED for repeated diphenhydramine overdoses and myriad psychiatric presentations. Initial physical exam revealed a disoriented, incoherent, tachycardic, and mydriatic female with dry mucous membranes and decreased bowel sounds. Intermittent twitching of the left leg was noted; no abnormal reflexes or clonus were documented. Home medications included fluphenazine depot injection (last received 10 days prior), mirtazapine, gabapentin, quetiapine, and diphenhydramine. Intravenous physostigmine (1.5 mg) was administered for presumed anticholinergic delirium, with no documented improvement in her mental status or her vital signs. She was admitted for evaluation of altered mental status of unclear etiology; toxicology was not consulted. Home mirtazapine was continued as needed for sleep, but other home medications were held. She was prescribed lorazepam as needed for agitation. Delirium and tachycardia persisted despite transfer to an inpatient psychiatric floor. She developed tachypnea, hypertension, tremor, lower extremity clonus, marked hypersalivation, moderate mioisis and profound diaphoresis. She repeatedly requested quetiapine and diphenhydramine. The toxicology service was consulted on hospital day 7 to evaluate for serotonin syndrome. She was found to have pronounced patellar reflexes and ankle clonus in addition to findings above. Mirtazapine was discontinued, and lorazepam and cyproheptadine were administered without objective improvement in symptoms; the patient noted subjective worsening. She acknowledged chronically ingesting 30–50 diphenhydramine tablets daily for many months prior to admission. Fifty milligrams of diphenhydramine were given, and her diaphoresis and drooling diminished within 2 h; she reported subjective improvement. Diphenhydramine 50 mg was initiated four times daily, with resolution of tachycardia, diaphoresis, hypersalivation, increased tone and clonus over 24 h. Mental status cleared. She was placed on an 8-day diphenhydramine taper which she completed prior to discharge.
Discussion: Diphenhydramine, an inexpensive over-the-counter medication widely considered to be safe, is commonly abused,

with physical tolerance and dependence previously described. Cholinergic upregulation is plausible in this context, and was present in this patient, whose history of substantial daily diphenhydramine intake placed the patient at risk of withdrawal with abrupt discontinuation of the drug. Upregulation of cholinergic receptors, increased acetylcholine production, or downregulation of cholinesterases may be contributory in this setting.
Conclusions: Although diphenhydramine dependence and tolerance has previously been described, acute diphenhydramine withdrawal heralded by the development of a state of cholinergic excess responsive to diphenhydramine replacement is not previously described. The serial assessment of this patient by multiple toxicologists strongly suggested the diagnosis.

KEYWORDS Diphenhydramine; withdrawal; substance use disorder

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126. Seven-year trends in the reporting of multiple agent exposures involving opioids and sedative-hypnotics/muscle relaxants to the ToxIC Registry, 2010–2016

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Introduction: Opioids (OPI), sedative-hypnotics (SED) and muscle relaxants (MR) contribute a major proportion of all agents reported by medical toxicologists to the Toxicology Investigators Consortium (ToxIC) case registry with these three drug classes responsible for over 20% of all agent fields. However, the relative contribution of each general class, as well as, individual agents has varied over time, often demonstrating a relatively flat or downward trend, particularly among opioids. The primary objective of this study was to determine trends in multi-drug use between these classes resulting in toxicological events.
Methods: The ToxIC Registry is a prospectively collected cohort of patients evaluated by medical toxicologists. This descriptive analysis included all cases reported 1 January 2010– 31 December 2016 for patients with toxic exposure related to >1 agent ($N = 16{,}633$, 32.5% of all cases). Multi-drug events were categorized for specific OPI:SED/MR combinations, by both individual drug and specific SED/MR groupings [benzodiazepines (BZ), non-benzodiazepines (NB), muscle relaxants, barbiturates (BA)]. Summary statistics included average annual percent change (AAPC) and significance testing of the proportions for trend (ptrend) using a 'case/total cases' metric (STATA/SE, Statacorp LP).
Results: An average of 258 cases involved exposure to at least one OPI:SED/MR combination annually over the 7-year period (range 189–322), representing 8.6–12.3% of multi-drug events in the registry (5-year average 10.9%). Linear tests for trend showed a consistent downward value (−5.1% AAPC, 26.127 X^2 26.127 $p<.0001$). Among the five most common opioids with any SED/MR, significant negative trends ($p<.05$) were observed for hydrocodone, methadone, and, oxycodone; and, a positive trend observed for heroin (X^2 5.390, $p=.02$). Events reporting clonazepam with any opioid also demonstrated a significant downward trend (X^2 4.352, $p=.037$), as did cyclobenzaprine, carisoprodol, and lorazepam. The OPI:alprazolam combination was negative but not significant. Utilizing BZ groupings in combination with individual OPI agents resulted in similar results – consistently negative trends with the exception of heroin:BZ (+18.8% AAPC, 5.487, $p=.02$). For NB, MR and BA groupings, relatively smaller numbers limited analysis by individual OPI; however, total OPI:MR combinations had a significant downward trend (−4.3% AAPC, X^2 9.411, $p=.002$).
Conclusions: Multiple drug events involving an OPI and SED/MR reported to the ToxIC demonstrated downward trends in their relative contribution to the registry over this 7-year period. The major observed exception being heroin, which demonstrated positive trends in involvement when analyzed for all SED/MRs combined or for benzodiazepines alone. As the Registry continues to increase in size and accumulated years, the ability to identify stable estimates of trend will continue to improve.

KEYWORDS Pharmacosurveillance; opioids; sedatives

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127. Toxic malingering: did methanol inhalation cause toxicity?

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Background: Intentional poisoning for the purpose of gaining benefits is uncommon. We present a case of alleged inhalational toxicity from methanol at the workplace, which is shown by toxicokinetic principles to be an implausible source of exposure.
Case report: A 45-year-old, previously healthy man presented to the emergency department (ED) with a burning headache and insomnia. He finished his third 12-h shift at a new job processing bio-fuels approximately 14 h prior and stated he was worried about exposure to methanol. He reported smelling "a sweet smell like methanol" for 15 min while working in an area of potential exposure. He used gloves and eye protection but no respirator. He denied any skin contact or inadvertent ingestion. He denied symptoms during the remaining 5 h of his shift. On the drive home, lights seemed brighter and he developed a headache. He reported no suicidal ideation, no ethanol consumption and no hobbies or other access to methanol containing product. The physical exam was normal. Complete blood count and chemistries were normal. A methanol level was drawn, but not available until the following day after the patient was discharged. The patient was contacted the following day when the methanol level was reported at 24 mg/dL. He returned to the ED 24 h later and received fomepizole. Blood chemistries remained normal. At the second presentation, he complained of headache, dizziness, confusion, and scotoma and was referred for follow up with ophthalmology and neurology with MRI. He was awarded benefits and did not return to work following the alleged poisoning due to continued symptoms. Air sampling in the work environment yielded a maximal methanol concentration of 330 parts per million.
Case discussion: Toxicokinetic principles rule out an inhalational exposure to methanol as the source of a blood methanol. Based upon a volume of distribution of 87L, an ingestion was at least 21 g. The potential inhalation exposure based on sampling data and maximal minute ventilation predicts a blood level of 0.372 mg/dL. Based upon 10 mg/dL/h dissipation rate, a substantially higher level would be predicted at the time of exposure with metabolic acidosis at presentation. These factors rule out an inhalation exposure and suggest an intentional ingestion prior to ED presentation.
Conclusions: Toxicokinetic principles can be applied to evaluate the plausibility that an inhalational exposure is the source of toxicity versus malingering.

KEYWORDS Methanol; malingering; toxicokinetics

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128. Characteristics of deceased illicit drug/alcohol abuse patients as potential organ donors

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Background: Despite efforts to increase the reservoir of organ donors, demand heavily outweighs supply. In April 2017, 118,017 individuals were listed as awaiting transplant. One area of opportunity to increase donor pools are victims of drug and alcohol.
Methods: A retrospective review was performed of one state's organ donors in the Gift of Hope Organ & Tissue Donation Network between September 2015 and March 2017. The characteristics of patients who were evaluated for organ procurement who died of drug overdose related causes were described.
Results: A total of 81 patients who died of acute drug or alcohol overdose were evaluated for organ procurement. A total of 279 unique organs were donated from this group. The majority of procured organs were liver or kidneys (see Table 1). The average age of these donors was 33 years; compared with donors who died of all causes which was 42 years. After unspecified drug overdoses, opioids were the second most common cause of death—reported in 26 (32.1%) cases (see Table 2). Of those who overdosed on opioids, five (19.2%) had evidence of intravenous drug abuse (IVDA) at the time of death. Overall, 42 donors (51.9%) had histories of IVDA in the preceding 12 months. A total of 9 donors tested positive for hepatitis B and/or C; and a history of IVDA was reported in seven (77.8%) of these cases. In 81 donors, high-risk features were identified in 57 (70.3%) of them. Of all organs transplanted, trhee organs (1.1%) were noted to have graft failure on follow up. Reasons listed for which organs were ruled out for transplant included diseased organ ($n = 29$ organs), ruled out after evaluation in OR ($n = 25$), time constraints ($n = 12$), infection and/or hepatitis ($n = 11$), poor organ function ($n = 11$), no recipient located ($n = 6$), ruled out after biopsy ($n = 3$), cardiac ejection fraction $< 50\%$ ($n = 3$), and restriction by the medical examiner ($n = 3$).
Conclusions: This study evaluated characteristics of organ donors who died of drug or alcohol related causes. Several interesting features of this group is the younger average age compared with donors who died of all causes. Additionally, the vast majority of them were considered high risk based on histories such as IVDA. Despite this, the graft failure rate was only 1.1%. Based on such data, this group of organ donors appears to be a potential valuable resource for organ donation despite engaging in often repetitive high risk behaviors.

KEYWORDS Organ donation; drug overdose; transplant

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Table 1. Types of Organs Procured and Graft Failure Rates

Organ	Died of Drug Abuse	Number of Graft Failure
Liver	61	1
Bilateral lungs	15	1
Left lung	5	0
Right lung	2	0
Left kidney	67	0
Right kidney	66	1
Bilateral kidneys	1	0
Heart	37	0
Pancreas	12	0
Intestine	0	0
Total	279	3

Table 2. Drugs Implicated in Donor Deaths

Reported Cause of Death	Incidence
Unspecified drug overdose	28
Opioid	26
Polypharmacy	21
Benzodiazepine	14
Intravenous drug abuse	13
Alcohol (including toxic alcohol)	8 (3 involved methanol)
Cocaine	4
Psychedelic mushrooms	1

129. Methadone-associated hypoglycemia with elevated serum insulin and C-peptide concentrations

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Background: Methadone has been associated with hypoglycemia. Few case reports and animal studies have shown this association, although the exact mechanism is not fully understood. We present a case of a patient who presented with coma due to methadone-associated hypoglycemia.
Case: A 63-year-old woman with a past medical history of Hepatitis C, CHF, ESRD, and COPD on daily methadone maintenance therapy presented to the Emergency Department (ED) by ambulance with unresponsiveness and hypoglycemia. Her fingerstick pre-hospital was 26 mg/dL, was then given glucagon 1mg IM. Her initial vital signs in ED were temperature of 94.5F rectal, HR 60, BP 166/79, RR 14, saturating 99% on room air. Initial fingerstick in the ED was 42 mg/dL. Patient was given dextrose with some improvement, but subsequently developed respiratory distress requiring intubation. She then required multiple other boluses of D50 IV with recurrent rebound hypoglycemia around 20 min later and again 2 h later. The patient was subsequently placed on a D10 infusion, given one dose of naloxone 0.4 mg IV,

and started nasogastric tube feeds. The patient did not have further episodes of hypoglycemia after being placed on a D10 drip. The labs were significant for an elevated insulin concentration at 21.2 IU/mL (Ref 3–17 IU/mL) and C-peptide concentration at 15.69 ng/mL (Ref 0.8–3.85 ng/mL). Her medications included methadone 110 mg daily, omeprazole, metoprolol, nifedipine, and amoxicillin. Subsequent serum sulfonylurea plasma testing was found to be negative and the patients serum methadone concentration was found to be 320ng/mL. Urine methadone and 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP) concentrations were 1400 ng/mL and 7400 ng/mL, respectively. History later obtained from the methadone clinic revealed that she likely ingested 4 d worth of her methadone shortly after receiving the medication.

Discussion: Case reports have shown an association between methadone and hypoglycemia. We have the first case report of methadone-associated hypoglycemia with elevated insulin and C-peptide concentrations in a patient with likely overdose. The etiology, however, is still yet to be elucidated. Hypoglycemia may result from insulin release or inhibition of hormones such as glucagon or epinephrine. Animal studies have shown that this effect is dose dependent and stereoselective, associated with the l-isomer of methadone. These studies also show the hypoglycemic effects were reversed with administration of naloxone, an opioid specific antagonist. Together this indicates the mechanism of action may be mu opioid receptor mediated though other mu receptor agonists such as fentanyl and oxycodone have not demonstrated similar hypoglycemic effects. In this patient, the hypoglycemia resolved after receiving a dose of naloxone and starting a D10 infusion.

Conclusions: Based on case reports and animal studies, it is reasonable to conclude that methadone is associated with hypoglycemia. We present the first case of methadone-associated hypoglycemia with elevated Insulin and C-peptide concentrations in a patient with likely overdose. However, further studies are needed to better understand the mechanism. Clinicians should be aware of this adverse effect in patients.

KEYWORDS Methadone; hypoglycemia; glucose

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130. Delayed fatality after chlorfenapyr ingestion

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Background: Chlorfenapyr is a pyrrole pro-insecticide that has been used in the US since 2001 to exterminate mites, termites, and thrips. It is converted to an active metabolite by mixed-function oxidases, yielding a potent mitochondria uncoupler, CL 303268. Human poisonings are rare, and they appear to be universally fatal. These prior reports collectively describe a 7–10 d post-ingestion quiescent period followed by profound irreversible cellular uncoupling, manifested as hyperthermia, tachypnea, and death. The most startling characteristic of this poison is its ability to exert delayed fatal toxicity. This case represents the first known reported fatality associated with a chlorfenapyr-ingestion in the United States.

Case: A 42-year-old male pest control worker with a medical history of alcohol and cannabis abuse presented to the ED with eight episodes of nausea, vomiting and abdominal pain roughly 2 h after ingesting approximately 300 mL of 21% chlorfenapyr and 500 mL vodka in a self-harm attempt. He was on no medications. His initial vital signs were the following: temp 97.8F, HR 109 bpm, BP 147/93 mmHg, RR 24 bpm, and O2 Sat. 98% on room air. His abdominal exam was benign, as was the remainder of his physical exam. His labs were significant for a hemoglobin of 18.6 g/dL, creatinine kinase of 432 μ/L, lacate of 7.9 mmol/L, ethanol level of 232 mg/dL, and pH of 7.4. His lactate normalized after fluid resuscitation with normal saline over 24 h. N-Acetylcysteine and coenzyme10 were administered in an effort to limit oxidative and mitochondrial damage. He was admitted to telemetry and monitored for alcohol withdrawal and observation for evidence of delayed chlorfenapyr toxicity. Two 30 g doses of activated charcoal were administered to limit further absorption as well as enterohepatic circulation. He remained lucid with normal vital signs, albeit with daily episodes of self-limited diaphoresis. On post-ingestion day 6, he became diaphoretic, tachypneic to a rate of 24, hyperthermic to an initial temperature of 101.3 and confused. He developed urinary retention and muscle rigidity. Hemodialysis was performed in an attempt to remove the active metabolite. Shortly after dialysis the patient's symptoms worsened; 2 h after dialysis his temperature increased to to 108F, at which point he suffered a PEA arrest. After 15 min of ACLS, the patient was pronounced dead.

Discussion: Chlorfenapyr has been postulated to uncouple oxidative phosphorylation, resulting in fatalities. Previous reports describe delayed hyperthermia, diaphoresis, vomiting, altered mental status, as well as rhabdomyolysis. Although it is a relatively small compound with a MW of 408 Da, virtually nothing is known about its Vd, or its *in vivo* protein binding. From our experience, it would appear that late hemodialysis is ineffective at mitigating toxicity.

Conclusions: Given the high delayed mortality and lack of effective treatment options for chlorfenapyr poisonings, further research into possible inhibitors of conversion into the active metabolite is warranted. We would advocate for aggressive early decontamination procedures and early attempts at extracorporeal removal of the parent compound until targeted antidotes are available.

KEYWORDS Chlorfenapyr; pesticide; fatality

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131. Ketamine exposures reported to United States poison control centers over a 15-year period

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Background: Ketamine use has been increasing in emergency departments and other health care settings. There has also been an increase in illicit use of ketamine in many parts of the US. This study sought to examine ketamine use reported to poison centers over the past 15 years and identify trends in use and outcomes.

Methods: A retrospective review was performed of all cases involving ketamine reported to the American Association of Poison Control Centers (AAPCC) from 1 January 2000 to 31 December 2015. Cases were divided into those involving ketamine as a single agent and those involving ketamine and other agents. Data collected included: age, gender, route and form of ketamine used, reason for exposure, and outcome. "Intentional use" cases were those coded as abuse, misuse and suspected suicide attempts, while "unintentional exposures" were defined as unintended exposure, unintended misuse, and therapeutic errors.

For outcomes, cases with "no effect", "not followed, judged as non-toxic exposure", "minor effects", and "not followed, minimal clinical effects possible" were grouped together as "minor". Reports of "moderate", "major", and "death" were grouped as named. Since not all cases contained each data point to be evaluated, the categorical totals differ and reflect only what data was available.

Results: A total of 6233 cases were available for evaluation. 1595 (51%) cases reported ketamine to be the only drug used, while 1514 (48.7%) cases involved multiple substances with ketamine. Of those single agent exposures to ketamine, the majority were males (67%) with an age range of 16–25 years (49%). The most common form of ketamine used as a single agent was liquid (45%, IV, IM, oral and rectal). Reports of single agent ketamine exposures peaked between the years 2000 and 2002, fell rather significantly and consistently until 2008; then gradually rebounded to previous peak levels until 2015 (Table). Intentional use (65% of all cases) was the most common reason for single agent ketamine exposures, while unintentional exposures occurred in 25% of single agent cases. About 53% of ketamine-only cases resulted in minor effects, with two cases of death. In contrast, ketamine use with multiple agents resulted in outcomes judged as moderate or worse, including 20 deaths in 62% of these cases.

Conclusions: Ketamine use reported to poison centers has rebounded to historical peaks in recent years, with the majority resulting from intentional use. Although there were two deaths in single agent users, our findings suggest that ketamine exposures involving multiple substances are at greater risk for serious toxicity.

KEYWORDS Ketamine; toxicity; outcome

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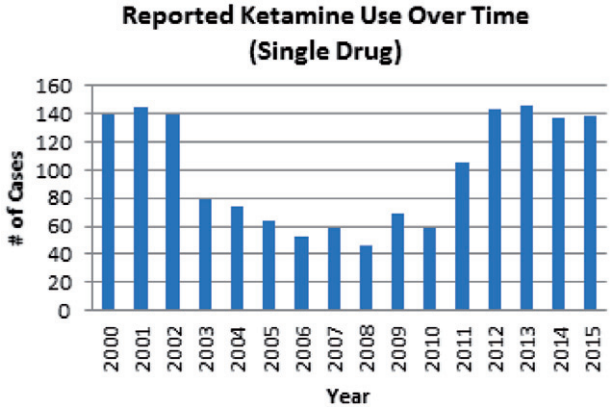

132. Five-year trend analysis of childhood exposure to single use laundry detergent packs in Canada

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Background: Single-use Laundry Detergent (LD) Packs were widely introduced in North America in early 2012. Prior to market introduction, a prospective, multi-center observational study was initiated among Poison Centers (PCs) in the US and Canada serving 24% and 42% of the respective populations. Previous reports from the ongoing study have been limited to the US experience. This is an analysis of accidental childhood LD Pack exposures reported in Canada.

Method: Trend analysis of LD Pack exposures (age <6 years) reported in Canada to a single PC participant in the ongoing prospective study (March 2012 through December 2016). Selected exposure data was transcribed from the complete PCC record using an IRB-approved case report form, including key demographic, morbidity, product, and situational variables. Reporting rates were normalized using Nielsen consumption data as a surrogate for household availability and expressed in terms of "exposures per million units sold".

Results: A total of 1347 childhood exposures (age <6 years) were reported during the five year period. Children age <=3 years were represented in 89.6% of all exposures, and ingestion (87.5%) and ocular (9.8%) were the major routes of exposure. Among exposures followed to known outcome, the percentage of cases with moderate or major outcome remained stable for ingestions (6.1%, $N = 52$) and ocular exposures (22.9%, $N = 19$). There was no discernable trend in the overall percentage of exposures managed in a healthcare facility for ingestions (34.3%) or ocular exposures (67.4%); however, the PCC referral rate for ingestions declined from 17.2% (2013) to 12.0% (2016) and remained lower than US PCC counterparts (28.9–16.1%, respectively). Children gained access to LD Packs outside of the original container in approximately 1/3 of the exposures, which is similar to previously reported findings in the US.

Conclusions: LD Pack exposure trends in Canada were similar to previously reported findings in the US except for HCF referral rates which were lower in Canada. Ongoing, collaborative efforts to reduce childhood exposures is needed.

KEYWORDS Laundry detergent packs; safety surveillance; Canada

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133. Poison center exposure management patterns and health seeking behavior associated with single-use liquid laundry detergent packs

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Background: US Poison Centers (PCs) frequently respond to accidental childhood exposures involving Single Use Liquid Laundry Detergent Packs (LLD Packs). Although the majority of accidental exposures do not result in serious injury, heightened concern following initial reports of life threatening respiratory distress and CNS depression (May 2012) continue to influence PC exposure management practices and consumer health seeking behavior.

Methods: This is an analysis of LLD Pack exposures (age <6 years) reported to 12 PCs participating in an ongoing, prospective observational study (serving 24% of US population). The case narrative was reviewed to verify coding accuracy (demographics, morbidity) and to confirm whether the PC maintained influence over medical care decisions, including referral timing and caregiver compliance with PC instructions. Exposures associated with a healthcare facility (HCF) referral were classified as "immediate" (PC referral during initial call) or "delayed" (PC referral during follow-up call). If the PC advised home observation, however, the caregiver/responder subsequently obtained medical care in a HCF

without notifying the PC, the exposure was classified as a "Self-Referral". Self-Referrals were further reviewed to determine whether the health seeking behavior was compliant with PC instructions to seek care in response to specific symptoms.
Results: During the period evaluated, PCs participating in the ongoing study influenced medical care decisions for 9671 childhood LD Pack exposures. Ingestion (84.1%) and ocular (12.5%) were the major routes of exposure. Among patients treated in a healthcare facility ($N = 2857$, 29.5%), 79.7% were classified as "PC Referrals" and 20.3% were classified as "Self-Referrals". The majority of Self Referrals (60.5%) were determined to be compliant with PC recommendations to seek HCF care in response to specific symptoms. PC Referrals declined annually (−43.1% overall), with the most significant reductions noted during the first 2 years. For ingestions ($N = 8130$), "immediate" PC Referrals were reduced by half (−49.5%), however, "delayed" PC Referrals remained stable (4.8%) and Self-Referrals nearly doubled (+97.8%). Among ocular exposures ($N = 1211$), PC Referrals declined (−33.5%) and Self-Referrals increased (+40.0%). Overall, PC Referrals resulting in an outcome of "no effect", "minor effect" or "no more than minor effect" remained stable for ingestions (79.4%) and ocular exposures (64.6%).
Conclusions: PC referral patterns appear to reflect increased comfort with managing childhood LLD Pack exposures in the home setting. A consensus triage guideline for LLD Pack exposures may facilitate further reductions in unnecessary medical care referrals.

KEYWORDS Laundry detergent packs; exposure management; health seeking behavior

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134. Hospital-treated opiate poisonings stemming from illicit drug use, prescription drug use, and deliberate self-harm

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Background: Ingestions of opiates are a major cause of medically serious poisoning events, yet such ingestions differ in fundamental ways including whether poisoning was intended (i.e., deliberate self-harm) or unintended, and whether the opiates were illicit or the source was a prescription. The purpose of the current study was to use the intention of the act and the source of the opiate to create *a priori* groups of opiate poisoning cases in order to compare them on key demographic and clinical variables based on the idea that the respective groups have differing characteristics and treatment needs.
Method: The sample is a subset of patients treated at a large, US, university medical center by a multidisciplinary, toxicology consultation team between 17 November 2010 and 30 December 2016. As they were treated, the cases herein were entered into a standard, de-identified, central database, and were subsequently downloaded by the study team for secondary analysis. The sample ($N = 435$) for the current analysis was selected based on (1) treatment for acute poisoning event, (2) ingestion of one or more opiates, (3) age 13 and over, and (4) a determination if the event

Table 1 Variable	Illicit Drug Poisoning (ID) (N=128) N (%)	Rx Drug Poisoning (Rx) (N=217) N (%)	DSH[a] Poisoning (SH) (N=90) N (%)	3-way comparison, $X^2(2)$ result (*p*-value)	2-way comparison (significant differences only)
Age 19+	121 (95)	197 (91)	76 (84)	6.3 (.042)	ID>SH
Male	84 (66)	117 (54)	38 (42)	11.9 (.003)	ID>SH,Rx
Co-Ingestion other drug	65 (51)	167 (77)	78 (87)	40.1 (<.001)	SH,Rx>ID
Moderate-high poisoning severity	82 (64)	96 (44)	64 (71)	9.1 (.011)	SH,ID>Rx
Nervous system affected	112 (88)	169 (78)	72 (80)	5.0 (.083)	N/A
Pulmonary sys. affected	68 (53)	68 (31)	30 (33)	17.3 (<.001)	ID>Rx,SH
Vital signs affected	49 (38)	50 (23)	27 (30)	9.1 (.010)	ID>Rx
Antidote provided	90 (70)	123 (57)	57 (63)	6.4 (.040)	ID>Rx
Non-pharm. support provided	52 (41)	77 (35)	43 (48)	4.1 (.128)	N/A
Pharmacological support provided	36 (28)	51 (24)	29 (32)	2.7 (.263)	N/A

Notes. Column percentages shown. [a]DSH = Deliberate Self-Harm. N=112 subjects missing data on poisoning severity. Moderate-to-high severity based on Poisoning Severity Score >2.

was unintentional or intentional, and if the opiate(s) was primarily illicit or prescription. These data were used to create three opiate poisoning groups for analysis: (1) deliberate self-harm (SH, $N = 90$); unintentional, illicit drug (ID, $N = 128$); and unintentional, prescription drug (Rx, $N = 217$). Chi-square tests were used to compare the groups on several variables including demographics (age, sex); co-ingestion of a non-opiate drug; poisoning severity; acute effects on three commonly affected organ systems (nervous, pulmonary, vital signs); and provision of three common treatments (antidote, non-pharmacological support, pharmacological support). The study was conducted with the approval of the local University's human subjects' review committee.
Results: Results for the comparisons of the three groups are shown in Table 1, column 5, and for follow-up two-way tests (where applicable) in column 6. ID patients differed from one or both of the other groups on several variables including more likely to be of adult age (than SH), male (than either group), to experience more severe poisoning (than Rx) including greater likelihood of deleterious effects to the pulmonary system (than either group) and vital signs (than Rx), and being more likely to require an antidote (than Rx). ID patients were also less likely to co-ingest another category of drug (i.e., a non-opiate) compared with the other groups. Finally, the RX and SH groups differed on just one variable, with SH patients showing greater poisoning severity.
Conclusions: The results suggest ID patients stand out from the other two groups in several ways, with the implication that tailored treatments for these patients in particular may be beneficial. Rx and SH patients did not show statistically significant differences, with the exception that the SH cases had greater poisoning severity. The study is limited by the cross-sectional research design and the results are unadjusted, with a plan to follow-up with multivariate analyses.

KEYWORDS Opiate; poisoning; overdose

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135. Respiratory depression after intentional misuse of tianeptine requiring prolonged naloxone treatment

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Background: Tianeptine is a dibenzothiazepine cyclic antidepressant with structural similarity to quetiapine. It is marketed in Europe for treatment of refractory depression. Its pharmacologic properties include increased serotonin, modification of the effects of glutamate and low potency mu and delta opioid receptor agonism. Sedation is not known to be a prominent side effect. We report a case of recreational use of tianeptine that produced respiratory depression successfully reversed with naloxone.
Case report: A 36-year-old male drank ethanol and intentionally injected an unknown amount of tianeptine intravenously to help him "see into the future." He was unresponsive upon EMS arrival and was given 1 mg naloxone IV with a positive response. On ED arrival the patient had miosis, CNS depression and a respiratory rate of 6 breaths per minute. Two additional doses of naloxone 0.4 mg IV temporarily reversed CNS and respiratory depression. The patient was subsequently placed on a naloxone infusion at 0.2 mg/h, and the infusion was titrated off over 9 h. After an additional 4 h of observation the patient was discharged. The urine drug screen was negative. Serum ethanol was 133 mg/dL, all other laboratory studies were unremarkable. Immunoassay screening tests by a tertiary lab were negative for barbiturates, benzodiazepines, cocaine, methadone, methaqualone, opiates, PCP, propoxyphene, THC, buprenorphine, oxycodone, tramadol, and total serum tricyclics. The presence of fentanyl and norfentanyl were not detected by LC/MS/MS. A liquid chromatography tandem mass spectrometry method specific for tianeptine was developed, and the patient's urine concentration was found to be 2 ng/mL.
Discussion: Tianeptine is not FDA approved in the United States, but is easily purchased over the internet. As such there is little clinical experience with the clinical effects and treatment of tianeptine toxicity outside of Europe. The drug has been detected in three post-mortem cases and in two case reports demonstrated reversal of respiratory depression with naloxone. Only recently have the mu and delta opioid receptor agonistic effects been described and considered therapeutically valuable in treating depression. Rare cases of misuse and dependence have been reported in France.
Conclusions: Tianeptine appears capable of producing significant CNS and respiratory depression following excessive doses, presumably due to mu opioid receptor binding. This case demonstrated the efficacy of naloxone to successfully reverse respiratory depression, and multiple boluses, an infusion and extended observation were required until effects resolved.

KEYWORDS Tianeptine; naloxone; misuse

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136. The availability of naloxone in California outpatient pharmacies

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Background: Between 2009 and 2013 five northern California (CA) counties had the highest age-adjusted opioid-related-deaths per 100,000 persons in the state: Plumas (24.51), Lake (22.50), Lassen (16.78), Humboldt (13.32), and Shasta (11.76). In September 2014, the governor signed AB1535 allowing pharmacists to dispense naloxone hydrochloride upon request and without a provider's prescription. AB1535 was supported by a number of public health, drug-treatment, and advocacy groups. To date, there is no published literature regarding the availability of naloxone over-the-counter in CA. We sought to determine knowledge of the bill and participation by pharmacies, availability of naloxone, future participation, and out-of-pocket cost to the consumer in the previously described 5 counties, Fresno County, and San Diego County.
Methods: All pharmacies in the seven counties were identified using the state Department of Consumer Affairs (DCA) website. Inpatient hospital pharmacies, specialty pharmacies (infusion, prison, long-term care, tribal) and pharmacies without "clear" status were excluded. Between January 30 and April 4 2017, pharmacies were contacted and the pharmacist-on-duty was asked the following questions: (1) Are you familiar with AB1535 that permits pharmacists to dispense naloxone without a prescription? (2) Are you currently participating in this program? If yes, do you currently have naloxone on the shelf and at what out-of-pocket cost? If not, do you plan to participate in the next six months? Responses were recorded and tabulated using Microsoft Excel 2011. Fresno-Central CA and San Diego-Southern CA were chosen

	Plumas (N=5)	Lake (N=13)	Lassen (N=5)	Humboldt (N=17)	Shasta (N=34)	Fresno (N=150)	San Diego (N=398)	Total (N=622)
Knowledge of Bill	5 (100%)	13 (100%)	5 (100%)	17 (100%)	31 (91%)	110 (73%)	308 (77%)	489 (79%)
Participation	1 (20%)	3 (23%)	0 (0%)	6 (35%)	10 (29%)	38 (25%)	172 (43%)	230 (37%)
Naloxone available immediately	1/1 (100%)	3/3 (100%)	NA	6/6 (100%)	10/10 (100%)	9/38 (24%)	135/172 (78%)	164/230 (71%)
Naloxone available next-day	NA	NA	NA	NA	NA	29/38 (76%)	11/172 (6%)	40/230 (17%)
Future Participation	1/4 (25%)	0/10 (0%)	0/5 (0%)	1/11 (9%)	0/24 (0%)	21/112 (19%)	59/226 (26%)	81/365 (21%)

Intranasal (IN)	1	1	0	6	10	34	152	204
Mean cost $	166.25	44.99	NA	85.83	130	77	122	112.62
Standard Deviation	0	0	NA	2	0	45	110	36.54
Median	NA	NA	NA	85	130	57.60	112	109.99
Range	NA	NA	NA	85-90	NA	44.90-200	46.74-260	44.90-260
Injectable (IMor IV)	0	2	0	0	0	10	20	32
Mean cost $	NA	70	NA	NA	NA	58.40	524.10	335.64
Standard Deviation	NNAA	0	NA	NA	NA	32	1265	1018.14
Median	NA	NA	NA	NA	NA	53.90	100	51.50
Range	NA	NA	NA	NA	NA	29-152.14	27-4500	27-4500

as representative of other geographical regions of CA to ensure that survey results were representative of the state as a whole.
Results: A total of 2,296 pharmacies were identified in the 7 counties using the DCA website. Of these, reasons for exclusion included: Cancelled (1505), revoked (12), probation/restricted (10), delinquent (4), hospital (59), prison (5), tribal (1), and specialty (52). Data were unable to be collected from additional 26 pharmacies as there was no answer when called on multiple occasions or there was a desire not to participate in the survey. Six hundred and twenty-two pharmacies were surveyed. Data are presented in Table 1. There was considerable variation in knowledge of AB1535, participation, immediate availability of naloxone, cost, and expressed future interest in participation.
Discussion: Overall rates of current (37%) or future planned participation (23%) are fairly low; higher rates are associated with participation by a regional or national pharmacy chain- all 10 participating pharmacies in Shasta were owned by the same parent company. Of the 230 total participating pharmacies, 123 were CVS branches (54%). Lassen County, despite a high rate of opioid-related-deaths has 0% current participation and 0% future interest in participation. There were considerable differences in out-of-pocket cost between pharmacies and counties; in many cases with costs that were arguably prohibitive to the end user.
Conclusions: Despite considerable support, the passage of AB1535 has not resulted in broad participation, availability, future interest, or an acceptable out-of-pocket cost for "prescription-free" naloxone hydrochloride.

KEYWORDS Naloxone; public health; opioid epidemic

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137. A descriptive study of the clinical characteristics of emergency department patients intoxicated with synthetic cannabinoids

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Background: We are currently in the midst of an epidemic of synthetic cannabinoid (SC) drug abuse. Pre-hospital providers, emergency physicians, hospitalists, and intensivists are challenged daily by the clinical consequences of this drug epidemic. Clinical effects of drug exposure are unpredictable and poorly characterized. The drugs are made in ad-hoc labs and the pharmaceutical characteristics of them are not entirely understood.
Objective: To describe the clinical features exhibited by patients under the influence of specifically identified SCs.
Methods: A convenience sample of emergency department (ED) patients presenting to a single urban academic ED with suspected SC exposure were enrolled in the study at the discretion of the treating provider. Blood and/or urine samples were obtained only if already ordered as part of the patient's routine clinical care. Specimens were sent to the Department of Health for identification of specific exposures using liquid chromatography-mass spectrometry. Clinical data including patient age, sex, clinical presentation, initial vital signs, and ultimate disposition was obtained from retrospective chart review.
Results: A total of 128 blood/urine samples were tested. Sevnty-two (56.3%) samples were found to be positive for SCs. Clinical data were extracted on 21 patients whose samples tested positive for the SCs AB-Chminaca 3-methyl-butanoic acid, ADB-Chminaca, AB-Chminaca, or a combination of the three. Five (23.8%) were

Patient	Sex	Age	Blood Pressure	MAP	Pulse	RR	Temp	Mental Status	Synthetic Cannabinoid
1	Male	45	140/90	107	92	16	37	Awake and alert	AB-Chminaca 3-methyl-butanoic acid
2	Male	27	102/53	69	61	18	36.7	Awake and alert	AB-Chminaca 3-methyl-butanoic acid
3	Male	50	98/68	78	102	16	36.8	Awake and alert	AB-Chminaca 3-methyl-butanoic acid
4	Male	41	143/79	100	88	16	36.5	Somnolent	AB-Chminaca 3-methyl-butanoic acid
5	Male	36	106/56	73	80		36.5	Awake and alert	AB-Chminaca 3-methyl-butanoic acid
6	Female	47	114/65	81	89	18	36.6	Somnolent	ADB-Chminaca
7	Male	21	133/78	96	123	14		Somnolent	ADB-Chminaca
8	Male	59	87/54	65	88	16	37	Somnolent	ADB-Chminaca
9	Male	53	109/56	74	107	16	36.7	Somnolent	ADB-Chminaca
10	Female	31	90/59	67	124	18	37	Agitated	ADB-Chminaca
11	Male	34	102/49	67	89	18		Agitated	ADB-Chminaca
12	Male	34	98/64	75	122	16	37	Somnolent	ADB-Chminaca
13	Male	45	82/53	63	72	15		Awake and alert	ADB-Chminaca
14	Male	33	90/57	68	103			Awake and alert	AB-Chminaca 3 methyl + ADB Chminaca
15	Male	42	206/102	137	46	30	36.4	Awake and alert	AB-Chminaca 3 methyl + ADB Chminaca
16	Female	50	135/76	93	78	18	37	Somnolent	AB-Chminaca 3 methyl + ADB Chminaca
17	Male	67	92/54	67	86	16	37	Awake and alert	AB-Chminaca 3 methyl + ADB Chminaca
18	Male	34	88/50	63	80		36.6	Somnolent	AB-Chminaca 3 methyl + ADB Chminaca
19	Male	35	152/78	103	119	18	36.7	Awake and alert	AB Chminaca
20	Male	35	94/53	67	113	16	36.9	Somnolent	ADB-Chminaca + AB Chminaca
21	Male	34	88/50	63	80		36.6	Somnolent	AB-Chminaca 3 methyl + ADB Chminaca + AB Chminaca

found to have a concomitant exposure of SC and another substance. Eighteen (85.7%) patients were male. Ages ranged from 21 to 67 years old. 15 (71.4%) patients had an initial presenting systolic blood pressure <115 mmHg while 11 (52.4%) had an initial SBP <100 mmHg. The average MAP of these 15 patients was 69 mmHg. The remaining six patients had an initial SBP >130 mmHg with an average MAP of 106 mmHg. Of these six patients, three were also positive for a non-synthetic substance. Mental status ranged between somnolent 10 (47.6%), awake and alert 9 (42.8%), to agitated 2 (9.5%). A basic metabolic profile (BMP) was checked on 16 patients. One patient had evidence of a metabolic acidosis with a CO2 = 17. The remaining 15 patients had no gross abnormalities detected. 2 patients were admitted to the hospital while the remaining 19 were discharged from the ED. (Table)

Conclusions: There continues to be widespread abuse of SCs. While there has been better characterization of the chemical constituents of these products, the clinical implications of their use remains largely anecdotal. This study collected clinical data on 21 patients that tested positive for the SCs AB-Chminaca 3-methyl-butanoic acid, ADB-Chminaca, or AB-Chminaca. Our descriptive findings showed that exposure to these specific SCs were associated with male gender, initial hypotension, and variation in mental status. Exposure was not seen to be associated with significant alterations in BMPs. Our study was limited by its small size and that all patients were from a single urban center. Future work would expand on the number of patients analyzed and collect more detailed information on clinical exam as well as co-morbidities.

KEYWORDS Cannabinoids; drug; K2

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138. Tianeptine, a poorly regulated "nootropic" with risk for abuse and physical

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Objectives: Tianeptine is a pharmaceutical that is available by prescription as an antidepressant in some countries, is controlled or banned in some countries, and is poorly regulated in others. In the United States, it is easily available for purchase as a "nootropic" from various websites without a prescription. Tianeptine was recently described as having mu opioid receptor agonist activity, suggesting a potential for both abuse and physical dependence. The objective of this study was to characterize the abuse potential and physical dependence of tianeptine based on the collective experience of one state's two Poison Control Centers (PCC).

Methods: This was a retrospective case series describing all exposures to tianeptine reported to a single state's PCC from 1/1/2000 through 4/1/2017. A single reviewer from each PCC extracted the following data from Toxicall®: patient demographics, reported dose and formulation of tianeptine, reported coingestants, vital signs, brief summary of patient's history and physical examination, and disposition.

Results: There were nine reported cases of tianeptine exposure. Seven of the nine were male. Mean age was 27 years. One case was an unintentional pediatric exposure. Three out of nine patients reported using tianeptine as a treatment for anxiety or

depression. Five out of nine cases reported abusing tianeptine. Five out of nine cases complained of symptoms after discontinuing tianeptine. Three of nine cases commented on dose of tianeptine: the unintentional pediatric exposure reported a dose of 12.5 mg; the other two cases reported abuse of 5 g daily and 10 g daily. Discontinuation symptoms reported among the five cases included anxiety, agitation, vomiting, diaphoresis, piloerection, lacrimation, and yawning. Two of nine cases were originally believed to be opioid overdoses and were administered naloxone for central nervous system depression and/or respiratory depression. In one case, naloxone administration improved the mental status and respiratory drive. In the other case, no effect was observed after naloxone administration. Five of nine cases were admitted to the hospital, and three of these cases were admitted to an intensive care unit. Outcomes reported in Toxicall® were minor in two cases, moderate in five cases, major in one case, and not reported in one case.
Conclusions: Tianeptine is an antidepressant and a mu opioid receptor agonist with risk for abuse and physical dependence. This product is poorly regulated in the United States and poses a risk to public health. Further study is necessary to understand its precise mechanism of action and need for governmental regulation.

KEYWORDS Tianeptine; drug abuse; physical dependence

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139. The dangerous internet purchase: an uncommon presentation of carbon monoxide toxicity with pulmonary edema, hemoptysis, and chemical pneumonitis

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Background: Formic and sulfuric acids are both corrosive substances that are commonly used in manufacturing. We report a patient who survived a suicide attempt after inhaling the carbon monoxide (CO) produced from mixing formic and sulfuric acids. They also have the potential to cause chemical burns and pneumonitis when inhaled. CH_2O_2(formic acid)+H_2O_2S(sulfuric acid)→ CO(carbon monoxide)+$H_2SO_2{\cdot}H_2O$ Figure 1. Chemical reaction that produces CO gas.
Case report: A 21-year-old healthy man purchased formic and sulfuric acids from a popular online shopping site. After he mixed them in a bowl in a suicide attempt, he placed his face over the bowl to inhale the formed CO. He then changed his mind and presented to the Emergency Department (ED) 1.5 h later awake and alert with frank hemoptysis. Initial vital signs were BP 110/73, HR 126, RR 32, O_2 sat 92% on room air, and T 101.4 F. He complained of chest and abdominal pain and was noted to have rhonchi on exam. He was placed on humidified oxygen, had a chest radiograph, carboxyhemoglobin level, and a pulmonary consult after a medical toxicologist was consulted through the poison center. He was intubated and ventilated within 30 min of presenting to ED due to desaturations and hemoptysis. His chest X-ray showed pulmonary edema from the caustic effects of the acids and chemical pneumonitis. He was started on levofloxacin and methylprednisolone. He had a leukocytosis of 23.37, initial ABG: pH 7.489, pCO_2 28.9, pO_2 53, HCO_3 29.1. Initial carboxyhemoglobin level was 27.4% which decreased to 3.3% and 1.6% at 2 and 25 h later, respectively. Chemistry panel was notable for a BUN 25 mg/dL and Cr 1.5 mg/dL. He was extubated 21 h after exposure but developed mild rhabdomyolysis with a CPK of 1781 mcg/L and oliguria, which was treated with IV fluids. He recovered fully.
Case discussion: We report a suicidal patient who survived from combining formic and sulfuric acid to produce CO resulting in severe toxicity. Another case reported by Scheir and Rentmeester (2016) discussed a 31-year-old man who mixed formic and sulfuric acids producing CO and was found unresponsive but survived with treatment. He also developed pulmonary injury, leukocytosis, rhabdomyolysis, and metabolic acidosis. However, he did not have hemoptysis and his pulmonary edema was due to volume overload. Both cases demonstrate that producing CO by mixing formic and sulfuric acids places patients and rescuers at risk.
Conclusions: Healthcare professionals and specialists of poison information (SPIs) should be aware of this uncommon and potentially fatal concoction, as well as caustic injury. As formic acid is not commonly used, if there is a formic acid exposure, SPIs should be sure to determine if there was also an exposure to any other strong acid, such as sulfuric acid, or a mixture of the two. This will help determine if there was a possible exposure to CO and guide management of patients, any nearby individuals, and first responders.

KEYWORDS Carbon monoxide; formic acid; sulfuric acid

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140. Refractory hypotension and death after intentional overdose of cilostazol and tamsulosin

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Background: Cilostazol, a quinolone derivative that inhibits phosphodiesterase III, is used to treat intermittent claudication. Tamsulosin, an alpha blocker, is used to treat benign prostatic hypertrophy. We report an unusual case of overdose of these two drugs that led to refractory hypotension and death.
Case report: A 72-year-old, non-English speaking male presented to the ED 5 h post-ingestion after admitting to his grandson that he had overdosed on his tamsulosin and cilostazol. His medications included those 2 and metformin. Initially he was well looking, with glucose of 222, blood pressure (BP) of 101/63 and heart rate (HR) of 96. He received a 2-L bolus of IV crystalloid, transiently raising his BP to 170/77. Within 2 h, he became agitated, confused, exhibited behavior changes, and complained of pain in his head and neck. A head CT performed revealed nothing acute. He complained of nausea which progressed to vomiting and diarrhea. He was admitted to the ICU and started on an IV infusion of crystalloid, but despite this his BP dropped to 70/40, his HR to 58, and his mental status continued to deteriorate. His BP decreased to 50/20 and norepinephrine was started. He was intubated and placed on a ventilator. Over the next 2 h, he was started on additional vasopressors including dopamine and vasopressin with no positive effect. The patient coded twice, and a full code was initiated each time. Additional medications reported as administered included calcium gluconate, sodium bicarbonate, hydrocortisone, and midazolam. A toxicology consult was offered and the therapies of lipid emulsion, phenylephrine, and methylene blue were recommended to assist with the refractory hypotension. None of

these were instituted, however, as the patient coded a third time, and was unable to be resuscitated, expiring 13 h post-ingestion.
Discussion: This patient developed hypotension that was refractory to all treatments initiated by the hospitalist during his admission. The combination of tamsulosin, an alpha 1A adrenergic blocker, with cilostazol, a drug that causes vasodilation through multiple mechanisms including phosphodiesterase III inhibition, suppression of cAMP degradation, and increase of cAMP within blood vessels, resulted in profound, refractory hypotension. While there are cautions against use of tamsulosin with phosphodiesterase five inhibitors, there are none that caution against use with phosphodiesterase III inhibitors. Therapeutic use of tamsulosin shows a peak effect at around 4–5 h post-ingestion in a fasting state, and 6–7 h if administered with food, suggesting the reason that this patient initially appeared well, but then rapidly deteriorated around 6–8 h following the overdose. No literature reports were discovered that discuss this interaction or this outcome for combining of cilostazol and tamsulosin in overdose. The deterioration after hour 6 was rapid and irreversible resulting in death 13 h post-ingestion.
Conclusions: The combination of two vasodilators such as tamsulosin and cilostazol in overdose may lead to hypotension that is refractory to standard treatments. Healthcare professionals should be aware that delayed presentation does not preclude the possibility of a rapid decline if multiple vasodilators are involved in a case.

KEYWORDS Cilostazol; tamsulosin; vasodilation

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141. Kratom from the user perspective – results from an online survey

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Background: Kratom (from the South Asian tree *Mitragyna speciosa*) use has become prevalent and a topic of discussion in the US in recent years with data suggesting an increase in prevalence of reported toxic exposures to the herbal preparation. An anonymous survey of current Kratom users evaluated self-perceived benefits and adverse effects of the extract as well as self-dosing.
Methods: The anonymous survey was administered via Kratom user websites in October 2016 until 10,000 responses were recorded. No personal health information was collected and IP monitoring was used to prevent ballot box stuffing. Only completed surveys were included in the analysis. Chi-square tests were used to compare nominal or ordinal data while *t*-test statistics with critical values at $p<.05$ compared scaled data. Demographic and health data were collected prior to self-reported use of Kratom.
Results: About 80% of respondents completed the survey and were included in the analysis. A majority of Kratom users were between the ages of 31 and 50 years, white, with middle income, and used the extract to self-treat pain and for emotional or mental conditions. After adjustment for state population, Kratom use was only significantly more frequent in Oregon and Idaho among respondents. The use of Kratom to treat symptoms of an illicit drug was more prevalent among 21–30 year old respondents. Symptom improvement was independent of weekly doses consumed which ranged from 1 to more than 48. However, the amount consumed per dose was higher for users utilizing Kratom to treat symptoms related to an illicit substance use disorder (more than 5 g per dose). Self-reported positive effects were increased energy, decreased pain, increased focus, and less depressive mood. Self-reported negative effects were nausea, constipation, dizziness or drowsiness, stomach upset, and vomiting.
Conclusions: Kratom is primarily used by a middle-aged population across the US for self-treatment of chronic pain and emotional or mental conditions which was also reflected by the self-reported positive effects. Kratom contains mitragynine and 7-OH-mitragynine which have been shown to act on opioid receptors. This may explain both the self-reported positive analgesic and adverse effects of nausea, constipation, and drowsiness. The results of this survey add to our understanding of Kratom use and its impact on the health of its users in the US. Limitations of the survey include anonymous self-reporting and distribution among current Kratom users through respective Kratom-advertising organizations that introduce bias into the study results.

KEYWORDS Kratom; epidemiolgy; online survey

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142. Extracorporeal treatments in poisonings from non-traditionally dialyzed drugs: a single center experience

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Background: Extracorporeal treatments (ECTRs) are routinely used to enhance the elimination of a limited number of toxins. A recent analysis of NPDS data showed significant use of ECTRs in patients poisoned from toxins not traditionally considered dialyzable. We hypothesized that the use of ECTRs in these cases was to treat either underlying medical illnesses or complications of the poisoning rather than for toxin removal.
Methods: Following institutional review board approval, we accessed all cases from 1 January 2000 through 16 December, 2016 from the Toxicall database of one Poison Control Center (PCC) in which ECTRs were listed for ingestions of acetaminophen (APAP), digoxin, tricyclic antidepressants (TCA), and opioids. These toxins were selected in part, based on the previously mentioned report. Data including notes fields were reviewed. A standardized tool was used to extract relevant data and accuracy of extraction was confirmed on 10% of cases. If ECTR was performed for toxin removal, the method used to determine efficacy was noted.
Results: One hundred thirty-nine unique cases met the inclusion criteria. Eleven were excluded because it was unclear whether ECTR was actually performed. An additional 36 were excluded because a traditionally dialyzable toxin was co-ingested. In the remaining 92 cases, the primary toxins involved were the following: APAP, 33; APAP/opioid combinations, 17; opioids, 16; TCAs, 2; digoxin, 24: The ECTRs used in these cases were: hemodialysis, 71; hemoperfusion, 0; CRRT, 19; MARS, 0; combined therapies, 2. Indications for ECTR were: kidney failure, 49; rhabdomyolysis, 1; acidosis, 15, fluid and electrolyte problems, 9; multiple reasons, 13; unclear, 3: In only one case, APAP was ECTR used to enhance toxin clearance. While ECTR is accepted to remove APAP in limited circumstances, in this case, the PCC had not recommended ECTR, and efficacy was not determined. One opioid poisoned

patient underwent ECTR to help preserve organ function prior to donation.
Conclusions: Over a 17-year period at a single PCC, only one patient had ECTR performed to primarily remove a toxin not traditionally considered dialyzable. In all other cases (99.1%) underlying medical conditions or complications of the poisoning confirmed that the indication for ECTR was not toxin removal. These results provide support for our hypothesis that although the absolute number of reported ECTRs are increasing in poisoned patients, this increase is not due to the misuse of ECTR in attempts to remove toxins known to be non-dialyzable. Analysis of reported NPDS statistics for the use of ECTR in toxins not traditionally dialyzable is potentially misleading. A true understanding of the indications for ECTRs can only be obtained through a detailed review of the case notes. In this single PCC, almost all uses of ECTRs in patients poisoned with toxins not traditionally dialyzable were for medical indications and complications of poisoning rather than toxin removal. A national study is underway to confirm the generalizability of these findings and address potential regional practice variations.

KEYWORDS Hemodialysis; NPDS; non-traditionally dialyzed drugs

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143. Extracorporeal treatments in poisonings from non-traditionally dialyzed drugs: a national study

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Background: Extracorporeal treatments (ECTRs) are routinely used to enhance the clearance of select toxins. A recent analysis of National Poison Data System (NPDS) data showed significant use of ECTRs in patients poisoned from non-traditionally dialyzed drugs. Additional analysis of 17 years of data from a single poison control center (PCC) confirmed that in over 99% of cases ECTRs were performed for either medical indications or complications of poisoning, and not toxin removal. In order to address potential regional practice variations, we sought to confirm these findings in a national sample of poison control centers (PCCs).
Methods: Following IRB and AAPCC approvals, NPDS data were obtained in which ECTRs were performed for ingestions of acetaminophen (APAP), digoxin, tricyclic antidepressants (TCAs), and opioids. In order to limit sample size, ambiguity and minimize variations in practice over time, only single substance exposures from the 3 most recent years of data were sampled. To prevent release of protected health information, individual PCCs were sent only the case number and year of their selected cases. Thus, data were accessed by PCC staff with rights to view the data. Each PCC was asked to review their cases including notes fields and complete a short survey that confirmed whether ECTR was performed. If ECTR was performed, the indication was requested. No protected health information was transmitted in the survey. Since the single center PCC study involved 92 cases, the target sample size for this study was at least 100 cases.
Results: Surveys were sent to all US PCCs and requested data on at total of 519 cases. One hundred and thirty-nine cases were received from 18 centers, covering the years: 2012, 33.3%; 2013, 38.5%; 2014, 28.1%. Three cases were excluded because ECTR was not performed and 2 other cases were excluded for missing data. In the remaining 134 cases, drugs involved were: APAP, 58; digoxin, 31; APAP in combined formulations with opioids or antihistamines, 20; opioids, 20. The following ECTRs were performed: hemodialysis, 95; CRRT, 30; Peritoneal Dialysis, 1; Hemoperfusion, 0; combined modalities, 8 (including one MARS case). The primary indication listed for ECRT was: kidney failure, 94; metabolic acidosis, 17; fluid and electrolyte abnormalities, 9; rhabdomyolysis induced kidney injury, 6; other/unclear, 6; toxin removal, 2 (APAP). Dialysis efficacy in one APAP case was determined by "falling levels and clinical improvement" while the other had no measure of efficacy reported.
Conclusions: A single PCC experience demonstrated that almost all uses of ECTRs in patients poisoned with non-traditionally dialyzed drugs were for medical confounding indications rather than toxin removal. These similar results obtained from 18 PCCs confirm that regional practice variations are not a cause for the increased use of ECTR described in NDPS statistics over the last decade. They also confirm that most cases (>98%) of ECTR associated with non-traditionally dialyzed drugs are performed for medical indications rather than toxin removal. Data from earlier years would be useful to characterize whether evolving trends, age and/or comorbid conditions play a role.

KEYWORDS Hemodialysis; NPDS; non-traditionally dialyzed drugs

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144. Aerotoxic syndrome: fuming about fumes while flying the friendly skies

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Background: According to the Federal Aviation Administration's Service Difficulty Reporting System, at least 0.86 flight crews per day report issues with fumes during flight requiring mechanical service. The most likely sources of in-flight fumes are believed to be engine oils and hydraulic fluids that leak into the engine due to faulty seals. Once heated, these toxic jet engine fluids combine with outside or "bleed" air and eventually released into the aircraft's passenger cabin.
Case Report 1: Three flight attendants presented to an occupational health clinic complaining of extreme fatigue, lightheadedness, headaches, dizziness, and nausea. The attendants stated they noticed a foul odor. After the 84 passenger plane emptied, the crew learned of an Exxon Mobil HyJet V hydraulic fluid engine leak. After supportive care, all were discharged after 8-h.
Case Report 2: Three flight attendants and two pilots reported an offensive smell in cabin and cockpit while on the tarmac readying for take-off. The flight crew complaints included dizziness, headaches, throat and ocular irritation, and nausea. The flight was aborted and the 139 passengers re-routed. The pilots reported the fumes were due to a Mobil Jet Oil II leak. After breathing treatments, all were released.
Case Report 3: Three flight attendants and a ground supervisor felt ill complaining of dizziness, coughing, and dyspnea while performing pre-boarding inspection of their aircraft. It was later learned that fumes resulted from an auxiliary power unit fluid leak. After being treated at a local healthcare facility, all were

discharged after 4 h. At a 6-month follow-up, all remained asymptomatic but concerned.
Discussion: Fume events typically occur during take-off and landing when the aircrafts engines can reach temperatures in excess of 500 °F, generating enough heat to create fumes if a leak is present. These fumes are best described as a foul "dirty gym sock" odor. Based on a national poison center survey targeting directors: 43% of 35 respondents were familiar with the term "aerotoxic syndrome" and 17% had at least one case of a fume event on an aircraft reported within the past 2 years. Aerotoxic ayndrome is associated with long-term, low level exposures and is not well understood, but animal models suggest inhalation of these fumes may affect multiple organ systems.
Conclusions: Repeated reports of noxious fumes being released into airplane cabins and causing symptoms in flight crews is disconcerting. The FAA needs to better address these fume events putting in place safeguards and solutions before more serious issues are realized, such as aerotoxic syndrome. Poison centers may be uniquely positioned to track and report these fume events.

KEYWORDS Aerotoxic; fume; flight

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145. Opioid prescription practices for sports related pediatric musculoskeletal injuries

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Background: The abuse and misuse of prescription opioids among adolescents has emerged as a serious concern. Opioid prescriptions for adolescents has been increasing. For adolescents, dentists, primary care and emergency medicine physicians are the leading prescribers of opioids. Participation in sports has increasingly become a larger part of society and a heavier importance placed on sports performance. Recovery from injury and pain control are important aspects in sports performance. It is unknown, however, whether aggressive pain control with opioids subjects adolescent athletes to the early risks of opioid dependence as seen among athletes in some professional sports. Therefore, the purpose of this study is to determine the opioid prescribing patterns for adolescents with musculoskeletal (MSK) injuries while playing sports in various clinical settings.
Methods: This retrospective case series reviewed patients aged 10–18 years evaluated at an urban, pediatric hospital for known or suspected musculoskeletal injury related to playing sports from September 2014 to September 2016. Data were extracted from electronic medical records based on inclusion query terms. Records for 14,172 initial visits with complete data for provider (Physician, Physician Assistant – PA, Nurse Practitioner – NP), department (ED, Orthopedics, Primary Care – PC), diagnosis (fracture, no fracture) and location of injury (upper extremity – UE, lower extremity – LE) were included. Demographics and prior opioid prescriptions were also collected and analyzed. Variables were compared using chi-squared tests and two-sample *t*-tests. Variables with significant differences in prescription practices in univariate logistic regression analysis were included in a multivariable analysis.
Results: Mean age was 13.2 years. Males received the majority of prescribed opioids (67.6%,OR 1.29; CI 1.08–1.54). Of patients receiving opioids, 79.7% had fractures while 20.3% had no fracture (OR 7.1; CI 5.81–8.68). ED providers were more likely prescribe an opioid (OR 10.33, CI 4.56–23.4 ED versus PC; OR 8.69, CI 7.15–10.57 ED versus Ortho). Opioids were prescribed in 5.9% of UE injuries, 3.6% of LE injuries, 9.4% of fractures and 1.9% of non-fracture injuries. ED providers prescribed 68.9% of the opioids in the study while seeing 27.7% of patients with MSK injuries. NPs were less likely to prescribe opioids than physicians and PAs (OR 0.49, CI 0.36–0.67 NP versus physician; OR 0.48, CI 0.37–0.62 NP versus PA).
Conclusions: For pediatric patients with sports related MSK injuries, most opioid prescriptions originated from an ED visit. The presence of a fracture and provider type also impacted opioid prescribing patterns.

KEYWORDS Opioid; adolescents; athletes

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146. Acetylcysteine regimens for acetaminophen overdose: a survey of poison center medical directors and medical toxicologists

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Background: Acetylcysteine has been used for the treatment of acetaminophen poisoning for nearly four decades. A commonly used acetylcysteine regimen is a three-bag, 21 h regimen in which half the total dose of acetylcysteine is delivered over 15 min or 1 h. This regimen has been associated with a high rate of adverse reactions including nausea, vomiting, and non-allergic anaphylactic reactions (NAARs). Recently, a two-bag, 20 h regimen has been studied demonstrating a significant reduction in adverse reactions and NAARs, and simplification of administration potentially reducing medication error. Sentiment in the US regarding the clinical advantages of the two-bag regimen is currently unknown. Therefore, the purpose of this study was to determine the recommendation preferences of acetylcysteine for acetaminophen overdose among practicing medical toxicologists and poison center (PC) medical directors.
Methods: A six question, cross-sectional survey was distributed to 51 poison center medical directors and 193 medical toxicologists. The survey covered the scenario of acute acetaminophen overdose and the various acetylcysteine regimens available for treatment. Descriptive statistics were performed.
Results: An invitation to participate in this survey was distributed to 51 poison center medical directors and 193 medical toxicologists. Among both PC medical directors and medical toxicologists, the majority responded that they primarily recommend intravenous (IV) acetylcysteine ($N = 30$, 75.0% and $N = 145$, 75.1%, respectively). PC medical directors responded preferentially recommending the three-bag acetylcysteine regimen ($N = 28$, 70.0%) and medical toxicologists responded recommending it in 66.8% of cases ($N = 127$). PC medical directors and medical toxicologists consistently recommend the two-bag regimen in the minority of cases ($N = 1$, 2.5% and $N = 2$, 1.1%, respectively). Among those who have recommended the two-bag regimen at least once, for both PC medical directors and medical

toxicologists fewer administration errors was the highest frequency response for the reason it was recommended ($N = 4$, 30.8% and $N = 24$, 24.0%, respectively).
Conclusions: The majority of PC medical directors and medical toxicologists in the US recommend the IV, three-bag regimen of acetylcysteine for acetaminophen overdose. The minority of survey respondents consistently recommend the two-bag regimen. Of those who have recommended the two-bag regimen, the highest frequency response was fewer administration errors as the reason for this choice. Clinicians should be aware of the existing data demonstrating a reduction in adverse reactions associated with the two-bag regimen as well as its simplification of administration.

KEYWORDS Acetaminophen; acetylcysteine; two-bag regimen

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147. Abuse of high-dose loperamide along with cimetidine to potentiate the "high"

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Background: Loperamide is an over-the-counter anti-diarrheal that slows intestinal peristalsis through its effects on peripheral μ-receptors. Loperamide was previously thought to be free of abuse potential due to its rapid metabolism, limited oral bioavailability, and poor blood brain barrier penetration. Nevertheless, loperamide abuse is becoming increasingly common with reports of associated life-threatening cardiac conduction disturbances and dysrhythmias. Online forums discuss the practice of co-ingesting substances which alter metabolism or transport of loperamide to enhance its euphoric effects. We describe the case of a patient who experienced prolonged recurrent life threatening cardiac arrhythmias and cardiac arrest in the setting of loperamide abuse while co-ingesting the medication cimetidine, a known inhibitor of loperamide metabolism.
Case: A 40-year-old woman with history of opioid abuse presented to the emergency department (ED) following an unwitnessed syncopal episode. Electrocardiogram showed normal sinus rhythm with a prolonged QTc of 583. Her laboratory workup was unremarkable. While in the ED, the patient developed cardiac arrest requiring intubation and cardiopulmonary rescucitation (CPR). She experienced recurrent episodes of torsades de pointes and ventricular tachycardia refractory to treatment with lidocaine, sodium bircarbonate, and repeated cardioversion. The patient's dysrhythmias were ultimately controlled on hospital day 2 after transvenous pacemaker placement. Overdrive pacing was continued for 8 d. The patient's QTc interval normalized after 2 weeks of observation. The patient admitted to chronic abuse of high-dose loperamide along with cimetidine to potentiate the "high."
Discussion: Patients are increasingly abusing loperamide in combination with several commonly used drugs to enhance its euphoric effects. These drugs may act synergistically to increase gastrointestinal absorption, decrease loperamide metabolism, or increase blood brain barrier penetration. Common examples include CYP3A4 inhibitors, CYP2C8 inhibitors, and P-glycoprotein inhibitors. This practice may increase loperamide blood levels and the risk of serious and prolonged cardiac events. Our patient likely co-ingested cimetidine, a CYP3A4 inhibitor, to slow loperamide metabolism and maximize its potential euphoric effects. Concomitant cimetidine use may have contributed to prolonged cardiac effects.
Conclusions: Loperamide cardiotoxicity represents a growing public health threat. Health care providers should be aware of the growing trend for drug users to combine multiple drugs with loperamide which may act synergistically to increase loperamide concentrations and the risk and duration of serious cardiac events.

KEYWORDS Loperamide misuse; intentional co-ingestion; drug synergy

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148. Truth is stranger than Pulp Fiction: a shot of adrenaline and a broken heart

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Background: Epinephrine is a commonly used medication administered for life-threatening conditions. Toxicity is usually the result of iatrogenic medication errors. Cases of intentional epinephrine poisoning are exceedingly rare. Overdose causes increased heart rate and cardiac contraction that can lead to myocardial infarction, cardiac arrest, and potentially lethal arrhythmias. We present a case of acute reversible myocardial ischemia and left ventricular dysfunction in the setting of self-inflicted epinephrine poisoning.
Case report: A 29-year-old female with extensive past psychiatric history including borderline personality disorder and multiple prior suicide attempts came to the Emergency Department (ED) for reported seizure activity eventually attributed to psychogenic non-epileptic seizures. On initial evaluation, her vital signs and physical examination were unremarkable. A few hours later, the patient broke into the ED crash cart and injected 1mg of epinephrine and 50mg of Benadryl into her neck with intent to end her life. She immediately developed chest pain, shortness of breath, and diaphoresis. Her heart rate increased to 150/min and blood pressure dropped to 73/38 mmHg. She was tachypneic, mildly hypoxic with O2 saturation 92%, and demonstrated rales on lung auscultation. A 12-lead EKG done immediately after the event showed regular tachycardia and lateral ST depressions. A chest X-ray revealed diffuse pulmonary edema. An echocardiogram showed depressed left ventricular systolic function with an ejection fraction (EF) of 20% and akinesis of the basal and mid segments of the left ventricle with sparing of the cardiac apex. Troponin I levels were elevated at 0.07 ng/mL and rose to a peak of 5.68 ng/mL at 15 h but eventually returned to normal. The patient was placed on oxygen and diuresed with intravenous furosemide. She was admitted to the ICU and gradually improved. A repeat echocardiogram obtained 48 h after the episode demonstrated improved systolic function with normal EF and chest X-ray showed resolution of pulmonary edema. On hospital day 3, she was discharged to the care of psychiatry in stable condition.
Discussion/conclusions: Catecholamine cardiotoxicity is rather uncommon but a serious and potentially lethal complication of epinephrine overdose. The pattern and time course of myocardial dysfunction in our patient is consistent with prior reports in the literature. The majority of prior cases have been the result of medical errors. To our knowledge, this is the first reported case of intentional epinephrine poisoning resulting in profound reversible myocardial dysfunction.

KEYWORDS Epinephrine toxicity; myocardial dysfunction; intentional ingestion

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149. Dinitrophenol exposures reported to a statewide poison control system

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Background: Dinitrophenol (DNP) is a mitochondrial uncoupling agent with potent toxic effects including cardiac dysrhythmias, acidosis, seizures, hyperthermia, and multiple organ failure. It is banned for human consumption by the Food and Drug Administration (FDA) but online sales of DNP as a weight loss agent and its many industrial uses have led to human exposures. This study aims to characterize DNP exposures reported to a statewide poison control system.
Methods: This was a retrospective, IRB-exempt study of deidentified cases which met coded or free text search for the term "dinitrophenol" between 1997 and 2016. Cases were excluded if the following criteria were met: information-only calls, non-human ingestion, wrong substances, and cases with no clinical data. Descriptive statistics was performed on the abstracted data using IBM SPSS.23 (SPSS Inc., Chicago, IL).
Results: There were 27 exposures identified. Ages ranged from 15 to 55years old (a median age of 33 years), and 23 (85%) patients were male. One-third of the exposures occurred in 1997, and the incidence slowly declined to an average of 1.5 cases/year. Sources and types of the DNP-containing products can be found in Table 1. Exposure intent varied, with nine cases of occupational exposure, six cases of adverse effects, five cases of environmental exposures, four cases of intentional misuse, and one case of self-harm. The adversely effected systems are listed in Table 2. The majority of exposures lead to no/minor outcomes (nine cases), while three cases had moderate effects, two cases had major effects, and there was one reported death. The single reported death occurred in a 27-year-old male who ingested an unknown amount of a dinitrophenol bodybuilding/weight loss supplement in a suicidal gesture. The patient presented to the emergency department awake, tachycardic (pulse 140s), hypertensive (blood pressure 190/80) and diaphoretic. Within an hour, the patient deteriorated with a rapid rise in body temperature. He then went into asystole and cardiac arrest and expired despite aggressive cardiopulmonary resuscitation measures. Public health investigation was done, confirming that the DNP was obtained via an online source originating in Eastern Europe.
Conclusions: DNP toxicity can be profound and rapid as observed in the reported death, such that clinicians should be aware of this type of exposure. Early decontamination and aggressive supportive measures should be instituted early in the course of a severe overdose.

KEYWORDS DNP; dinitrophenol; poison control center

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TABLE 1. Type of DNP Exposures

Type	Exposures; N = 27cases
Herbal Supplements	11 cases (40.7%)
Herbicide	8 cases (29.6%)
Laboratory Chemicals	2 cases (7.4%)
Explosives	2 cases (7.4%)
Fungicides	2 cases (7.4%)
Insecticides	1 case (3.7%)
Paint	1 case (3.7%)

TABE 2. Adverse Effects

Adverse Effect/Intervention	Exposures; N = 27 cases
Dermatologic*	13 cases
Cardiac	5 cases
Respiratory	4 cases
Metabolic	3 cases
Central nervous system	6 cases
Gastrointestinal	1 case
Ocular	1 case
* These cases were mostly dermatologic exposures	

150. Kratom exposures reported to a statewide poison control system, 2007–2016

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Background: Kratom is a Southeast Asian plant with psychoactive effects ranging from stimulation to sedation as a result of actions at opioid and NMDA receptors. Reports of kratom use are increasing in popularity for both recreational use and as a detoxification agent for opioid withdrawal. This study characterizes the use and clinical effects of kratom as reported to a statewide poison control system.
Methods: This was a retrospective, IRB-exempt study of deidentified cases which met coded or free text search for the term "kratom" between 2007 and 2016. Cases were excluded if the following criteria were met: information-only calls, non-human ingestion, wrong substances, and cases with no clinical data. Descriptive statistics was performed on the abstracted data using IBM SPSS v.23 (SPSS Inc., Chicago, IL).
Results: A total of 50 cases met the inclusion criteria, of which 35 (70%) were male between 17 and 59 years old. The majority of these exposures were intentional for self-harm, self-medication, or recreational purposes (44 cases), two cases were accidental pediatric ingestions, and four cases unknown/unlisted intent. The incidence increased over time, with 38% of cases occurring in the final year of the date range (2016). Outcomes: 19 cases (38%) experienced moderate/severe outcomes with 13 (26%) treated and released from the emergency department, four (8%) admitted to a critical care unit, one (2%) admitted to a medical floor, and

one (2%) lost to follow-up. Major adverse effects by system included: 33 cases (66%) central nervous system effects (altered mental status, agitation, seizures, tremors, confusion, hallucinations), 17 cases (34%) cardiac effects (tachycardia, chest pain, hypertension, conduction disturbances), 12 cases (24%) gastrointestinal effects (diarrhea and vomiting), 10 cases (20%) metabolic effects (acidosis, electrolyte or chemical abnormalities), and seven cases (14%) of hyperthermia.
Conclusions: Kratom exposures demonstrated a dramatic increase based on calls to a large statewide poison control system over the last 9 years, likely realted to its use as an opioid substitute or detoxification agent. A broad range of toxic effects was noted. More investigations are needed to delineate a dose-response effect and specific treatments for kratom toxicity.

KEYWORDS Kratom; Mitragyna; poison control system

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151. Aluminum phosphide pesticide use results in deaths of four family members

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Background: Aluminum phosphide, often used as a grain fumigant, is a restricted pesticide that, when exposed to moisture, releases toxic phosphine gas. Acute exposure to phosphine results in interference with enzymes and protein synthesis and has the greatest effect on the heart and lungs. Toxicity can result in pulmonary edema, circulatory collapse, and cardiac arrest.
Case report: The father in the home of a family of ten, obtained Weevil-Cide (aluminum phosphide) pellets from an undisclosed source and spread the pellets under his mobile home in an effort to eliminate mice. Soon afterwards family members began complaining of an odor in the home. Four days later, family members complained of abdominal pain and vomiting, were seen in the emergency room, and were discharged with presumed "flu". That evening, the father attempted to wash away the pellets using a water hose. Early the following morning, an older child awoke and found that she could not awake some family members so she called 9-1-1. All occupants were ill and some had difficulty breathing. Carbon monoxide (CO) was initially suspected by first responders, but no CO was detected. Two responding police officers found a child in full cardiac arrest and CPR was initiated. The HAZMAT team was dispatched. Although a language barrier was present, at least one occupant suspected that the pesticide was responsible for illnesses and shared this information. All victims but one were transported to the ED. The 7-year-old child was pronounced dead at the scene and an 11-year-old arrived in full cardiac arrest. The other victims,though ill, could communicate, although the parents required translators. The father had disposed of the pesticide canister in the trash bin behind the home. It was recovered and had contained aluminum phosphide, confirming phosphine as the agent of exposure. Less than 1 h from arrival, the 9-year-old child arrested and quickly expired. The 17-year-old arrested 3 h after arrival and quickly expired. The 45-year-old mother deteriorated more gradually. At the poison center's recommendation, she was taken to the cath lab where an Impella circulatory assist device was inserted. The poison center located the nearest receiving facility offering adult ECMO/ECLS support and facilitated her transport to this facility. The mother required prolonged supportive care but was eventually discharged to the family's temporary home. The remaining five occupants of the home were treated and eventually released within 3–4 d. Also of note,one of the family's outdoor dogs expired during whelping approximately 7 d following the incident while in the custody of animal control. Necropsy indicated the presence of diphacinone, indicating exposure to an anticoagulant pesticide. Hepatic central lobular cytoplasmic vacuolar degeneration was also noted, but judged as "minimal".
Case discussion/conclusions: Aluminum phosphide pesticide, although restricted, may still find its way into homescreating an extreme hazard for occupants, particularly children. In the eventof phosphine gas exposure, providers should urgently prepare for the initiationof aggressive hemodynamic support.

KEYWORDS Phosphine; aluminum phosphide; poisoning

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152. Keeping pace in the NPS race: opioids and benzodiazepines in samples submitted to a large reference laboratory

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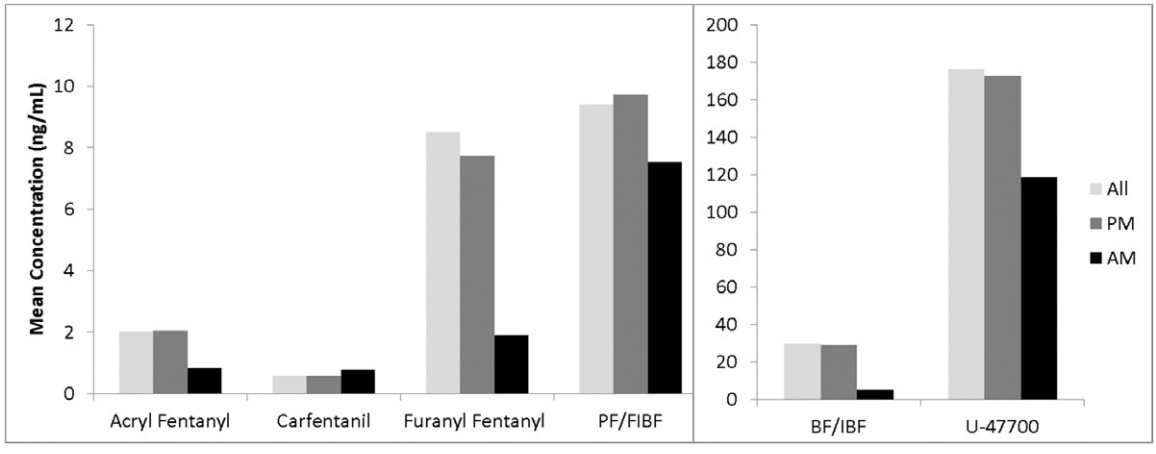
Background: Novel psychoactive substances (NPS) continue to challenge clinicians, medical toxicologists, poison control centers, law enforcement, death investigators, and laboratories. "Designer"



	% POS	Range (ng/mL)	Mean ± std dev (ng/mL)
Opioids			
4-Methoxybutyryl Fentanyl	0.0	-	-
4-Methylphenethyl Acetyl Fentanyl	0.0	-	-
Acryl Fentanyl	10.8	0.11 - 29	2.01 ± 3.21
AH-7921	0.0	-	-
alpha-Methyl Fentanyl	0.0	-	-
Beta-hydroxythiofentanyl	0.0	-	-
Butyryl Fentanyl/Isobutyryl Fentanyl (BF/IBF)*	4.8	0.12 - 180	29.95 ± 38.2
Carfentanil	19.9	0.1 - 14	0.58 ± 1.01
para-Fluorobutyryl/fluoro-isobutryl fentanyl (PF/FIBF)*	12.1	0.1 - 164	9.4 ± 24.22
Furanyl Fentanyl	45.1	0.1 - 710	8.51 ± 35.92
MT-45	0.0	-	-
ortho-Fluorofentanyl	0.1	2.4	-
para-Fluorofentanyl	0.5	0.1 - 0.29	0.18 ± 0.07
U-47700	13.7	0.2 - 3800	176.34 ± 419.73
U-50488	0.0	-	-
Valeryl Fentanyl	0.0	-	-
Benzodiazepines			
Etizolam	44.0	2.9 - 1100	131.4 ± 236.8
Flubromazolam	8.3	7.4 - 230	76.4 ± 74.7
Flubromazepam	9.2	20 - 7900	1271 ± 2364.3
Meclonazepam	0.9	10	-
Nifoxipam	0.0	-	-
Phenazepam	0.9	100	-
Pyrazolam	0.0	-	-
Bromazepam	6.4	5.7 - 430	198.4 ± 198.3
Clonazolam	2.8	5.2 - 13	9.7 ± 4.1
Delorazepam†	22.9	5 - 330	88.3 ± 82.2
Deschloroetizolam	0.0	-	-
Diclazepam	12.8	6.4 - 110	40.2 ± 30.9

opioids and benzodiazepines are examples of the classes of NPS that have gained popularity in the past several years. "Designer" opioids include analytes such as U47700 which was developed by a pharmaceutical company but never brought to market and compounds that are structurally related to fentanyl while the benzodiazepine group includes drugs that are used in other countries such as Etizolam and truly novel substances such as Flubromazepam. There is a dearth of data with respect to concentrations detected in biological samples after exposure and little information available to aid in interpretation of the results.

Methods: In order to routinely monitor, the appearance of NPS in submitted samples was developed and based on the prevalence of specific substances methods to quantify the results were validated. These data were then evaluated to identify the gender and age of users, concentration ranges of positive results, and determine if these ranges differ in antemortem (AM) and postmortem (PM) samples. Data from quantitative analyses of blood, serum or plasma from the start date of quantitative testing –31 March 2017 – were exported from the Laboratory Information Management system along with available demographic information.

Results: Between October 2016 and March 2017, 1425 blood, serum, and plasma samples were analyzed for designer opioids and 109 were analyzed for designer benzodiazepines. The table includes the analytes included in both tests, % of positive samples, concentration ranges and average concentrations. All samples submitted by medical examiner/coroner's offices or with a sample source labeled aortic, cardiac, femoral, or central were considered PM and any sample submitted for cases involving driving-under-the-influence were considered AM. The majority of samples were post-mortem; 93% and 80% for opioids and benzodiazepines, respectively. For all analytes, the concentration ranges for AM and PM cases overlapped. Overall, cases that were positive for opioids contained and average of 1.6 analytes and there was no difference between AM and PM Cases, but 12% of positive PM cases contained 3 or 4 different analytes while only 2 AM cases had 3 analytes. The figure displays the average concentration for all cases, PM and AM samples for opioid. It should be noted that an AM case with 770 ng/mL furanyl fentanyl was not included in the data when calculating the average AM concentration. There were too few AM benzodiazepine cases for a meaningful comparison.

Conclusions: The available data provide important quantitative information for analytes which several analytes which do not have any published data provided. However, the majority of cases tested in this laboratory are from PM cases. This may be due to an overall lack of testing in individuals who present to the emergency department (ED) and are treated and released. Data will be updated as more samples are analyzed.

KEYWORDS Novel psychoactive substances; fentanyl analogs; opioid abuse

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153. Blood heavy metals in the users of different nicotine delivery products

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Background: Heavy metals, including cadmium, arsenic, lead, and chromium may be found in cigarette products both in the US and internationally. The presence of these metals has been demonstrated in mainstream and side-stream smoke. In addition to tobacco smoke, these metals are also classified as human carcinogens by the International Agency for Research and Cancer (IARC). The objective of this study was to query the National Health Assessment and Nutrition Examination Survey (NHANES) database to analyze blood levels of heavy metals in smokers using a variety of nicotine delivery products (NDP) including e-cigarettes, hookah, cigarette smokers, pipes, cigar, or a combination of methods.
Methods: The NHANES database was queried from 2013 to 2014 for the use of NDP and blood heavy metal levels. Inclusion criteria included individuals 18 years or old with blood heavy metal levels and who completed the tobacco questionnaire. Blood metal levels were analyzed for users of each type of NDP including e-cigarettes, hookah, cigarette smokers, pipes, cigar, or a combination of methods. The whole blood specimen was analyzed by mass spectrometry. A Kruskal–Wallis analysis was performed to determine if blood metal levels varied by the type of NDP used.
Results: Mean age of the population analyzed was 50.6 years (range 18–80 years). Blood cadmium and inorganic mercury varied significantly by the type of NDP used. Hookah smokers had the highest concentrations of both metals compared with other NDPs. Blood lead, selenium, and manganese levels did not vary significantly with the type of NDP used. Participants only used e-cigarettes in combination with another NDP.
Conclusions: To our knowledge, this is the first retrospective epidemiological study to report blood heavy metal levels among smokers with different type of NDPs. The use of combination of different methods of smoking may affect the levels of heavy metals in the blood. Hookah smoking is associated with increased blood cadmium and inorganic mercury levels compared with the other NDPs.

KEYWORDS Metal levels; smokers; hookah

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154. Mushroom exposures in the United States reported to the Toxicology Investigator's Consortium (ToxIC) registry

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Objective: The objective of this study was to characterize cases involving mushroom exposure as reported in the Toxicology Investigators Consortium (ToxIC) registry.
Methods: The ToxIC registry was queried for cases involving mushroom exposure from January 2010 to September 2016. We used descriptive statistics to report the distribution of age, sex, type of mushroom exposure, clinical presentation, and therapeutic interventions.
Results: A total of 44 cases involving mushroom exposures were identified during the 6-year study period. Exposures occurred in persons ranging from age 3 to 76 years, with the median age being 28 years, and were more common in males (55.3%) than females (38.3%). The majority of cases(56.8%) were intentional in nature, with the primary reason (12 cases) for intentional use being "to get high." The most commonly identified mushrooms were Psilocybe spp. (20.4%), Amanita phalloides (6.8%), Amanita muscaria (2.8%), and Ganoderma spp. (2.27%), although a specific mushroom was not known in most cases (68.2%). Clinical symptoms were present in 86.4% of cases. The most commonly reported symptoms were hallucinations (22.7%) and agitation (27.7%). Hallucinations occurred more frequently in conjunction with Psilocybe (42%) exposure, while hepatotoxicity was reported most frequently with exposure to Amanita phalloides (66.7%). Serotonin syndrome was diagnosed in two cases involving Psilocybe mushroom exposure. The most commonly reported interventions were decontamination by activated charcoal (4.5%), symptomatic relief with benzodiazepines (25%), and *N*-acetylcysteine for hepatotoxicity in six cases (13.6%).
Conclusions: We report frequency descriptive statistics for mushroom poisoning as reported to the ToxIC registry from 2010 to 2016. Limitations of our study include the small number of mushroom exposures reported to the registry.

KEYWORDS Mushroom; hepatotoxicity; *N*-acetylcysteine

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Heavy metals	Hookah	Smoker	Cigar	Pipe	Combination of NDPs	None	P-value
Lead	1.23ug/dL	1.70ug/dL	2.43ug/dL	1.37ug/dL	1.46ug/dL	1.54ug/dL	0.44
Cadmium	1.74 ug/L	1.10 ug/L	0.43 ug/L	0.26 ug/L	0.98 ug/L	0.40 ug/L	<0.001
Selenium	192.78 ug/L	194.85ug/L	193.22ug/L	188.19ug/L	191.90 ug/L	199.00ug/L	0.35
Manganese	8.19 ug/L	9.76 ug/L	8.11 ug/L	9.20 ug/L	8.83 ug/L	9.88 ug/L	0.06
Mercury, inorganic	0.44 ug/L	0.23 ug/L	0.22 ug/L	0.19 ug/L	0.21 ug/L	0.27 ug/L	<0.001

155. Impact of recreational marijuana legalization on synthetic cannabinoid use

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Background: Synthetic cannabinoid receptor agonists (SCRAs) were initially viewed by some as a legal alternative to plant marijuana. Due to the unpredictable and sometimes serious health effects of SCRAs, various forms of legislation have been instituted in an attempt to curb their availability and use. However, modifications to their chemical composition and targeted marketing have resulted in continued availability. Since some of the historic appeal of SCRAs was as an alternative to marijuana, we hypothesized that legalization of recreational marijuana (RM) by some states might decrease the demand for SCRAs. The purpose of this study was to determine if there is a relationship between the legal status of RM and the incidence of SCRA exposures based on National Poison Data System reports.
Methods: Data on SCRA exposure cases were requested from the American Association of Poison Control Centers' (AAPCC) National Poison Data System from 1/1/2011 through 12/31/2016. Cases were broken down by state and by year in order to compare states with and without legalized RM. During the study period, legalized RM became effective in Colorado, Washington, Oregon, Alaska, and Washington, DC. Negative binomial models were used to determine whether there was a difference in the rate of SCRA exposure by legalization status over time. The total number of calls to the PC was used to normalize the rate.
Results: During the study period, 29,044 SCRA exposures were reported to PCs. Annual exposure cases nationwide declined from 6968 in 2011 to 2668 in 2013 and peaked at 7797 in 2015. When considered by state, SCRA cases declined in Washington after RM legalization (December 2012) from 175 cases in 2011 to 28 in 2016 (p=.017). A similar decline occurred in Oregon (RM legalized July 2015) from 39 SCRA cases in 2011 to 14 in 2016 (p=.012). However, there was not a statistically significant change in SCRA cases for Colorado, Alaska, or Washington, DC. When combining states with and without legalized RM over the study period, there was no significant difference between the groups with regard to frequency of SCRA cases reported to PCs (p=.41).
Discussion: Since 2011, there have been sporadic outbreaks of SCRA intoxication in a number of regions around the US including states with and without legalized RM. Factors influencing the timing and location of these events are likely complex and not fully understood. This study was limited by the fact that PC SCRA cases obtained from AAPCC were provided by year, and changes in RM legal status sometimes became effective mid-year. Additionally, individual state numbers were low and might reflect underreporting of SCRA exposures to PCs.
Conclusions: There appears to be no correlation between the frequency of SCRA exposures reported to poison centers and legal status of recreational marijuana. Additional study may be warranted to better understand and address the ongoing interest in SCRAs as drugs of abuse.

KEYWORDS Synthetic cannabinoid; marijuana; poison centers

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156. Successful treatment of acetaminophen/iron-induced fulminant hepatic failure with acetylcysteine, deferoxamine, and early transplantation

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Background: Although rare, combined overdose of acetaminophen (APAP) and iron appears to be particularly dangerous. A small case series (Audimoolam, *Transpl Int* 2011) suggested high mortality despite N-acetylcysteine (NAC), deferoxamine (DFO), and transplantation. We report a patient with fulminant hepatic failure (FHF) successfully treated with NAC, DFO, and early transplant.
Case report: An 18-year-old female presented with nausea and vomiting after intentional ingestion of ibuprofen, iron (unknown formulation), and Midol. She was alert with stable vital signs and diffuse abdominal tenderness without rebound. Initial lab results included APAP 52 mcg/mL (reportedly 4 h post-ingestion), iron 423 mcg/dL, AST 23 U/L, ALT 18 U/L, creatinine (Cr) 0.92 mg/dL, and negative abdominal film. The patient was treated with supportive care. The next day she had persistent vomiting. Repeat labs (23 h after initial) included AST 1989, ALT 1704, bilirubin 3.4 mg/dL, and INR 9. The patient was started on NAC, given fresh frozen plasma, and transferred to a regional transplant center (RTC). DFO was started after transfer and continued for 36 h. Upon arrival at the RTC the patient remained alert with BP 117/59, HR 112, and T 36.6. Labs included AST 7476, ALT 6720, lactate 15.7 mmol/L, APAP <10, iron 322, and INR 3.5. NAC was continued. The patient was evaluated and listed for transplant within 18 h of transfer. On day 3, she had worsening encephalopathy with decerebrate posturing and seizure activity. She was intubated and had a negative head CT. Liver transplant was performed on day 5. The patient required repeat surgery the same day for evacuation of 1500 mL clot and ligation of the splenic artery. The explant showed acute hepatitis with extensive bridging necrosis, cholestasis, and marked hepatocellular damage consistent with drug-induced liver injury. On POD1, mental status did not improve. Repeat CT showed cerebral edema. This was treated with permissive hypertension and mannitol. Hospital course was complicated by kidney failure requiring dialysis, thrombocytopenia, and bacteremia. Kidney function recovered (Cr 2.7 mg/dL) such that dialysis was no longer needed. The patient was discharged home on day 36 with normal mental status.
Case discussion: Concomitant ingestion of APAP and iron may subject the liver to a "double hit," targeting different hepatic zones and making regeneration less likely. In this case, treatment delay due to inaccurate history regarding ingestion time likely exacerbated the patient's liver failure.
Conclusions: FHF due to combined APAP and iron overdose is uncommon but is associated with high mortality. In this case the patient recovered with NAC, DFO, and early liver transplantation.

KEYWORDS Acetaminophen; iron; liver transplant

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157. Massive caffeine overdose treated successfully with intensive supportive care and high flux haemodialysis

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Background: Caffeine is a xanthine derivative similar to theophylline. Many health stores sell oral tablets as energy and exercise supplements. We report a case of ingestion of 40 g caffeine, leading to seizures and cardiac arrest.
Case report: A 32-year-old man with no significant past medical history was brought to the emergency department (ED) by ambulance following an acute ingestion of 200 × 200 mg caffeine tablets dissolved in water. Initial vitals with emergency medical services (EMS) included blood pressure 88/41 mmHg, heart rate 88 beats/min (regular), O_2 saturation 98%, and GCS 13. Dimenhydrinate 50 mg IV was given by EMS for emesis. Sixty minutes post-ingestion, the patient lost pulses during ED triage. Return of spontaneous circulation occurred after 18 min of CPR and four defibrillations for ventricular fibrillation and ventricular tachycardia. Post-resuscitation ECG showed atrial flutter with a corrected QT interval (QTc) of 566 ms. Several brief seizures followed responding to benzodiazepines. Oral activated charcoal (AC) was administered. The patient was admitted to ICU on a phenylephrine infusion for refractory hypotension. Beta-antagonists (esmolol, propranolol) were considered for refractory hypotension, although not required. High flux haemodialysis (HD) was initiated for severe caffeine toxicity 3.5 h after ingestion and continued for 6 h. Serum caffeine concentrations pre- and post-dialysis were 125 μg/mL (641 μmol/L) and 65 μg/mL (333 μmol/L), respectively. There were no further dysrhythmias or seizures post-dialysis and QTc one day later was 458 ms. The patient was extubated after one day in ICU; he was alert with normal neurologic function. On day 2, he was transferred to a medical ward and discharged from hospital on day 7.
Case discussion: Caffeine toxicity and fatality occurs at doses beyond 50 mg/kg and 200 mg/kg, respectively. Our patient consumed 40 g of caffeine (570 mg/kg) with serum concentration well above documented lethal levels. Absorption was likely accelerated by ingesting a solution of caffeine leading to seizures and cardiac arrest within 60 min. The patient was defibrillated, then stabilized with phenylephrine until HD rapidly cleared serum caffeine to less toxic levels. High flux HD resulted in reduced caffeine half-life in our patient (approximately 5.9 h) compared with previous large caffeine ingestion without extracorporeal elimination (16 h) and similar half-life in a patient who received combined charcoal haemoperfusion and HD (4.5 h).
Conclusions: This case demonstrates effective treatment of a massive caffeine overdose with intensive supportive care and rapid high flux HD, leading to survival with normal neurologic function.

KEYWORDS Overdose; caffeine; hemodialysis

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158. Loperamide misuse to avoid opioid withdrawal: high doses, high risk

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Introduction: Loperamide is a readily accessible non-prescription medication that is emerging as an opioid substitute, used to alleviate the symptoms of acute opioid withdrawal. As the opioid epidemic evolves, loperamide exposures are increasing. The objective of this study was to determine the clinical characteristics of patients with loperamide toxicity.
Methods: The ToxIC registry, a nationwide, prospectively collected cohort of patients evaluated by medical toxicologists was searched from November 2011 to December 2016 for patients in which loperamide was listed as a substance of exposure. Each identified record was reviewed by several investigators to determine the circumstances, dose, clinical presentations, treatment, and outcomes associated with loperamide use.
Results: Twenty-six cases were identified, and both the number and the relative proportion of cases increased progressively (Figure 1). The median age was 27 (range 2–89, IQR 17.5, 36) and 54% were male. Race was identified in 46% ($n = 12$) and was predominantly Caucasian ($n = 10$, 83%). Of cases with known intent ($n = 18$), 12 (67%) were misuse/abuse, three (17%) were self harm/suicide, and three (17%) were pediatric exploratory ingestions. Specific circumstances for misuse/abuse included taking higher doses than labeled ($n = 7$), attempting to avoid withdrawal ($n = 6$), and abuse (gaining a pleasurable sensation ($n = 4$)). The dose was reported in nine cases and ranged from 4 (pediatric exploratory ingestion) to 400mg. In patients seeking to avoid withdrawal, doses were 160–400 mg/d; the most common reported dose was 200mg. ECG abnormalities included 10 cases of prolonged QTc (>500 ms), which consisted exclusively of misuse/abuse ($n = 6$) and self-harm ($n = 1$) exposures. Other ECG findings: six prolonged QRS (>120 ms), two 1st degree AV block. Ventricular dysrhythmias were reported in seven cases (27%), five of which were single agent exposures. All but one had prolonged QTc, with a range of 566–749 ms; all patients with dysrhythmias in which dose was reported ingested 200 mg or greater. Reported QTc values were 464–749 ms. When treatment was reported (17 patients), the most common were naloxone/nalmefene ($n = 6$, 23%), sodium bicarbonate ($n = 4$, 15%), intubation with ventilatory management ($n = 4$), and pacemaker ($n = 4$). There were no deaths.
Conclusions: The majority of patients in this cohort had loperamide toxicity due to misuse/abuse, in line with national trends. In patients taking loperamide to avoid withdrawal, doses in excess of 100mg were repeatedly observed. When taken in large doses, particularly those exceeding 200mg, loperamide may cause significant cardiovascular effects, including QT prolongation and ventricular dysrhythmias.

KEYWORDS Loperamide; substance abuse; cardiac arrhythmia

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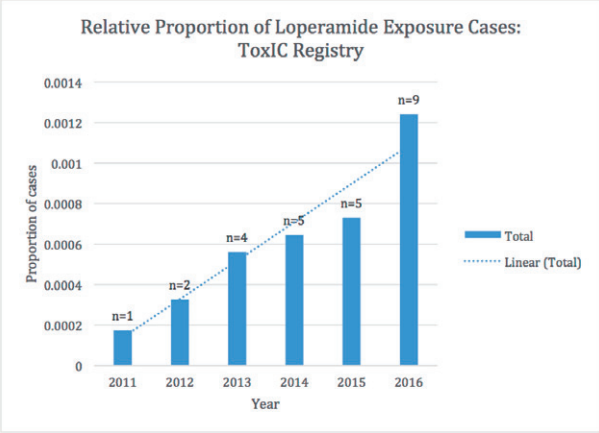

Figure 1. Relative Proportion of Loperamide Exposure Cases: ToxIC Registry.

159. Limited opioid withdrawal with utilization of transdermal buprenorphine to bridge to sublingual buprenorphrine/naloxone: a case series

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Background: Buprenorphine/naloxone is an effective and safe treatment option for opioid use disorders (OUD). As a partial opioid agonist, the degree of potential respiratory depression is minimal compared with other available opioid substitution therapies (OST) or continued opioid use. A pre-requisite period of moderate withdrawal when transitioning between existing full opioid agonist therapy (OAT) and buprenorphine/naloxone is a major barrier for treatment initiation and is often considered unacceptable. By introducing buprenorphine in low doses (buprenorphine 5mcg/h or 20mcg/h transdermal (TD) = 0.12mg–0.48mg/24h) for an average of 12–48 h to a patient still on full OAT, slow displacement and preferential occupancy of unoccupied mu-opioid receptors can limit the sudden displacement that a typical initiation dose (buprenorphine 2–4mg sublingual) may precipitate and may limit the extent of withdrawal. Benefits may also extend to facilitating the tolerability of admission in hospitalized patients with OUD, who are otherwise at high-risk of leaving hospital to use. To date, this method has not been described in the inpatient population.

Methods: Eight patients were identified by St. Michael's Hospital Addictions Consultation service from 1 January 2015 to 29 December 2016. These patients had current OUD or opioid physical dependence, admission requiring inpatient stay for delivery of primary treatment and apprehension for initiating buprenorphine/naloxone due to pre-requisite opioid withdrawal.

Results: The baseline characteristics are summarized in Table 1. One patient was on methadone 102mg daily and two patients were on high-dose (200–800 Morphine Equivalent Daily Dose (MEDD)) or ultra-high dose (>1000 MEDD) opioid therapy; their estimated use was 800 MEDD and 1572 MEDD, respectively. Two of these patients underwent intentional opioid tapers prior to patch initiation. The average opioid dose prior to patch application was 370.6 MEDD. Seven patients were bridged with buprenorphine 20mcg/h patch and one with 5 mcg/h patch. Six patients were initiated on sublingual buprenorphine/naloxone after 12–48h of patch application. The sublingual initiation of two patients was delayed >48h due to reasons unrelated to the protocol.

Table 1: Baseline characteristics

Variables	N=8
Age (mean years +/- standard deviation)	47.5 +/- 11years
Male	37.5%
Previous OUD diagnosis	63%
Previous pharmacologic OST	50%
Duration of opioid use (years)	10 years
Best estimated baseline mean MEDD [1,2]	378.5 MEDD
Mean MEDD prior to patch application	370.6 MEDD
Opioid withdrawal experienced during transition	25%

OUD: Opioid Use Disorder, OST: Opioid Substitution Therapy, MEDD: Morphine Equivalent Daily Dose
[1]Fentanyl conversion as per http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b08.html
[2]Likely underestimated as one patient on methadone and MEDD conversion not established

Table 2: Outcomes

Primary outcomes	N=8
Receipt of primary treatment	100%
Hospitalization retention for duration of primary treatment	100%
Discharged on buprenorphine/naloxone	100%
Mean discharge buprenorphine/naloxone dose	11.3 mg/d
Secondary outcomes	
Outpatient addiction treatment within 4 weeks [1]	88%
Buprenorphine/naloxone treatment at 4 weeks [1]	88%

[1]One patient lost to follow-up

Six patients tolerated the transition well without symptoms. The two patients that experienced mild opioid withdrawal (Clinical Opiate Withdrawal Score of 11 and 14, respectively) had received an opioid taper. Notably, one patient on 800 MEDD at baseline, who did not undergo taper, tolerated the transition without withdrawal. All patients received their intended primary treatment and were discharged on sublingual buprenorphine/naloxone at an average dose of 11mg. All patients, except one lost to follow-up, remained adherent and attended outpatient addictions treatment 4 weeks post-discharge (Table 2). Weaknesses include small sample size, lack of comparator group, variability of protocol (patch strength, duration of application) and underestimation of baseline MEDD.

Conclusions: The administration of a buprenorphine patch prior to sublingual buprenorphine/naloxone therapy to patients receiving full OAT was well-tolerated and may have limited the extent of opioid withdrawal even in patients on high dose opioid therapy. Practically, this may have contributed to inpatient retention and adherence to maintenance treatment after hospital discharge. Further study is warranted to definitively assess the clinical efficacy and tolerability of this novel intervention.

KEYWORDS Opioid substitution therapy; buprenorphine; opioid use disorders

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160. Treatment and outcomes for patients with recurrent methanol poisoning: a case series

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Introduction: The toxic effects of methanol poisoning are well established and a generally accepted treatment threshold exists. However, there are patients who recurrently present to the Emergency Department (ED) with a methanol concentration above the recommended treatment threshold of >6.2 mmol/L (>20 mg/dL) with no acidosis or end organ damage. Some literature suggests that using this concentration as a guideline for treatment may be overly cautious. Hence, it is unclear whether it is necessary to initiate costly therapies such as alcohol dehydrogenase inhibitors (ADHi) in patients who present repeatedly. We sought to identify patients presenting with recurrent methanol poisoning with methanol concentrations above 6.2 mmol/L who

Table 1: Emergency Department visits by patients with recurrent methanol poisoning presenting with serum methanol concentrations > 6.2mmol/L and not treated with alcohol dehydrogenase inhibition or hemodialysis.

Patient	[Methanol] on arrival, mmol/L (mg/dL)	[Ethanol] on arrival, mmol/L (mg/dL)	GCS on arrival	Patient-reported route and source of methanol poisoning
A	9 (28.8)	6 (27.7)	15	Huffing paint thinner
B	7 (22.4)	Undetectable	15	Ingesting paint thinner
B	7 (22.4)	46.8 (215.7)	10	Huffing lacquer thinner
B	7 (22.4)	7.9 (36.4)	15	Huffing lacquer thinner
B	7 (22.4)	30.6 (141)	15	Ingesting "methanol"
B	7 (22.4)	51 (235)	11	Ingesting lacquer thinner
B	8 (25.6)	27.7 (127.7)	15	Ingesting lacquer thinner
B	8 (25.6)	5.8 (26.7)	15	Ingesting lacquer thinner
B	8 (25.6)	50.7 (233.6)	9	Ingesting lacquer thinner
B	8 (25.6)	Undetectable	15	Ingesting paint thinner
B	8 (25.6)	25.2 (116.1)	15	Ingesting lacquer thinner
B	9 (28.8)	48 (221.2)	15	Ingesting paint thinner
B	10 (32)	20 (92.2)	14	Huffing paint thinner
B	11 (35.3)	Undetectable	15	Huffing lacquer thinner
B	11 (35.3)	43.5 (200.5)	12	Ingesting lacquer thinner
C	10 (32)	24.2 (111.5)	15	Huffing lacquer thinner
D	7 (22.4)	Undetectable	15	Huffing lacquer thinner

* GCS denotes Glasgow Coma Scale

Table 2: Secondary outcomes of all visits by patients with recurrent methanol poisoning.

Proportion of visits with visual acuity documented, %		5.3 (6/113 visits)
Proportion of visits with ophthalmology follow-up arranged, %		1.8 (2/113 visits)
Proportion of visits with adherence to AACT guideline	Folate or folinic acid, %	74.3 (84/113 visits)
	NaHCO3 for visits with documented pH < 7.3, %	57.1 (4/7 visits)
	ADHi (ethanol or fomepizole) for visits meeting one of the AACT guideline criteria for ADH inhibitor, %	76.6 (72/94 visits)
	Hemodialysis for visits meeting one of the AACT criteria for HD, %	75.7 (28/37 visits)
Proportion of visits with Toxicology consult documented, %		67.3 (76/113 visits)
Median length of ED stay, hours		14
Proportion of visits requiring hospitalization, %		28.3 (32/113 visits)
Proportion of visits requiring ICU admission, %		6.2 (7/113 visits)
Proportion of visits treated with ADHi, %		68.1 (77/113 visits)
Mean amount of fomepizole used per visit among visits during which fomepizole was used, mg		2821
Proportion of visits requiring HD, %		33.6 (38/113 visits)
Mean duration of HD when HD was used, hours		8.6

* AACT guideline denotes 2002 American Academy of Clinical Toxicology practice guideline on the treatment of methanol poisoning, ADHi denotes alcohol dehydrogenase inhibition, HD denotes hemodialysis, ED denotes Emergency Department, ICU denotes Intensive Care Unit.

were not treated with ADHi (ethanol or fomepizole) or hemodialysis (HD) and to examine for any serious adverse outcomes. Secondary objectives were to review the adherence to the American Academy of Clinical Toxicology (AACT) toxic alcohol management guideline recommendations, visual acuity documentation and ophthalmology follow-up, and to estimate these patients' health care resource utilization.

Method: We performed a retrospective medical record review of all methanol poisoning related visits by patients with recurrent methanol poisoning to four EDs from 2002 to 2015. We defined recurrent methanol poisoning as patients with three or more ED visits for methanol poisoning (ICD9: 980.1 or ICD10: T51.1). We excluded visits unrelated to methanol poisoning. The primary outcome was the prevalence of serious adverse outcomes (blindness or death) among patients with recurrent methanol poisoning presenting with a serum methanol concentration >6.2 mmol/L (>20 mg/dL) without acidosis or end organ damage at ED presentation and not treated with ADHi or HD. Secondary outcomes included the proportion of ED visits with visual acuity documentation, referral to outpatient ophthalmology follow-up, adherence to the AACT management guideline, and resource utilization outcomes including ED length of stay, hospital/ICU admissions, and use of fomepizole/HD.

Results: A total of 113 visits by 10 patients met inclusion criteria. For the primary outcome, there were no serious adverse outcomes for the 17 visits by four patients presenting with methanol concentrations on arrival >6.2 mmol/L (>20 mg/dL) and not treated with ADHi or HD. None had visual symptoms on arrival or a serum pH < 7.30. Methanol concentrations on arrival ranged from 7 to 11 mmol/L (22.4–35.3 mg/dL). Four had undetectable ethanol concentrations on arrival. Seven were due to huffing rather than ingestion. All patients survived to subsequent ED visit with no documented visual symptoms (Table 1). Six (5.3%) of visits had visual acuity documentation, and two (1.8%) had ophthalmology follow up arranged. Table 2 describes all secondary outcomes.

Conclusions: In this case series of patients with recurrent methanol poisoning, serum methanol concentrations up to 11 mmol/L (35.3 mg/dL) without treatment with ADHi or HD did not result in blindness or death. However, subtle visual deterioration could not be determined. Future study is needed to formally evaluate the safety of using a higher treatment threshold in patients with repeated methanol exposures.

KEYWORDS Methanol; fomepizole; recurrent methanol poisoning

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161. Severe acute lead toxicity due to extra-articular retained bullet fragments

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Lead toxicity due to retained bullet fragments has been well documented in the literature through numerous case reports. However, these case reports typically involve retained intra-articular fragments or projectiles dispersed over a large surface area from a shotgun blast. This case documents life-threatening acute lead toxicity in a patient nine years after receiving gunshot wounds to the left femur and chest. Shortly after experiencing acute left thigh pain with exertion, the patient gradually developed intensifying abdominal pain and anorexia, with a 60 lbs weight loss over 2 months. The symptoms included a progressive, ascending neuropathy with associated muscle weakness. Three and one-half months after onset of symptoms, the patient was bed-bound, unable to move his lower and upper extremities against gravity. At this time, the lead level was 129 μg/dL. He was hospitalized and received two rounds of chelation with intramuscular British anti-Lewisite and parenteral EDTA Calcium Disodium in addition to surgical removal of bullet fragments. This was followed by 2 months of in-patient rehabilitation and 16 months of out-patient therapy during which time the patient received 10 courses of chelation with oral Dimercaptosuccinic acid (500mg TID for 21 d). Despite therapy, blood lead levels remained in the 50–70 μg/mL range. His clinical course has improved significantly with full ambulation and few limitations in activities of daily living. He has persistent mild chronic motor and sensory polyneuropathies. The free and zinc protoporpyhrin levels have fallen throughout the treatment course and the red blood cell indices have normalized. The Adult Blood Lead Epidemiology and Surveillance Program from 2003 to 2012, reported that approximately 5% of levels over 80ug/dL were due to retained bullet fragments. Typically bullet fragments involving intra-articular joints are linked to elevated lead levels as synovial fluid prevents the formation of a surrounding capsule and promotes fragment dissolution. The acute onset of left thigh pain in this patient was temporally associated with the development of abdominal colic, microcytic anemia, and progressive muscle weakness starting approximately 2 weeks after the acute left thigh pain. All of the subsequent, well-described signs and symptoms of severe lead toxicity were consistent with the rapid release of previously sequestered lead from a ruptured capsule. During the acute in-patient parenteral chelation and bullet removal phase whole blood lead levels decreased by 60%, then plateaued during chronic intermittent oral chelation. Since 1975, protoporhyrin levels have been studied as a measure of chronic lead exposure. The potential for false positives with concurrent iron deficiency and a time lag after exposure may have limited its role during acute exposure. Protoporhyrin levels correlated well with clinical improvement in this patient with chronic exposure. This case, highlighted by a life threatening quadriparesis, demonstrates the dangers of acute lead toxicity resulting from encapsulated extra-articular bullet fragments following acute capsular disruption. It also underscores the limited utility of blood lead levels during prolonged chelation with a high total lead burden. Free and zinc protoporhyrin may provide a better measure of chelation effectiveness in these clinical situations.

KEYWORDS Lead toxicity; lead chelation; retained bullet

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162. Postmortem analysis of carfentanil associated overdose deaths

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Background: Carfentanil is approved for large animal sedation in veterinary medicine. Relative potency of carfentanil is estimated to be 100× that of fentanyl. In 2016, illicit use of carfentanil and associated deaths were reported in a number of states including Ohio, West Virginia, Florida, Michigan, Kentucky, and Pennsylvania. Carfentanil has been seized in bulk form as well as being found as an adulterant in, or replacement of heroin. In February 2017, carfentanil along with three similar synthetic opioids, furanyl fentanyl, acryl fentanyl, and valeryl fentanyl, were banned as exports from China in response to international pressure to reduce the flow of synthetic opioids into the United States. In November and December 2016, the first three deaths associated with carfentanil in our service area were reported. To date, there are no published post-mortem levels of carfentanil associated with death.
Case reports: We performed a retrospective review of postmortem blood toxicology reports in deaths associated with carfentanil reported to the regional poison center. Levels were quantified using high-performance liquid chromatography tandem mass spectroscopy. In each case detectable post-mortem blood levels of carfentanil were found.
Case 1: A 24-year-old woman with a peripheral blood carfentanil level of 0.53ng/mL. Other substances identified included delta-9 THC (0.84 ng/mL) benzoylegonine (200ng/mL), dextrorphan (200ng/mL), chlopheniramine (240ng/mL), and dextromethoraphan (2800 ng/mL).
Case 2: A 21-year-old man with a peripheral blood carfentanil level of 0.34 ng/mL. The remainder of his toxicology report indicated a qualitative positive result for naloxone and quantitated delta-9 THC (0.62 ng/mL), dextrorphan (91ng/mL), dextromethorphan (280 ng/mL), and chlorpheniramine (210ng/mL).
Case 3: A 20-year-old woman with a cardiac blood carfentanil level of 0.2ng/mL. Additional cardiac blood levels were furanyl fentanyl (2.5ng/mL), alprazolam (19ng/mL), cocaine (84 ng/mL), benzoylecgonine (2000 ng/mL), delta-9 THC (0.59ng/mL), and cyclobenzaprine (80 ng/mL)
Discussion: Human clinical and postmortem data regarding carfentanil toxicity and forensic analysis are limited. We report three cases of deaths and associated postmortem carfentanil levels. Understanding postmortem distribution and relative contribution to deaths will be critical in further investigation of this emerging synthetic opioid. In all cases, carfentanil was likely the primary cause of death. In Case 3, furanyl fentanyl and alprazolam may have contributed to death. Post-mortem furanyl fentanyl levels have been reported in the range of 2.5–76ng/mL and usually in the presence of additional opioids. Alprazolam would be much less likely to cause death in isolation but could have had a synergistic effect on respiratory drive in the presence of carfentanil and furanyl fentanyl. Determination of relative contribution to death by a drug is complex and dependent on a variety of factors including baseline comorbidities, relative tolerance to a given drug, and presence of additional intoxicants among others.
Conclusions: The levels reported in these caseswere relatively similar and indicate a range of postmortem levels 1–2 orders of magnitude lower than those typically reported for fentanyl, consistent with carfentanil's reported relative potency. Further research is needed to quantify levels of carfentanil associated with death and survival

KEYWORDS Carfentanil; postmortem; opioid

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163. Substance use treatment and referral: novel use of poison center services

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Background: In 2014, 20.2 million Americans suffered from substance use disorders. The number of annual unintentional overdose deaths continues to rise including more than 52,000 in 2015. The causes of this alarming trend are multifactorial, demanding innovative and coordinated responses. Poison centers are ideally suited to respond with preventive education, immediate treatment recommendations, as well as data collection and analysis. Traditionally, poison centers have not participated in recovery treatment and referral. Evidence suggests that intervention including referral to appropriate treatment resources can improve engagement in substance use treatment. The objective of this study is to demonstrate proof of concept that poison centers can provide substance use disorder treatment and referral in addition to traditional poison center activities.
Methods: Poison center staff were trained in the brief evaluation of patients with substance use disorders for identification of potentially life-threatening withdrawal syndromes that would necessitate inpatient treatment. Decision algorithms based on classes of substances, presenting symptoms, and location (hospital, ED, physician office, home) were developed. Substances include opioids and GABA agonists. Callers from home were referred to an ED or provided outpatient referral resources based on need, assistance in locating naloxone in the case of opioids, and referred to their County based drug and alcohol agency. Healthcare provider callers were assisted in the evaluation of patients' toxicity and potential withdrawal, provided, by fax, treatment recommendations including pre-completed prescriptions for symptom-based opioid withdrawal medications and naloxone, discharge instructions discussing substance use disorders and follow up, and a list of treatment facilities in the patient's home county. All patients were contacted on days 1 and 7 following the initial call to provide motivation and assess engagement. With consent, patients from the center's home county had their information provided directly to the county drug and alcohol office to facilitate follow up and engagement.
Results: In the first 5 months of availability, 19 callers from five counties contacted the center specifically for enrollment in this program. Ten were men and callers ranged in age from 18 to 60. Public callers accounted for 6/19 (32%) calls while 13 calls originated from hospital Emergency Departments (EDs). Eighteen calls were related to opioids (12/18 heroin, 6/18 prescription opioids), while another was due to gabapentin misuse and symptomatic withdrawal. Of the 19 patients, two were admitted to the hospital. One patient was admitted due to hypoxemia as a result of drug toxicity and one was admitted because of complicating medical comorbidities. Three callers were reached on both days 1 and 7. All three indicated that they had not used since discharge and were engaged in treatment. The remaining patients either refused follow up, did not answer or had non-working numbers.
Conclusions: Poison centers can expand their roles to include the treatment of patients with substance use disorders and withdrawal, referral to treatment, and follow up engagement. Critical opportunities to optimize such service include coordinating with existing programs, enhanced program awareness through public and provider education, and accurate documentation of patient phone numbers particularly when provided by a third party.

KEYWORDS Substance use disorders; Poison center; addiction

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164. Induction of buprenorphine/naloxone for opioid withdrawal in an academic emergency department

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Background: Opioid withdrawal is an increasingly common presentation to the emergency department (ED) and while it is not fatal, it poses a significant symptomatic burden on these patients. Currently, the ED physician has limited resources to manage these patients symptoms or to support them in their transition to an opioid treatment program. We present a case of opioid withdrawal treated with Buprenorphine/Naloxone (BNX) by a medical toxicology consult service in the ED.
Case report: A 30-year-old male presented to the ED reporting anorexia, vomiting, diarrhea, and myalgias for 24 h after abrupt cessation of heroin. On exam, he was diaphoretic and restless with mydriasis, fine tremor, and mild tachycardia. His initial COWS(clinical opiate withdrawal scale) was 21, indicating moderate withdrawal. BNX induction was performed by the consulting toxicologist with 2mg/0.5mg test dose to evaluate for precipitation of withdrawal, followed by 6mg/1.5mg 1 h later with improvement of his COWS score to <2. The patient was discharged directly from the emergency department with a 1 week bridging prescription of BNX and a scheduled follow up appointment with a BNX clinic.
Case discussion: There is growing evidence that BNX may not only effectively manage opioid withdrawal symptoms as shown in the case above but also may increase enrollment and adherence to an addiction treatment program by two-fold when the regimen is started in the ED compared with referral alone. Currently, few emergency physicians utilize BNX for their patients as they are only allowed to administer, but not prescribe, this medication unless they obtain a Data 2000 waiver. This situation provides a unique opportunity for a medical toxicologist to assess the patient while acutely in opiate withdrawal, improve their symptoms, and help them to establish care within the toxicologist's own practice or within a community BNX clinic.
Conclusions: Through the use of a medical toxicology consult service, induction of BNX in the setting of acute opioid withdrawal created a safe and effective disposition for the patient with appropriate follow up directly from the emergency department.

KEYWORDS Buprenorphine; suboxone; opioid

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165. Intrathecal bupivacaine and morphine toxicity leading to transient neurogenic shock and delayed status epilepticus

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Background: Local anesthetic systemic toxicity (LAST) most commonly occurs in the setting of regional anesthesia complicated by intravascular injection. High doses can cause dysrhythmia, seizures, and coma. Lipid emulsion therapy is a recommend

treatment for LAST, but experience with the toxicodynamics and treatment of intrathecal local anesthetic toxicity is limited.
Case study: A 74-year-old woman with a chronic pain managed with an intrathecal bupivacaine/morphine pump placed 4 years prior presented to the emergency department directly from her anesthesiologist's office where her pump was refilled with 50mL solution (35 mg/mL morphine, 10 mg/mL bupivacaine), injected directly into the reservoir. She immediately reported loss of sensation in her legs. This was followed by obtundation, hypotension, and lower extremity flaccidity. Her anesthesiologist deactivated the pump, and on aspiration was only able to recover 40cc of the solution, suggesting the patient received 100 mg bupivacaine and 350 mg morphine intrathecally. She became more responsive after 0.8 mg intravenous naloxone but she demonstrated crystalloid-responsive hypotension (initial blood pressure 67/32 mmHg) with persistent sensorimotor neuropathy. Her motor function gradually improved. Three hours after injection, she developed generalized tonic-clonic seizure activity refractory to 4 mg of intravenous lorazepam. An EKG was obtained showing a normal sinus rhythm with a QRS of 84 ms. Because of persistent seizures, the patient received a 1.5 cc/kg bolus of 20% intravenous lipid emulsion followed by infusion of 0.25 cc/kg/min for 30 min. Nevertheless, seizures persisted despite administration of 10 mg of IV midazolam. The patient was intubated, loaded with 1000 mg intravenous phenobarbital, and started on propofol infusion with abatement of seizure activity. No epileptiform activity observed on electroencephalogram on the first day of admission. She was extubated on day two and eventually discharged from the hospital with plans to remove her pump as an outpatient.
Discussion: The patient developed intrathecal local anesthetic and opiate toxicity after pump malfunction during refill. She initially manifested signs of opioid toxidrome and neurogenic shock. Her flaccid paralysis from spinal local anesthetic effect was followed by status epilepticus, likely secondary to caudocranial spread of bupivacaine. Our patient received a much larger dose than that typically given in spinal anesthesia, where generally less than 10mg of bupivacaine is administered. In this case, no local anesthetic cardiotoxicity developed likely due to CNS sequestration of bupivicaine. Likewise, poor CNS penetration of intravenous lipid emulsion may have negated any antidotal effect.
Conclusions: We present a case of bupivacaine toxicity leading to spinal shock, progressive altered mental status, and status epilepticus refractory to intravenous lipid emulsion. Though all potential therapies should be attempted, aggressive management of status epilepticus with benzodiazepines and barbiturates may be more effective than lipids in cases of toxicity from intrathecal administration of bupivicaine.

KEYWORDS Intrathecal; intravenous lipid emulsion; bupivacaine

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166. Persistent prolongation of QT interval and QRS secondary to loperamide toxicity

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Background: Loperamide is an over-the-counter antidiarrheal agent, which is frequently prescribed for diarrheal illness and used off-label for opioid withdrawal. In therapeutic doses its absorption is limited. It represents an emerging drug of abuse, and, in significantly higher doses, loperamide can have systemic opioid agonist effects that can also be complicated by cardiac conduction aberrancies
Case report: A 25-year-old female with history of chronic pain and opioid use disorder presented with generalized weakness. She stated she had been ingesting "handfuls," of 60mg loperamide multiple times per day. Initial EKG showed prolonged QT interval, with QTc of 603 ms. QRS interval was also noted to be prolonged at 174 ms. She had no personal or family history of QT prolongation or dysrhythmias. She had recently discontinued her haloperidol. Only other medication or substance use was an OTC cough medicine containing chlorpheniramine and dextromethorphan, which she denied misusing. Urine gas chromatography/mass spectroscopy showed only loperamide, dextromethorphan, chlorpheniramine, and haloperidol metabolite. She was given intravenous magnesium sulfate and sodium chloride, and admitted for cardiac monitoring. Serial EKGs showed persistence of QT prolongation, with maximum QTC of 742 ms more than 25 h after her initial presentation. QRS improved but remained prolonged greater than 130 ms. On hospital day 3, and 67 h after initial presentation, her EKG normalized with QTc 529 and QRS of 120, and she was discharged home in stable condition.
Discussion: Loperamide is an opioid receptor agonist, which targets the μ-opioid receptors of the myenteric plexus of the large intestine to decrease tone of the intestinal wall muscles. Systemic circulation is limited by P-glycoprotein in the intestine and extensive first pass hepatic metabolism. Similar to methadone, high-dose loperamide ingestions have been associated with cardiotoxic effects ranging from QT-interval prolongation to ventricular dysrhythmias, including torsade des pointes, and have been associated with syncope and death. Loperamide has a relatively long half-life of 12–14 h, and we present a case of persistent and prolonged cardiotoxicity requiring 3 d until resolution. Cardiotoxicity is likely secondary to potassium channel dysfunction, with dose-dependent additive effects from calcium and sodium channels. Loperamide is similar in its chemical structure to haloperidol, which has known QT-prolonging effects.
Conclusions: In large overdose, loperamide can cause systemic toxicity, including cardiotoxicity and prolongation of the QT interval, which improve with clearance of the medication.

KEYWORDS Loperamide; qt prolongation; dysrhythmias

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167. Laboratory confirmed intravenous carfentanil exposure requiring naloxone infusion

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Background: Carfentanil is a synthetic μ-opioid agonist with reported potency approximately 10,000 times that of morphine and 100 times that of fentanyl. Its only approved use is to incapacitate, sedate and anesthetize large animals, giving it the popular nickname, "elephant tranquilizer." Most existing data on carfentanil comes from animal studies. Human exposures are not well documented. We present a case of confirmed, intentional intravenous carfentanil exposure.
Case report: A 26-year-old man with a history of polysubstance abuse obtained 100mg of carfentanil via a "dark web" source. He injected approximately 60 mcg, and ingested 4.9mg of what he believed to be "clonazolam," obtained from a separate online source. He was found unresponsive and bradypneic by his parents. In the emergency department, he was given a total of 4.4 mg of naloxone intravenously, with partial arousal and improvement in respiratory rate. Subsequently, a naloxone

infusion was initiated at 5 mg/h and maintained for 7 h. The infusion was discontinued when patient had returned to baseline. Initial laboratory workup showed mild transaminase elevation and rhabdomyolysis, with peak CPK 6885 IU/L. Toxicologic studies were notable for urine immunoassay positive for opiates, benzodiazepines and cocaine. Of note, the patient also endorses using cocaine and heroin in the days prior. Benzodiazepine confirmation test was positive for alprazolam, and opiate confirmation test was positive for codeine, hydromorphone, or hydrocodone metabolite and dihydromorphine or dihydrocodeine metabolite. Urine gas chromatography/mass spectrometry (GC/MS) analysis was positive for caffeine, cocaine metabolite, and nicotine. Specific analysis for carfentanil with serum high-performance liquid chromatography/tandem mass spectrometry (LC-MS/MS) was positive (1.1 ng/mL).
Case discussion: The elevated serum level suggests the substance he obtained from the "dark web" source was indeed carfentanil. Although this patient endorses polysubstance abuse, including heroin and cocaine, the temporal relation to carfentanil use suggests its role in this patient's critical illness. Despite the presence of alprazolam and previously used opioids, a serum level of 1.1 ng/mL likely represents a level associated with toxicity. Although we have the carfentanil spectrum in our lab's urine GC/MS library, it was not identified, suggesting that carfentanil is difficult to detect by this method. Finally, he required escalating and prolonged reversal therapy with naloxone, consistent with previous reports of fentanyl derivative toxicity.
Conclusions: Our case demonstrates that carfentanil can be easily obtained from unregulated Internet sources, and this patient's clinical course suggests large doses of naloxone may be required for reversal of carfentanil toxicity.

KEYWORDS Carfentanil; Internet; naloxone

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168. Can initial findings predict outcome in inhalational phosphine exposures?

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Background: Rapid, seemingly unpredictable deterioration may occur following inhalational phosphine (PH3) exposure.
Case reports: A family composed of two parents and eight children were unintentionally poisoned in their home by PH3. They all appeared to have sub acute lower level exposure for 3–4 d and developed gastrointestinal symptoms and headache. The night before their presentation, the father tried to remedy the problem by dissolving the phosphide tablet that he laid under their prefabricated home with water from his garden hose. Their initial hemodynamic findings and whether and when they developed a cardiac arrest are found in the table below. The three youngest children (7, 9, and 11 years) and a 17-year-old sibling succumbed to this exposure. None of those four patients had an echocardiogram performed. The 45-year-old mother deteriorated more slowly giving her physicians time to insert an Impella

Age	K	Mg	PO4	Ca	Cr	SpO2
7						Ventilated
9	3.8	3.5		9.4	1.64	
11						Ventilated
13	3.4L			9.6	0.97	99%RA
16	3.5L	1.9	2.8	9.2	0.61	100%RA
17	3.1L	2.0	7.5H	8.6	1.33H	BV Mask
19	3.0L	1.8	2.3L	8.6	0.55L	100%RA
21	3.5L	1.7	2.5L	8.9	0.85	100%RA
45	3.4L	1.5L	2.4L	7.21	0.81	Ventimask
53	3.0L	2.0	5.4H	9.1	1.3	100%RA

Age	BP	HR	CO2	pH	Lactate	EF	Outcome
7	0/0	0					CA At Scene
9	112/80	90	8	6.83			CA < 1 hour
11	0	0		<6.5			CA Enroute
13	94/57	108	18	7.26	7.3	>=55%	Hypotensive Survived
16	121/74	79	24	7.40	2.5	60-65%	Survived
17	77/55	107	14	7.22			3 hours
19	118/74	98	21	7.45			Survived
21	124/66	87	29	7.32	5.1	60-65%	Survived
45	86/55	88	15	7.35	4.7	<10%	5 hours -> Impella Survived
53	119/71	98	24	7.42	4.4	60-65%	Survived

circulatory assist device and to fly her to the nearest facility capable of implementing emergency extracorporeal life support (ECLS). The 13-year-old* sibling developed persistent hypotension (high 80's to mid 90's) but was treated only with fluids and did not require pressors. His echocardiogram done 4 h after arrival was mildly depressed. Their initial lab and pulse oximetry values are found in the other table below. Hypokalemia was seen in 7/8 patients, one had hypo and one hypermagnesemia, 3/6 had hypo and one had hyperphosphatemia, only one had a low total calcium, two had an elevated creatinine indication acute kidney injury (AKI), and both had a cardiac arrest.
Discussion: Rapid echocardiographic assessment of myocardial contractility is often done in hospitals who are used to seeing phosphine ingestons. Some emergency physicians have acquired the skill to do informal bedside cardiac ultrasound evaluations to assess contractility. Serum bicarbonate levels appear to correlate with lactate and venous pH.
Conclusions: Early echocardiography is beneficial in evaluating these patients. Early and serial lactates, bicarbonates and pH's are also be useful in assessing prognosis. Most of the electrolyte levels in our table are not useful prognostically. AKI appears to be a specific but in sensitive indicator of poor outcome. Because of our small number of patients, these findings are not conclusive and need to be further evaluated with a larger case series with early and serial measurements done routinely.

KEYWORDS Phosphine; prognosis; poisoning

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169. Perceived risk of drug substance among pregnant women

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Background: Substance abuse is a major public health problem in the United States. In 2014, over 10% of the population used illicit substances, and 23% reported binge alcohol use. Substance abuse among pregnant women represents a unique challenge as use of alcohol, tobacco and illicit drugs can have serious consequences for both the mother and the developing fetus. The objective of this study was to determine whether pregnancy status affected women's perceptions and use of alcohol, tobacco and illicit drugs.
Methods: The National Survey on Drug Use and Health (NSDUH) is a questionnaire administered to approximately 67,500 people aged 12 and older in the United States each year. Responses to the NSDUH questionnaire for women aged 12–44-years-old were queried regarding their risk perception of tobacco, alcohol, marijuana, cocaine, and heroin use. Ordinal logistic regression was performed to determine the effect of pregnancy status on women's risk perception of drug use after controlling for age, race, and education level. Chi-squared analysis was used to assess differences in substance use by trimester.
Results: A total of 290,802 women fell into age group 12–44 years over a 12-year study period (2002–2013). Most women were aged 18–25 years-old (39.8%) or 12–17 years-old (36.3%), with fewer respondents in the 26–34 (12.3%) and 35–44 (11.6%) age groups. A majority of respondents identified as White (60.8%), Hispanic (16.7%) or Black (13.8%). There were 10,707 (3.4%) women who reported being pregnant. Gestational age was evenly distributed between first (30%), second (36%) and third (33%) trimesters. When compared with non-pregnant females, pregnant women were significantly more likely to ascribe greater risk to alcohol use ($p<.005$), heavy smoking (1 pack/d) ($p<.005$), smoking marijuana once a month ($p<.005$) or 1–2 times per week ($p=.022$), using cocaine once a month ($p<.005$), and trying heroin once or twice ($p<.005$). There was no statistical difference between pregnant and non-pregnant women in risk perception of using cocaine or heroin 1–2 times a week. Among pregnant women who did use alcohol, tobacco, marijuana, cocaine or heroin, there was a significant decrease in the frequency of use as their pregnancy advanced ($p<.005$).
Conclusions: Pregnant women were more likely to ascribe greater risk to using alcohol, tobacco, and other illicit substances than non-pregnant women. This increased perception of risk was reflected in a decrease in substance use by trimester. It is important to continue to educate women on the risks of substance use during pregnancy.

KEYWORDS Drug use in pregnancy; drug abuse; NSDUH

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170. Clinical presentations of alcohol naïve patients with very high blood alcohol concentrations

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Background: Alcohol intoxication is a common presentation in the Emergency Department. Previous literature reports a dose response effect of clinical intoxication and a Blood Alcohol Concentration (BAC) >90mmol/L (414 mg/dL) is reported to be lethal. However, previous studies report that this BAC is not associated with life-threatening central nervous system (CNS) or respiratory depression in chronic alcoholics. Clinical experience suggests that individuals without a history of chronic heavy alcohol consumption (alcohol naïve individuals) are more likely to be severely intoxicated. Hypothesis: We hypothesize that a BAC >90mmol/L (414 mg/dL) is associated with life-threatening CNS and respiratory depression in alcohol naïve individuals.
Methods: We performed a retrospective cohort study of patients presenting to a Canadian, core area, tertiary care hospital with both adult and pediatric emergency departments, from January 2008 to June 2014. Medical records of consecutive patients with BAC >90mmol/L (414 mg/dL) were reviewed for evidence of alcohol naivety. Patients were determined be alcohol naïve if they fit into one of two categories: patients ≤20 years of age, or adult patients ≥21 years of age without multiple positive BAC results and without a history of chronic heavy alcohol consumption documented in the medical record. Electronic medical records of all other emergency departments and urgent care centers in the city were cross-referenced to identify patients with recurrent presentations with alcohol intoxication. Data collected included evidence of CNS or respiratory depression, evidence of co-ingestion and historical, physical, or imaging results suggestive of concomitant trauma.
Results: Thirty-six patients with BAC >90 mmol/L (414 mg/dL) met our inclusion criteria. Twenty-one were ≤20 years of age and 86% of these were female, while only 20% of adult patients were female. The mean lowest recorded Glasgow Coma Scale for all individuals was 7.4. Half of all individuals required airway support including 28% requiring intubation. Eleven percent of patients

had episodes of hypoxia, and 11% had hypotension. The mean emergency department length of stay was 7 h 34 min and 11% of patients were admitted to the intensive care unit. There were no episodes of hypoglycemia and no patients had imaging evidence of intracranial injury. Four ≤20-year-old patients had evidence of co-ingestion that may have contributed to their clinical findings.
Conclusions: In patients without a history of chronic alcohol consumption, a BAC >90mmol/L (414 mg/dL) may be associated with significant and potentially life-threatening CNS and respiratory depression. The incidence of severe intoxication appears to be higher in adolescent girls than boys. Further study may be helpful to identify factors contributing to the disproportionate presentation in this vulnerable population.

KEYWORDS Alcohol; blood alcohol concentration; CNS depression

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171. Systemic lead poisoning in an infant after gunshot injury to the spine and brain

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Background: Lead is a well-known toxic metal and developmental toxin in children. Cases of systemic absorption and toxicity from lead ingestion are common. Far more unusual is lead absorption and toxicity from non-ingested lead foreign bodies (LFBs), such as bullets. When this occurs, it is most likely because the LFB is in contact with circulating fluid, such as synovial fluid and possibly cerebrospinal fluid. We describe a case of lead poisoning in an infant after gunshot injury to the head and neck with LFBs in the central nervous system (CNS).
Case report: The guardian of a 5-month-old female was attempting to fix a rifle when it discharged. The bullet ricocheted and struck the girl in her neck and thorax. She was stabilized at an outside hospital and transferred to a level one pediatric trauma center. Imaging revealed extensive soft tissue shrapnel in left neck, thorax, and occipital head. There were LFBs in the spinal canal at C4 and T2. LFB also tracked into the left cerebellum, penetrating to the midline brain near the cerebral aquaduct. Initial examination showed no movement in upper extremities and withdrawal to touch in bilateral lower extremities in a stable, intubated and sedated patient. Soft tissue was tattooed with black substance; LFBs and shrapnel were present. Debridement removed visible fragments. She had a C4-5 and T2-3 laminectomy with intradural LFB removal. Post-operative imaging revealed residual LFBs in the left cerebellar hemisphere, fourth ventricle, and occipital soft tissue. Two days after injury, a capillary blood lead level (BLL) was 27 mcg/dL. Thereafter, she was able to wean from the ventilator, smile, make eye contact and regain some extremity function. Constipation occurred that was attributed to medications and critical illness. Serial BLLs went up to 50 mcg/dL at 3 weeks post-injury. Succimer was started at standard dosing. BLLs initially decreased during succimer therapy, but quickly rebounded. Using a threshold of 45 mcg/dL for chelation, she required three courses of succimer in the 6 months since her injury. Highest BLL was 59 mcg/dL. She has not developed signs of neurotoxicity, hypertension, anemia or constipation. She is meeting appropriate language and social developmental milestones with motor limited as expected from her spinal injuries.
Case discussion: Any symptoms of lead toxicity in this child are complicated by her young age and her co-occurring injuries. Her BLL may have risen rapidly secondary to initial high surface area exposure. Her ongoing source of lead is likely LFBs in contact with CSF. This type of exposure may result in chronic lead toxicity and potentially greater neurotoxicity. Unfortunately, the location of these LFBs also makes removal too risky to attempt. The role that potentially higher CSF lead burden may play is unstudied. The few pediatric reports of CNS LFB include no infants and no long-term outcomes.
Conclusions: Elevated blood lead levels in an infant are complicated by retained lead foreign bodies in the CNS. For this rare scenario, no precedence was found in published cases to guide chelation therapy or predict long-term outcomes.

KEYWORDS Lead; pediatric; bullet

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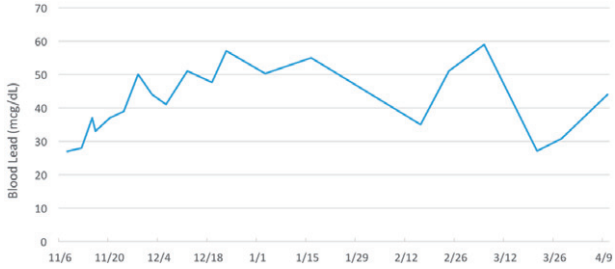

172. Tobacco as a source of lead poisoning in a 12-year-old child

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Background: In many Southeast Asian countries, including Thailand, tobacco is both smoked, and added to a "quid" (a mixture of betel leaf, areca nut, tobacco, and slaked lime), that is then chewed. We report a case of lead poisoning in a child from tobacco imported from Thailand.
Case report: A 12-year-old Thailand refugee boy was found to have a blood lead level (BLL) of 72 mcg/dL (reference < 10 mcg/dL). Six months prior, his BLL was 6 mcg/dL. He was asymptomatic and the rest of his workup was unremarkable. His father, mother and two of his five siblings had elevated BLLs of 53 mcg/dL, 24 mcg/dL, 22 mcg/dL, and 19 mcg/dL, respectively. Health Department interviewed the family and conducted thorough site investigation that included taking samples of home products in addition to the use of x-ray fluorescence spectrometry. All of the tested products, including the usual suspects of paints and imported spices, as well as the father's areca nut and betel leaf, tested negative. However, a sample of the father's dried tobacco leaves imported from Thailand contained 36.12 ppm (mcg/kg) of lead. The mother reported that the father both smokes the tobacco using a pipe, and adds it to his chewed betel quid. The tobacco was removed from the home and the patient was treated with oral succimer for 21 d (10mg/kg/dose BID for 5 d, then TID for 14 d). His BLL decreased to 13 mcg/dL after treatment and the BLLs of his affected family members also decreased on follow-up.
Discussion: Tobacco is usually prepared from partly fermented and unprocessed sun-dried leaves of Nicotiana rustica and Nicotiana tabacum. Tobacco is often overlooked in evaluating exposure to heavy metals. The tobacco is sometimes added to a quid mixture. A study carried among northern Thai hill tribes and rural Thai found that 83% of betel-quid chewers used tobacco,

but the chewing habit seems to be declining in Thailand. One study reported high toxic metals including lead in different Chinese Tobacco cigarettes. Another reported exposure to arsenic, cadmium, and lead from betel quids. In our case, the source of the lead exposure was clearly the imported tobacco, but the route of exposure was not clear, whether it is directly by the child chewing or smoking imitating his father or if he was exposed from second-hand smoke or debris contact. The former seems more likely as his BLL was significantly higher than the rest of household exposed to second-hand smoke.
Conclusions: Tobacco can have unsafe levels of contaminants such as lead, which if smoked or chewed, can cause a high blood lead level. Awareness of cultural practices and imported products especially from Asian countries is of paramount importance when evaluating patients with elevated lead levels.

KEYWORDS Thailand; tobacco; lead

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173. Trends in alcohol intoxication among students presenting to a university hospital emmergency department using code-based records

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Background: While the burden of excessive alcohol use among college students is well-documented, few studies have explored the epidemiology of hazardous drinking among students in the emergency department (ED). This study examined demographic trends in ED visits due to alcohol intoxication among college students in an ED associated with a major public university.
Methods: ED electronic medical records from 2009–2010 to 2014–2015 academic years were linked to student academic data. Alcohol-related visits were identified from ICD-9 codes reported in the medical records. Descriptive statistics were performed to determine frequency alcohol-related visits by academic year and demographic characteristics. A chart review of 100 patients randomly selected from each of the first and last years of the study period was performed by two independent reviewers to evaluate the completeness of code-based recording of alcohol-related visits.
Results: There were 9616 student visits (48% male) to the ED during the study period. Over 88% of students were aged 18–24 years, 80% were undergraduate, and 21% were affiliated with the Interfraternity/Sorority Councils. There were 1001 (10.4%) visits due to alcohol intoxication, of which 242 (24%) had co-occurring diagnoses indicating injury or trauma. The rate of alcohol intoxication (per 100 ED visits) was higher in males (11.1%) than in females (9.7%), and higher in white (10.7%), Hispanic (9.8%), and Asian (9.7%) students than in African-American (7.8%) and US non-resident students (5.3%). The rate was also higher in undergraduate (11.9%) than in graduate students (3.8%) and in students affiliated with Interfraternity/Sorority Councils (13.6%) than in those who were not (9.6%). The rate varied greatly by academic program, ranging from 1% to 12%. The rate decreased linearly with age: 16% in students aged <20 years (p for trend <.01), 8.3% in ages 20–25, and 3.5% in ages >25. Using code-based data, we found the rate of alcohol-related visits increased significantly from 7.9% in 2009–2010 to 12.3% in 2014–2015 (p <.01). The increase was greater among students aged <20 (from 10.8% to 17.6%, p <.001). However, the chart review found that in the 2009–2010 academic year, only eight out of 15 (53%) visits related to alcohol intoxication were coded, while in 2014–2015, 13 out of 17 (76.4%) were coded.
Conclusions: Alcohol intoxication contributes a significant proportion of total ED visits in college students and varies across sociodemographic strata. Undergraduate students aged <20 years appear to be the most vulnerable group. A significant proportion of ED visits due to alcohol intoxication were not captured by ICD-9 codes, and was higher in 2009–2010 than in 2015–2016. Code-based diagnoses appear to underestimate the true burden of alcohol intoxication among students presenting to ED. Information from clinical notes must be used in epidemiological studies of hazardous drinking among students in the emergency department (ED) to capture the true burden.

KEYWORDS Alcohol intoxication; emergency department; college students

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174. Fatal iron overdose without gastrointestinal signs

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Background: Iron is absorbed via oxidative damage to the gastrointestinal (GI) endothelium, and the lack of GI signs and symptoms has been proposed as a sensitive prognostic marker against development of significant toxicity. We present a case of fatal iron overdose with no evidence of GI signs that was refractory to treatment with chelation therapy, hemodialysis, and Molecular Adsorbent Recirculating System (MARS).
Case report: A 30-year-old female was noted to be normal at 02:45 by her significant other. Approximately 15 min later, he heard a "thump" and found the patient down in the bathroom. Paramedics intubated the patient. A suicide text message was later discovered. The patient was hemodynamically stable on arrival to the emergency department. Her initial labs showed glucose 241 mg/dL, serum acetaminophen 375 mcg/mL, and urine drug screen positive for cocaine and opioids. Her electrocardiogram showed QRS 118 ms and QTc 500 ms, and a 4-mm terminal R wave in aVR. The patient was treated with intravenous (IV) sodium bicarbonate, with subsequent narrowing of the QRS interval to 82 ms. Serum acetaminophen concentration at 4.5 h post-ingestion was 369 mcg/mL, and IV N-acetylcysteine was started. Ten hours after her presumed ingestion, the patient demonstrated hemodynamic instability, with heart rate 135 and blood pressure 105/64. Her labs at that time were otherwise notable for leukocytosis (WBC 33.0), hyperglycemia (584 mg/dL), worsening renal function (creatinine 1.0 from 0.7), elevated lactic acid (11 mmol/L), and acidemia (arterial pH 6.81). Acute iron ingestion was suspected as a possible etiology for the profound acidosis based on the patient's medication. An abdominal radiograph showed no radio-opaque pill fragments. The patient had no hematochezia or melena, and no blood was noted via nasogastric tube. Serum iron concentration was obtained and was 1457 mcg/dL. The patient was started on IV deferoxamine therapy; IV sodium bicarbonate was continued. She received norepinephrine and epinephrine for blood pressure support and insulin infusion for hyperglycemia. Repeat labs showed transaminase of AST 5169 U/L and ALT 3410 U/L; these increased over the following day to >7000 U/L each. The patient's clinical condition

deteriorated and she was treated with hemodialysis and MARS. Despite these interventions, the patient ultimately suffered multisystem organ failure and death.
Discussion: Reasons for lack of GI symptoms in this severe iron overdose are explored. This patient was intubated, paralyzed, and sedated, and thus may not have manifested GI symptoms otherwise suggestive of the first stage of iron toxicity. These interventions may have also physiologically impaired her GI motility. Her initial electrocardiogram suggests a co-ingested medication with tricyclic antidepressant effects. Both antimuscarinic toxicity and opioid use (based on positive urine tox screen) may have caused slowed or stagnant GI motility, thereby masking any hematochezia or hematemesis. Neither cross-sectional abdominal imaging nor endoscopy/colonoscopy was performed, so the extent of any GI ulceration and/or necrosis cannot be assessed. The elevated serum iron and the remainder of the patient's clinical course, including leukocytosis, hyperglycemia, shock and multiorgan system failure, are otherwise consistent with severe iron toxicity.

KEYWORDS Iron; fatal; gastrointestinal

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175. Geographical trends of heroin abuse in the United States

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Background: Heroin use has quadrupled since 2002 with reports that this has disproportionately affected rural areas. The aim of this abstract is to describe heroin abuse trends for different population areas from 2005 to 2016.
Methods: Reports of heroin use were obtained from the National Poison Data System (NPDS) from 2005 through 2016. Inclusion criteria consisted of living within the continental United States and providing a zip code of residence. Census population data from 2010 were used to define rural and urban regions into four levels (A, B, C, D) based on US Census Bureau definitions of metropolitan areas; population levels ranged from most densely populated to least densely populated (A: populations of one million or more; B: 250,000–999,999; C: 100,000–249,999; D: less than 100,000). Cities with three digit zip codes covered in multiple levels were assigned to the most populous level contained in the zip code. Cases were then assigned and summed over year and population level. A saturated Poisson regression model was run estimating the mean at each time point for each population level. Case counts were compared from 2005 to the 2016 count within each population level.
Results: A total of 25,665 heroin abuse calls were reported to NPDS from 2005 to 2016. Of these, 24,248 had a residential zip code provided that could be categorized into one of the four population levels. The overall number of heroin abuse calls reported in 2005 was 989 and increased to 5010 calls reported in 2016. All population levels showed a significant increase in heroin abuse cases over time ($p<.001$). Both population levels A and B showed a fourfold increase in the number of heroin abuse cases in 2016 compared with 2005 (4.37 (95% CI: 4.01, 4.73) and 4.77 (95% CI: 4.06, 5.60), respectively). The more rural population levels (C and D) had the most substantial increase from 2005 to 2016, with the number of heroin abuse cases increasing by nearly 11-fold (10.66 (95% CI: 7.98, 14.24) and 10.45 (95% CI: 7.84, 13.93), respectively).
Conclusions: Heroin abuse continues to increase across all population area levels within the United States, not solely major metropolitan cities. Interventions to curb heroin abuse should be considered in both metropolitan areas as well as rural areas where it is becoming more prominent. Rural areas (population areas less than 250,000) have seen the largest increase in heroin abuse cases over time which may indicate that the heroin epidemic is spreading from large cities to surrounding areas.

KEYWORDS Heroin abuse; urban versus rural; trends over time

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176. A study regarding follow-ups after Green Pit Viper (*Trimeresurus spp*) bites according to the clinical practice guideline published by the Ministry of Public Health

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Introduction: The Ministry of Public Health in Thailand published a venomous snakebite guideline in 2004. For a patient who gets bitten by a Green Pit Viper (GPV), the guideline suggests a physician orders blood tests immediately after arrival and repeat it once 2 h later when the first tests come back normal. If the second tests are still normal, the patient can be discharged and scheduled for follow-ups at 24, 48, and 72 h (0, 2, 24, 48, and 72 h plan). Since the guideline was published, there has been no large study validating its efficiency and safety especially to those who are discharged home and are followed up as outpatients.
Objectives: To study the prevalence of abnormal blood tests at the second draw, when the first tests came back normal. To determine the prevalence of adverse outcomes in those who could be discharged home and were scheduled for follow-ups as outpatients at 24 ± 6 h after bites.
Methods: This was a retrospective chart review study. The inclusion criteria were (1) those with suspected/confirmed green pit viper bites, (2) at least 15 years old, (3) presenting to our hospital from January 2008 to December 2015, (4) had at least two blood draws (immediately after arrival and 2 h apart). We excluded those with other known types of animal bite that were not from GPV. We had two chart extractors who were blinded to the objectives to reduce potential bias. They were instructed how to extract data from medical records using a standard data record form. Inter-rater reliability among the two extractors was calculated and the kappa was 0.805.
Results: During the study period, 320 cases were finally enrolled. The majority were male (56.3%) and median age was 44 years old (interquartile range: 30-55). There were only four cases (1.3%) with the abnormal Venous Clotting Time (VCT)/platelet count (PC) results of the second blood draws when the first sets of the tests were normal. Only one of the four cases received antivenom. For those who could be discharged after the second blood draws and had outpatient follow-ups at 24 ± 6 h after bites, the early unplanned revisits were found in only three out of 284 cases (1.1%). None of these were related to the systemic envenomation and nobody has received antivenom. The patients with abnormal VCT/PC results at 24 ± 6, 48 ± 6, and 72 ± 6 h were 7, 3, and 1 cases, respectively. Overall, only 21 cases (6.6%), received the F(ab')2 equine-derived antivenom and none of them had any hypersensitivity reactions.
Conclusions: This study with 320 GPV bites over the 8-year-period showed a very low prevalence of abnormal blood tests at 2 h after a normal first set of tests. This study also confirms safety

of having an outpatient follow-up at 24 h after bite as recommended by the Ministry of Public Health when the blood tests at time 0 and 2 h later are normal. This study also demonstrated safety of the F(ab')2 equine-derived antivenom.

KEYWORDS Snakebite; pit viper; venous clotting time

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177. Presence of new psychoactive substances as likely adjuvants formulated in conjunction with LSD: a case report of three patients

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Background: New psychoactive substances (NPS) are an emerging and serious threat to public health. Clandestine laboratories are constantly producing new chemicals and combinations of substances with intent to augment the drug user's experience. We report three cases of dramatic psychostimulant toxicity involving a combination of NPS and lysergic acid diethylamide (LSD).
Cases: Three 20-year-old college students presented to the emergency department with altered mental status after using blotter paper sold to them as "acid" before a football game. They all used the same product. All three patients had mydriasis, delirium, psychosis with visual and auditory hallucinations, and combative behavior requiring chemical sedation and physical restraint. One patient sustained minor head trauma after repeatedly hitting her head on a wall but had a normal CT brain. Initial vital signs in all patients were remarkable for tachycardia and hypertension with normal temperature and oxygen saturation. Laboratory evaluations for all three patients showed normal values on CBC, CPK, and chemistry panels; ECGs showed normal intervals. Urine drug screens were negative for amfetamines and cocaine in all patients; one patient was positive for THC. All three patients were admitted and improved after 24 h of observation with no sequela. Initial serum samples obtained on ED presentation were analyzed using liquid chromatography-quadrupole time-of-flight mass spectrometry to evaluate the presence of NPS. Serum analysis for all three patients confirmed the presence of LSD, *N*-propyl-3,4-methylenedioxyamfetamine (3,4-MDPA), 3-methoxy-2-keto-1-(1-phenylcyclohexyl)-pyrrolidine (3-MeO-2-keto-PCPy), and 4-Acetyloxy-*N*,*N*-diallyltryptamine (4-AcO-DALT).
Discussion: 3,4-MDPA is a psychoactive substituted phenethylamine and thought to be an enhancer for hallucinogenic drugs. 3-MeO-2-keto-PCPy is a novel dissociative drug and analog of phencylidine. 4-AcO-DALT is a novel tryptamine compound that is chemically similar to psilocybin. All three of these substances are believed to act as enhancers/adjuvants for hallucinogenic drugs. In our cases, patients exhibited sympathomimetic and psychostimulant effects with self-injurious behavior. The duration of effects observed in our patients was about 24 h and all improved with no sequela.
Conclusions: Our cases show that 3,4-MDPA, 3-Meo-2-keto-PCPy, and 4-AcO-DALT can be present in combination with hallucinogenic drugs like LSD, and produce dramatic psychostimulant effects on users. Toxicologists should anticipate the presence of NPS when evaluating patients with severe or unusual toxidromes.

KEYWORDS 3,4-MDPA; 3-Meo-2-keto-PCPy; 4-AcO-DALT

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178. Emergence of a potent synthetic cannabinoid "SGT-78" (4-cyano-cumyl-BUTINACA): a case report

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Background: Synthetic cannabinoids (SC) in circulation among users and confirmed by clinical laboratories have distinct trends and change over time. First generation SCs like the JWH compounds are rarely encountered today, while new and more potent SCs continue to emerge. We report a case of a new potent SC resulting in severe toxicity in a patient who purchased the drug online.
Case report: A 24-year-old male presented to the ED after he was found down by his parents at home. Upon arrival he was combative, maintaining his airway, with GCS 10. Physical exam was notable for periorbital ecchymosis and dilated (5mm) reactive pupils. Initial vital signs were HR 105, BP 180/100, *T* 39 °C, RR 23, and SpO2 99% on room air. Initial laboratory evaluation showed a metabolic acidosis (pH 7.28, HCO3 18, lactate 5.1), acute kidney injury with rhabdomyolysis (Cr 4.7, CPK 19,267), and leukocytosis (WBC 25). Urine drug screen was negative. ECG showed sinus rhythm with normal intervals. The patient was initially managed for sepsis with concern for meningitis. His CT brain and lumbar puncture results were normal. Over subsequent days the patient remained altered and Cr peaked at 9.7 with adequate urine output, cultures were negative for infection. His mental status improved after two sessions of hemodialysis on days 5 and 6. At that time, he admitted purchasing "synthetic marijuana" over the internet 3 d prior to presentation, from a supplier he had previously used. After smoking the drug, he recalled having visual hallucinations but otherwise could not remember events. The patient was discharged AMA on day 10 with a Cr of 7 and CPK of 2825, with intact mental status and neurological exam. The initial serum samples obtained at ED presentation were analyzed using liquid chromatography-quadrupole time-of-flight mass spectrometry. Serum analysis detected the presence of 4-cyano-cumyl-BUTINACA.
Discussion: 4-Cyano-cumyl-BUTINACA, also known as "SGT-78", is a novel SC that was initially reported in Hungary and was confirmed by the Welch Emerging Drugs and Identification of Novel Substances Project (WEDINOS). According to unofficial sources, it is believed to be 4–5 × stronger than 5F-MDMB-PINACA (5F-ADB) and 3 × more potent than 5F-CUMYL-PINACA (SGT-25), which are indazole-based SCs from the indazole-3-carboxamide family. Users described its effects as similar to MDMB-CHMICA with a shorter duration. MDMB-CHMICA and other potent SCs have been linked to fatalities and high morbidity, including altered mental status, rhabdomyolysis, and acute kidney injury, among others. Our case involved severe toxicity and multi-organ dysfunction, suggesting that 4-cyano-cumyl-BUTINACA is another potent SC. It is also notable that our patient's mental status improved after dialysis several days after presentation, which suggests that the drug or its metabolites are renally eliminated and could have a prolonged duration of action.
Conclusions: 4-Cyano-cumyl-BUTINACA is an emerging, and likely potent, SC that can be associated with severe sympathomimetic effects on users resulting in multi-organ dysfunction and prolonged hospital stay.

KEYWORDS 4-Cyano-cumyl-BUTINACA; synthetic cannabinoid; renal failure

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179. Characteristics and predictors of oxycodone misuse: results from the 2015 National Survey on Drug Use and Health

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Background: The abuse and diversion of prescription medications, especially opioids, continue to be a serious public health concern. Oxycodone is one of the most commonly prescribed and abused opioids in the US. The objective of the current study is to identify predictors of oxycodone abuse using the nationally representative National Survey of Drug Use and Health (NSDUH) data.

Methods: The 2015 NSDUH public use cross-sectional data were analyzed. The respondents were classified into two groups, past year oxycodone users and misusers, based on the screening questions assessing past year use and misuse of oxycodone products. The prevalence of selected demographic, clinical factors and substance use and abuse, including prescription medications, was assessed descriptively for the two population groups using cross tabulated frequencies and chi-square tests. Logistic regression was used to identify predictors of oxycodone abuse adjusting for covariates. Odds ratios (OR) and corresponding 95% confidence intervals (CI) were calculated.

Results: Overall, the 2015 NSDUH survey comprised of 57,146 respondents, of which 5,698 respondents (9.9%) reported using oxycodone products over the last year. About 1174 respondents reported misuse, accounting for 20.6% of the total oxycodone users or 2.6% of the survey sample. Past year oxycodone misusers were more likely to be males (54.9% versus 41.2%, $p<.001$), unmarried (66.6% versus 44%, $p<.001$), and non-Hispanic whites (66.1 versus 65.6, $p<.001$) or Hispanics (14.9% versus 9.3%, $p<.001$). The prevalence of use and misuse of other substances in the previous year was significantly higher in the oxycodone misusers. Previous year marijuana use (OR: 1.41, 95% CI: 1.06–1.86, $p=.01$), heroin use (OR: 2.79, 95% CI: 1.21–6.40, $p=.01$), and hallucinogen use (OR: 2.38, 95% CI: 1.24–4.54, $p=.008$) were significant predictors of oxycodone misuse. Similarly, respondents reporting source of pain relievers to be drug dealers were 4.2 times more likely to be oxycodone misusers (OR: 4.23, 95% CI: 1.98–9.04, $p<.001$). Hispanics (OR: 1.47, 95% CI: 1.03–2.10, $p=.03$) had a significantly higher probability to misuse oxycodone. Oxycodone misuse was significantly more likely among misusers of other opioids including tramadol (OR: 1.82, 95% CI: 1.10–3.02, $p=.001$), morphine (OR: 4.46, 95% CI: 2.04–9.73, $p=.0002$), hydrocodone (OR: 1.42, 95% CI: 1.04–1.94, $p=.02$), and buprenorphine (OR: 3.39, 95% CI: 1.35–8.51, $p=.009$). In contrast, previous year cocaine users (OR: 0.59, 95% CI: 0.38–0.92, $p=.02$) were significantly less likely to misuse oxycodone products in the past year.

Conclusions: The results indicate a high prevalence of oxycodone misuse based on the analysis of a nationally representative sample of survey respondents. Important demographic and clinical differences exist in the respondents who reported using and misusing oxycodone products. The use and the misuse of marijuana, hallucinogens and other opioids as well as source of pain relieving medications appear to be important predictors of oxycodone misuse.

KEYWORDS Oxycodone; misuse; predictors

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180. Age and gender are risk factors for pediatric poisoning suicides

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Background: Recent analysis from the CDC shows that suicide rates have increased since the late 1990s and may be increasing most in adolescents. Other data show that there may be unique trends in mechanism of suicide and gender in adolescent populations. The purpose of this study was to evaluate trends in reported suicides (attempted and completed) to the National Poison Data System (NPDS) involving children and adolescents aged 6–20 years.

Methods: NPDS exposures in 6–20 year olds from 2009 to 2016 that involved an exposure reason of intentional suspected suicide were extracted. Annual counts by age are described. Trends in age and gender were examined using Poisson regression adjusting for population by age and gender. Top substances involved were also described.

Results: About 539,080 suicide exposures involving 6–20 year olds were reported between 2009 and 2016. Annual counts increased 55% from 56,528 in 2009 to 87,872 in 2016. The largest increase occurred among 6–12 year olds (184% increase; Table 1). Of all exposures, 74% involved females and 26% involved males. On an average, exposures increased 12% per year for female adolescents and 4% per year for males (Table 2). The increase in 6–12 year old females (21%) was significantly larger than the increase in 13–17 year old females (13%) and 18–20 year old females (5%). In all three age groups, the increase among females was significantly larger than the increase among males. Miscellaneous sedative/hypnotic/antipsychotics (12.4%), non-steroidal antiiflammatory drugs (12.4%), and selective serotonin reuptake drugs (9.4%) were the most common substances reported, but trends were not apparent by age group.

Conclusions: From 2009 to 2016, suicide exposure rates increased significantly among 6–20 year olds. Trends in suicides are conventionally examined in older adolescents, but our analysis showed that poisoning suicides in younger children are rapidly increasing and pre-teen girls represent an alarmingly high-risk group. Poison center trends in substances involved and other characteristics may yield insights into the factors that put young children at risk and should be further examined.

KEYWORDS Suicide trends; adolescents; NPDS data trends

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Table 1. Counts by age and year

Age (yrs)	2009	2010	2011	2012	2013	2014	2015	2016	% Increase (2009 to 2016)
6-12	1,295	1,429	1,507	1,892	2,465	2,998	3,311	3,674	**183.7%**
13-17	32,157	31,246	32,710	36,159	42,389	49,808	54,575	57,095	**77.6%**
18-20	22,859	22,358	22,125	21,536	21,129	21,819	24,269	26,953	**17.9%**

Table 2. Mean annual rate of change by age and gender

Age (yrs)	Female (95% CI) (n=400,903)	Male (95% CI) (n=137,681)
6-12	21% (18%, 23%)	8% (4%, 12%)
13-17	13% (11%, 14%)	5% (2%, 8%)
18-20	5% (3%, 7%)	0% (-2%, 3%)
TOTAL	**12% (11%, 14%)**	**4% (2%, 6%)**

181. Essential oil exposures in pediatric population: a 6-year review

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Background: Annually, the highest percentage of calls to poison centers across the United States are pediatric exposures. As natural remedies become more popular forms of therapy across the culture, children are at a potential risk of being exposed to essential oils used at home. Limited data exists beyond case reports about the clinical effects and outcomes of children who get exposed to essential oils. The purpose of our study was to retrospectively review data collected by the National Poison Data System (NPDS) over the last 6 years in order to characterize pediatric exposures to essential oils.
Methods: The NPDS was retrospectively queried to collect all closed, human exposures to essential oils between 1 January 2011 and 31 December 2016. The analysis was farther restricted to children and young adults up to 19 years of age. The AAPCC codes 0201023, 0201022, 0201024, 0077360, 0201025, and 0201026 were utilized to define the essential oil exposures. Several clinical factors were assessed to determine the key characteristics of essential oil exposures including exposure site, level of health care facility care (HCF), management site, and medical outcome. Demographic variables analyzed included age and gender. Descriptive analyses were carried out and frequencies were reported.
Results: During the study period, the number of essential oil exposures in children and young adults increased from 9282 in 2011 to 16,051 in the year 2016. Eucalyptus oil (408 versus 934) and tea tree oil (1050 versus 2907) demonstrated significant increases in reports during the study period. In majority of the cases, the exposure site was residence (97.8%) and the most common route of exposure was ingestion (75.9%). Most cases were managed on site (86.9%) and the most frequent medical outcome was minor effects (62.3%). Unintentional causes accounted for 90% of the cases. Demographically, males (50.4%) and females (49.1%) has similar propensity to be exposed to these oils. Children under the age of 6 years (86.2%) were significantly more likely to be exposed. Among the specific clinical effects, ocular irritation and pain (5.7%), vomiting (5.6%), and oral irritation (5.4%) were the most common effects seen in cases. There was only a single reported case of death and 33 cases of seizures over the study period. The predominant therapies recommended or performed for essential oil exposures included Dilute/irrigate/wash (77.4%) and providing a food or snack (15%).
Conclusions: Essential oil exposures are increasing in the pediatric population, but fortunately the majority of exposures cause minor clinical effects and can be managed safely at home.

KEYWORDS Essential oil; pediatric; exposure

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182. A survey of buprenorphine use and misuse among opioid users in the emergency department

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Introduction: Buprenorphine, a partial opioid agonist, is an approved treatment for opioid use disorder. While arguably less effective than methadone, buprenorphine appears to be safer and more convenient, and is likely underutilized. This underutilization may be multifactoral and likely a result of limited licensed care providers, lack of provider awareness and government regulations that make incorporating buprenorphine prescribing into an established practice impractical for many care providers. Despite limited availability of buprenorphine, diversion has been reported. Reported sources of diverted buprenorphine include friends and family with an appropriately obtained prescription, street dealers and on-line pharmacies. Individuals may seek buprenorphine treatment for a number of reasons, including self-treatment of withdrawal, self-treatment of opioid use disorder, and euphoria from the drug itself.
Objectives: In this study, we examined the awareness, availability, and utilization of buprenorphine among heroin users presenting to the Emergency Department (ED). Additionally, we sought to determine the motivation for buprenorphine use among heroin users in the ED. Finally, we attempted to discern the degree of buprenorphine diversion by heroin users.
Methods: This is an interim analysis of a cross-sectional study conducted in the Emergency Department of a large inner city university hospital. Patients were eligible to participate in the study if they presented with opioid intoxication or after an opioid overdose and were 18 years of age and older. This study received IRB approval.
Results: There were 153 patients enrolled in the study. Of the respondents, 73.2% were male. About 66.6% were between 20 and 40 years old (36.6% between 20 and 30 and 30% between 30 and 40), 61.4% identified as Caucasian, 17% African American and 17% Hispanic. 88% had used heroin in the last 6 months and 26% had used buprenorphine. About 82% endorsed familiarity with buprenorphine, 74% had used it at some point in their life, and 50% had received a prescription from a physician. Of those receiving a prescription, 59% admitted to sharing, trading or selling their buprenorphine. Patients taking buprenorphine without a prescription had mostly obtained it from a dealer (74%) or a friend (26%). About 56% of patients without prescriptions used the buprenorphine to avoid withdrawal, paid an average of $10 per pill/film and used an average dose of 8 mg per dose.
Discussion: Awareness of buprenorphine among heroin users is high but there appears to be a discordance between overall use and prescription based use. This most likely demonstrates a substantial lack of resources available to heroin users. Only half obtain the buprenorphine from a physician and close to 60% of those receiving a prescription admit to diversion. In addition, most of the non-prescription buprenorphine was obtained from a dealer (74%) and was used to treat withdrawal, not as maintenance treatment, and the average dose used was lower than the standard 16 mg dose used in opioid use disorder.

KEYWORDS Buprenorphine; diversion; addiction

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183. Cardiac arrest following an acute-on-chronic ingestion of lacosamide

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Background: Lacosamide is an antiepileptic agent that selectively enhances slow inactivation of voltage-gated sodium channels. Previous reports of lacosamide toxicity have noted an array of cardiac disturbances, including cardiac arrest. However, these reports are confounded by multidrug ingestions involving other medications known to cause cardiac disturbances in overdose. We report a rare case of lacosamide-induced QRS prolongation leading to cardiac arrest following ingestion of lacosamide alone.
Case report: A 20-year-old female with history of epilepsy presented to the ED after ingesting an unknown amount of her own lacosamide 100 mg tablets. Prior to ambulance transport, she developed status epilepticus. Upon arrival to the ED, an ECG revealed a QRS duration of 146 ms, QTc interval of 513 ms, and a terminal R wave in lead aVR. Coingestants were ruled out by verifying pill counts of the patient's other medications. Initial labs were significant for an arterial pH of 6.60 and a serum lacosamide level of 89.3 mcg/mL (therapeutic <15 mcg/mL). Shortly after arrival, the patient suffered asystolic cardiac arrest. ROSC was achieved after a brief resuscitation. Shortly thereafter she developed hypotension (80/46 mmHg) and tachycardia (139 bpm). Repeated ECG showed a QRS duration of 200 ms, QTc of 512 ms, and continued presence of a terminal R wave in lead aVR. A sodium bicarbonate infusion was initiated for progressively widening QRS. The repeat ECG after initiation of IV sodium bicarbonate revealed resolution of the previously seen conduction disturbances. The remainder of the patient's hospitalization was complicated by rhabdomyolysis and ventilator-associated pneumonia. These complications eventually resolved and she was discharged to an inpatient psychiatric unit 14 d post-exposure with no documented neurologic deficits or persistent end-organ damage.
Case discussion: Lacosamide has been documented to cause cardiac conduction disturbances and dysrhythmias, often in the presence other known cardiotoxic agents. Previous reports have utilized IV sodium bicarbonate therapy for suspected sodium channel blockade, based on lacosamide's therapeutic mechanism of action and characteristic ECG changes. We add to the existing literature with this case of a confirmed isolated acute-on-chronic ingestion of lacosamide resulting in seizures, QRS prolongation, and asystolic cardiac arrest treated successfully with sodium bicarbonate therapy.
Conclusions: Seizures, hypotension, QRS widening, and cardiac arrest are possible following ingestion of lacosamide alone. Sodium bicarbonate therapy is likely to be beneficial in cases of sodium channel blockade due to lacosamide toxicity.

KEYWORDS Lacosamide overdose; cardiac arrest after lacosamide ingestion; sodium bicarbonate for lacosamide toxicity

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184. Trends in gabapentin abuse reported to poison centers, 2012–2015

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Background: Gabapentin is a newer antiepileptic medication that shares structural homology with gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the brain. While it does not cause full agonism of the GABA receptor, it has several other mechanisms that lead to sedation in overdose, both alone and when in combination with other sedating agents. In overdose, it has been reported to cause euphoria and sedation, making it a potential substrate for drug abuse. Due to a widespread rise in availability, we predict rates of gabapentin abuse reported to US poison centers will increase in the years since its introduction as a treatment for neuropathic pain.
Methods: We retrospectively analyzed all adult cases (age greater than 17 years) of gabapentin abuse reported to the National Poison Data System (NPDS) between January 2012 and December 2015, using search terms, "gabapentin" and "abuse". Demographic information, medical outcomes, and treatments administered were collected. All analyses used descriptive statistics.
Results: We identified 6239 cases of gabapentin abuse reported to poison centers during the study period. Gabapentin was the sole agent of abuse in 2195 (35.2%) cases. Major effects were observed in 5.48% of patients, 28.7% had moderate effects, and 31.8% described minor effects. Men comprised 48.1% of patients. Health care facilities initiated 76.5% of calls. Mean annual prevalence of gabapentin abuse reported to poison centers rose from 2.69 cases per million in 2012 to 9.18 cases/million in 2015. West Virginia and Kentucky have the highest average prevalence during this period (35.5 and 33.6 cases/million, respectively). Intubation occurred in 369 cases, and of these, only 34.9% were associated with gabapentin abuse alone. Sedation was the most common reported effect in 45.9% of cases of gabapentin abuse alone. Deaths comprised 22 cases, and were more likely to be associated with polysubstance ingestion (95%).
Discussion: Rates of gabapentin abuse have steadily risen during the period between 2012 and 2015. Approximately two-thirds of gabapentin abuse occurs with other substances. A potential reason for the observed rise in abuse rates may relate to its off-label usage as a treatment for neuropathic pain, and lack of DEA schedule designation compared with similar agents (such as pregabalin). The inability to detect gabapentin on routine drug testing may be another reason for its rise in popularity.
Conclusions: The rates of gabapentin abuse have steadily risen during the period between 2012 and 2015, possibly secondary to the rise in off-label applications, widespread availability, and lack of DEA schedule designation.

KEYWORDS Gabapentin; NPDS; abuse

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185. Pediatric ondansetron overdose resulting in obtundation, respiratory failure and QTc prolongation

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Background: Ondansetron is a commonly prescribed anti-emetic. Although well tolerated in therapeutic doses, there is limited data on toxicity in pediatric overdose. Ondansetron antagonizes serotonin sub-type 3 (5-HT3) receptors in the central nervous system. There is a single case report of obtundation, hypotension, liver enzyme elevation, QTC prolongation, serotonin syndrome, and seizures in a pediatric overdose. We report a similar case.
Case report: A 24-month-old healthy female presented with obtundation, seizure-like activity, respiratory failure and QTc prolongation. The mother found the child with four opened blister packs of 8mg ondansetron ODT tablets (dose 3.56 mg/kg, recommended dose 0.1–0.15 mg/kg). Within an hour, the child seemed sluggish and developed "shaking" movements of her upper extremities. The mother placed her in a cool bath to "revive" her. When she did not wake up she took her to the Emergency Department. On arrival to the ED she was unresponsive reacting only to painful stimuli. Her abnormal vitals were as follows: HR 115 (bpm), BP 97/38 (mHg), Temp 33.8˚C. Her pupils were 7mm bilaterally and minimally reactive. There was no clonus, hyperreflexia, or rigidity. While in the ED, the patient developed a tonic–clonic seizure and desaturated on pulse oximetry to 60%. She was administered iv midazolam and morphine, as part of RSI, and intubated. Her initial EKG showed sinus rhythm with a QTC prolongation of 498 ms. Laboratory data revealed a potassium level of 3.1 mEq/L and a glucose of 160 mg/dL (the CBC and remainder of the BMP were normal). Acetaminophen, aspirin, and ethanol levels were negative. A urine drug screen performed after intubation was positive for benzodiazepines and opioids consistent with the RSI medications. A CT of the brain was negative. The child was transferred to a pediatric intensive care unit. EEG performed hours after intubation and sedation showed diffuse slowing consistent with encephalopathy. Within 8 h of initial ingestion, the patient became more alert and was successfully extubated. A repeat EKG the following day showed her QTC normalized to 410ms and the child was discharged home.
Case discussion: Our case is like the one prior case report of severe toxicity after pediatric ondansetron overdose. In that case, the child also presented with obtundation, seizure, and QTc prolongation. Additionally that case also had abnormal liver function tests as well as clonus and hyperreflexia concerning for serotonin syndrome. In our case, liver function was normal and serotonin syndrome was not observed. Supportive care was initiated and the patient had resolution of her symptoms within several hours. Given the history, ondansetron was thought to be the single agent responsible.
Conclusions: With the widespread use of ondansetron, this medication is frequently found in households with children. Although rarely reported, severe toxicity can occur with overdose. Treatment is primarily supportive with attention to airway, seizure precautions and QTc monitoring. More literature regarding the frequency, presenting symptoms, complications, and mechanisms of toxicity, would assist clinicians in caring for patients with suspected ondansetron ingestions.

KEYWORDS Ondansetron; pediatric; unintentional overdose

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186. Heroin, cocaine and methamfetamine exposures reported to US poison centers (NPDS): 2005–2016

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Introduction: Abuse of heroin, cocaine, and methamfetamine remains persistent in the US. We examined temporal and demographic changes of these three drugs of abuse over a 12-year period.
Methods: retrospective evaluation of the National Poison Data System (NPDS) for cases involving heroin, methamfetamine and cocaine reported to US poison centers from 2005 to 2016. Severe outcomes were defined as moderate effect, major effect or death.
Results: There were 41,882 cases involving heroin (mean 3490/year) with a significant increase (314%) from 1878 cases/year in 2005 to 7774 cases/year in 2016. The increase per year escalated dramatically in 2010 from a mean annual increase of 4%/year (2005–2010) to 33%/year during 2010–2016. Heroin exposures occurred primarily in adults (>19years), increasing from 82% of cases in 2005 to 91% of cases in 2016. The percentage of heroin cases involving adolescents (12–19 years) decreased 51% with a change noted in 2010 from a mean annual increase of 2.9%/year to a decrease of 9.6%/year from 2005 to 2010 and 2010 to 2016, respectively. There were 68,576 cases involving cocaine (mean 5714/year) with a 24% decrease from 7706 cases/year in 2005 to 5318 cases/year in 2016. The cases/yr for cocaine decreased until 2014 with a mean annual decrease of 4%/year from 2005 to 2014 and an increase of 6%/year for 2014–2016. The percentage of cocaine cases involving adolescents (12–19/years) decreased 33% overall, with a mean annual decrease of 5%/year from 2005 to 2014 and an increase of 6%/year for 2014–2016. There were 41,470 cases involving methamfetamine (mean 3455/year). After 2007, there was a sustained linear increase (486%) from 1119 cases/year in 2007 to 6558 cases/year in 2016. The percentage of methamfetamine cases involving adolescents (12–19/years) decreased 56% from 14.5% of total cases/year to 6.4% cases/year. Severe outcomes increased proportionally with total cases for heroin and methamfetamine: severe heroin cases increased 396% from 903/year in 2005 to 4676/year in 2016 and severe methamfetamine cases increased 722% from 377/year in 2007 to 3100/year in 2016.
Discussion: Heroin and methamfetamine cases have increased dramatically, with cocaine showing a smaller but consistent decrease. The enormous increase in methamfetamine, despite controls on pseudoephedrine supplies, is previously unreported. The increase in heroin and methamfetamine appears to be occurring in adults, with percentage of adolescent abuse of heroin, methamfetamine and cocaine all showing significant declines.

KEYWORDS Heroin; methamfetamine; cocaine

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187. Trends in fatal overdoses, with a focus on opioids, analogs and polysubstance overdoses

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Background: Opioid intoxication has been increasing for more than two decades. For much of this time period, prescription opioid drug diversion was the primary source of the increase. Coordinated efforts at controlling the number of dispensed opioids have shown results in decrease prescriptions dispensed. However, in the same period, deaths caused by lethal intoxication have increased.
Methods: Review of Franklin county coroner's office records from 2012 to 2016 for lethal intoxication. The office also provides service for 6 surrounding counties, providing a service for central Ohio. The drugs attributed to the fatality were based on the

coroner's legal determination after autopsy and post-mortem toxicology analysis.
Results: Between 2012 and 2016, 1748 deaths were attributed to lethal intoxications (OD). There was a 34% increase from 305 deaths in 2012 to 409 deaths in 2016. About 1533 (77.7%) of OD deaths were attributed to an opiate/opioid or polysubstance intoxication including an opioid with a benzodiazepine or cocaine. During this period, there was 40% increase in the opioid or opioid/poly-substance related deaths. The increase in the opioid or opioid/poly-substance group was entirely responsible for the rise in total lethal intoxications. Two notable and significant increases occurred involving fentanyl/analogs (676% increase, 17–132/year) and cocaine (90% increase, 70–133/year). The significant increase as well as the presence of fentanyl analogs was not seen until 2015 and 2016. Heroin OD related deaths increased 80% until 2015, but fell 21% in 2016 (170–133/year) Lethal intoxications involving a prescription opioid or benzodiazepine remained steady: Rx-opioids excluding oxycodone (mean 82/year), oxycodone (mean 57/year) and benzodiazepines (mean 46/year). Methamfetamine related deaths occurred but were less than 1–2% (1–9/year).
Discussion: The increase in lethal intoxications in the study period is attributed to dramatic increase in illicit heroin and illicit non-pharmaceutical fentanyl fatalities. Prior to 2015 the source of fentanyl was prescription drug diversion (patch). In 2015, illicit fentanyl via the heroin distribution market appeared and is responsible for the sudden increase. The increase in cocaine/poly-substance OD deaths is also concerning. Users report the belief that adding a stimulant to their drug mix will help keep them awake (and alive) when using the more potent fentanyls. During this same period, there was no change in prescription opioid fatalities.
Conclusions: Opioid/opiate fatalities continue to increase, despite a decrease in available prescription opioids. The increase appears related to illicit heroin and illicit fentanyl and fentanyl analogs.

KEYWORDS Fentanyl analogs; heroin; cocaine

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188. Pediatric marijuana ingestions: the ToxIC experience 2010–2016

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Background: Decriminalization, legalization, and medical use of marijuana have increased availability and diversified exposures. This is particularly true of pediatric exposures to marijuana and marijuana edible products. The clinical effects of marijuana on children may be different and potentially more severe when compared with adults. Previous research has looked at subsets of pediatric marijuana exposures, and significant clinical outcomes requiring ICU admission have been reported. More data are needed regarding the clinical features and circumstances surrounding pediatric marijuana exposures.
Methods: Cases involving marijuana as the primary exposure in the pediatric (age ≤12) population reported to the ToxIC Registry between 1 January 2010 and 31 December 2016 were reviewed. Cases were excluded if more than one primary exposure was present. Data collected included demographics, exposure year and conditions, clinical outcomes, and treatment.
Results: Thirty-five cases listing marijuana as the primary agent were identified. Five cases were excluded for the presence of another primary coingestant, which included nicotine, methamfetamine, ethanol, and cocaine, leaving a total of 30 cases. Sixteen (53%) were female. Most cases were from Arizona (23%), Colorado (23%), and New York (17%), see Figure 1. Twelve (40%) were under 2 years of age, 12 (40%) were 2–6 years of age, and 6 (20%) were 7–12 years of age. The number of cases increased significantly after 2013: 2010 (0%), 2011 (6.7%), 2012 (0%), 2013 (10%), 2014 (33.3%), 2015 (13.3%), and 2016 (36.7%). Most cases (87%) involved unintentional exposures. The majority (63%) were oral ingestions, two (6.7%) were inhalational, and in nine cases (30%), the route of ingestion not reported. Twenty-eight (93.3%) reported signs or symptoms of toxicity. The only reported toxidrome was sedative hypnotic (30%) syndrome. Coma/CNS depression was common, occurring in 21 cases (64.5%). Reported signs are detailed on Table 1. Toxicologic treatment was given in nine (30%) cases: six (20%) were given fluid resuscitation, two (10%) were given benzodiazepines, and two (6.7%) patients were intubated. No deaths were reported.
Conclusions: Thirty unique cases of pediatric marijuana exposures were reported to the ToxIC Registry between 2010 and 2016, with a trend of increasing exposures over the study years. The majority of cases were unintentional oral exposures. Depressed mental status was common and intubation was uncommon. This study is limited by absence of confirmatory testing.

KEYWORDS Marijuana; pediatric; accidental

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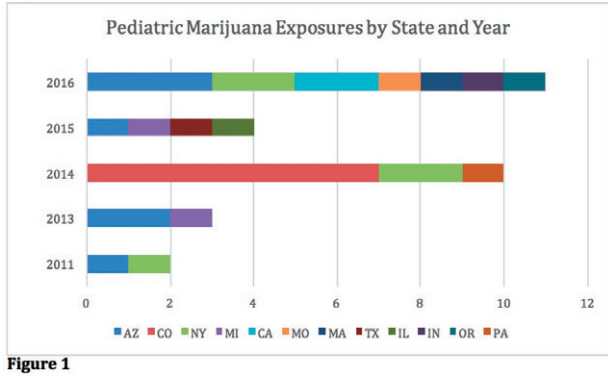

Figure 1

Table 1: Clinical Signs after Marijuana Exposure in Children

Signs	Number of patients
Coma/CNS depression	21
Hyperreflexia/myoclonus/clonus/tremor	3
Delirium/Toxic psychosis	2
Seizure	2
Hallucination	2
Agitation	2
Respiratory depression	2
Tachycardia (HR >140)	2
Hypotension (BP <80)	1

189. Changes with time in analytically confirmed exposure to novel psychoactive substances in patients with severe clinical toxicity in the UK

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Objective: The Identification Of Novel psychoActive substances (IONA) study has been collecting clinical data and biological samples from patients presenting to multiple hospitals in the United Kingdom (UK) with severe toxicity suspected to be caused by novel psychoactive substances. The study aims to identify the novel psychoactive substance (NPS) involved and link these to documented clinical features. Here we present analytical findings for 182 patients recruited between March 2015 and January 2017 and examine temporal changes in substances identified.

Methods: With ethical approval, patients (≥16 year) presenting to 16 participating hospitals with severe acute toxicity (specifically pre-defined) after suspected NPS exposure were recruited with informed consent, or in those lacking capacity at the time of enrolment, the agreement of an appropriate relative/representative. Clinical features were recorded using a structured data collection sheet. Blood and urine samples were collected and analysed by liquid chromatography-tandem mass spectrometry. Temporal changes were examined by comparing data from patients recruited over three time periods (Table), with the third following legal control of NPS in the UK by the Psychoactive Substances Act (May 2016).

Results: Clinical and analytical data were available for 182 participants. Their median age was 32 years (range 16–61 years) and 136 (75%) were male. NPS were detected in at least one sample from 112 (62%) patients, conventional drugs of misuse in 109 (60%) and both in 65 (36%). No drug of misuse was identified in any samples from 26 (14%). The most commonly identified NPS were synthetic cannabinoid receptor agonists (SCRA, $n = 66$), cathinones (21), methiopropamine (13), and NBOMe compounds (13). The eight most common conventional drugs of misuse (or their metabolites) identified were methadone (57), diazepam (32), MDMA (23), amfetamine (21), methamfetamine (19), MDA (12), cocaine (9), and MDEA (6). Reductions in the proportion of patients with samples positive for methiopropamine (legal control in November 2015) and MDMB-CHMICA were seen after 2015, but there were increases for 5F-ADB, 5F-NPB-22, and FUB-AMB (also called AMB-FUBINACA). From June 2016, a reduction in the proportion of samples positive for SCRA overall was observed, but no important changes were detected for other NPS groups. Small reductions in the proportion of patients with samples positive for NPS overall were offset by increases for conventional drugs of misuse.

Conclusions: SCRAs have been the most common NPS detected in episodes of severe NPS-related toxicity in the UK over the study period. Conventional substances are also commonly involved. The substances most commonly implicated have changed over the course of the study. Legal control may contribute to changes in the affected substances but other factors may also influence the findings.

KEYWORDS Drugs of misuse; epidemiology; mass spectrometry

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Table. Temporal changes in numbers (proportions, %) patientswith at least one positive sample

	A - March to December 2015	B - January to May 2016	C - June 2016 to January 2017	Overall
n	49	66	67	182
Any NPS	34 (69%)	43 (65%)	35 (52%)	112 (62%)
Any conventional	26 (53%)	37 (56%)	46 (69%)	109 (60%)
SCRA (Any)	19 (39%)	30 (45%)	17 (25%)	66 (36%)
Cathinone	5 (10%)	8 (12%)	8 (12%)	21 (12%)
Methiopropamine	9 (18%)	2 (3%)	2 (3%)	13 (7%)
NBOMe compounds	7 (14%)	0 (0%)	6 (9%)	13 (7%)
Specific SCRAs				
5F-ADB	0 (0%)	19 (29%)	11 (16%)	30 (16%)
5F-NPB-22	1 (2%)	8 (12%)	6 (9%)	15 (8%)
FUB-AMB (AMB-FUBINACA)	0 (0%)	5 (8%)	5 (7%)	10 (5%)
MDMB-CHMICA	7 (14%)	1 (2%)	0 (0%)	8 (4%)
5F-PB-22	3 (6%)	4 (6%)	1 (1%)	8 (4%)
5F-AKB-48	3 (6%)	2 (3%)	2 (3%)	7 (4%)

190. In stock highs? Inventory of research chemical internet vendors

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Background: The misuse and abuse of novel psychoactive substances (NPS) is facilitated by their distribution as "research chemicals" via the Internet. However, there are few studies examining these research chemical internet vendors (RCIVs). We performed a 24-week study of research chemical internet vendors to better characterize their listed inventory.
Methods: This was a prospective observational study. RCIVs were identified using a Google search term "Research Chemical Buy" performed 1 week prior to the study start date. The top 12 consecutive working vendor websites were included in the study. Vendor websites that had a broken URL, closed permanently, or for body building compounds only were excluded. Inventory was taken of all single substance, non-brand name RCs and the websites were re-inventoried every week for 24 weeks from 6/2016 to 11/2016. Newly listed RCs and those that disappeared from the websites were recorded. When the same research chemical was present multiple times on the same website it was counted only once. When the same research chemical was present on multiple website, it was counted one time per website. Each RC was classified into one of the following 13 NPS types: synthetic cathinone, synthetic cannabinoid, benzodiazepine, opioid, arylcyclohexylamine, tryptamine, LSD analogs, 2C, aminoindane, benzofuran, phenidate derivative, amfetamine, and other. The United States DEA schedule status of each substance was evaluated and recorded.
Results: During the study period, three vendors became nonfunctional but were included in the final analysis. The mean number of RCs per site was 55 (range 11–146, SD 36) for a total of 658 RCs. There was at least one example of all 13 NPS types identified. The two most common types of RC listed were synthetic cathinones and synthetic cannabinoids with a mean of 17 (range 0–39, SD 11)) and 14 (range 0–34, SD 10) per site, respectively. The least common type of RC encountered was LSD analogs with total of 11 documented across all sites. Table 1 shows the total number of each group encountered. A total of 78 new RCs were added to website inventories during the study period. Synthetic cathinones were the most common newly listed RC ($n = 27$). A total of 47 RCs disappeared during the study period. Synthetic cannabinoids were the most common RC to disappear ($n = 17$). On an average, there were eight DEA Schedule I substances listed per website (range 0–37, SD 10).
Conclusions: Distribution of NPS as RCs via the internet is a known challenge. This study demonstrates a large, varied and dynamic inventory of RCs can be found online. A limitation of this study is that we could not verify the veracity of the listed substances. Further studies are warranted to better understand the factors that drive the inventory of RCIVs.

KEYWORDS Novel psychoactive substance; research chemicals; cathinones

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Class	Number of Products
Synthetic Cathinones	200
Synthetic Cannabinoids	169
Benzodiazepines	45
Arylcyclohexylamines	34
2C	26
Benzofuran	25
Phenidate Derivative	25
Amphetamine	21
Tryptamine	17
Aminoindanes	13
Opioids	12
LSD-analogs	11
Other	60

191. Where's the withdrawal? Retrospective review of benzodiazepine withdrawal

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Background: Benzodiazepines are widely misused or abused. Acute withdrawal from benzodiazepines is often compared with ethanol withdrawal and there is concern for similar morbidity and mortality. However, there is paucity of medical literature regarding clinical characteristics, treatment and outcomes of acute benzodiazepine withdrawal. We sought to better characterize acute benzodiazepine withdrawal by examining cases treated at an academic medical center.
Methods: This was a retrospective study. The electronic medical record database of an academic medical center was queried for all patients admitted or discharged with a diagnosis of benzodiazepine withdrawal, drug withdrawal, sedative-hypnotic withdrawal or withdrawal-NOS from 1/1/2011 to 1/1/2016. Iatrogenic benzodiazepine withdrawal cases were excluded. For all cases age, sex, month/year of encounter, initial vital signs and type of drug withdrawal (alcohol, opioid, benzodiazepine, or other) were collected. In cases determined to involve benzodiazepine withdrawal then the following additional data was collected: which type of benzodiazepine withdrawing from, disposition, duration of hospital stay, presence of seizures, intubation or death and pharmacological treatment. Initially all authors abstracted the same eight encounters and results reviewed to assure inter-rater agreement.
Results: A total of 250 cases were initially identified. After authors' evaluation, only 59 cases were determined to involve benzodiazepine withdrawal. Opioid withdrawal ($N = 132$) was the most common diagnosis in the 191 non-benzodiazepine drug withdrawal cases. From 2011 till 2013, there was an average of 8 cases per year identified. This increased to 14 in 2014 and to 22 in 2015. Among the 59 benzodiazepine withdrawal cases, there were two groups identified: The benzodiazepine withdrawal only group ($n = 34$) and benzodiazepine plus other drug withdrawal group ($N = 25$). Concomitant opioid withdrawal ($N = 20$) was the most commonly identified other drug withdrawal in the benzodiazepine plus other drug withdrawal group. Table 1 shows the

clinical characteristics of these two groups. In both groups, alprazolam was the most commonly implicated benzodiazepine to be withdrawing from. Eight cases had seizures reported. No endotracheal intubation was reported. Eighty-three ($N = 49$) of all patients were treated with a benzodiazepine. Lorazepam was the most commonly used benzodiazepine but diazepam, alprazolam, midazolam, chlordiazepoxide and clonazepam were all used. For the 23 cases treated only with lorazepam, the average dose was 8.75 mg [SD 11.5]. In 15 cases, more than one type of benzodiazepine was used. Phenobarbital was used in two cases. No propofol, dexmedetomidine, or ketamine use was reported in either group. No deaths were reported. Of patients discharged, 27 (46%) received a prescription for a benzodiazepine.

Conclusions: While cases of benzodiazepine withdrawal appear to be increasing, significant morbidity was rare and mortality was absent in this study. Treatment with benzodiazepines was common but highly variable. Further multi-center studies are warranted to better characterize the incidence and characteristics of acute benzodiazepine withdrawal.

KEYWORDS Benzodiazepine withdrawal; alprazolam; drug withdrawal

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	Benzodiazepine Withdrawal Only	Benzodiazepine Plus Other Drug Withdrawal
Number	34	25
Age [SD]	46.3 [14.6]	43.7 [14.4]
% Female	50% (N=17)	72% (N=18)
Initial HR [SD]	100 [18]	95 [20]
Initial BP [SD]	140 [27]	137 [27]
Initial Temp [SD]	36.8 [0.3]	36.8[0.2]
Admitted to non-critical care unit	62% (N=21)	56% (N=14)
Admitted to ICU	3% (N=1)	4% (N=1)
Duration of Hospital Stay (Days)[SD]	5.2 [4.9]	6.2 [3.4]
Seizures Reported	18% (N=6)	8% (N=2)
Benzodiazepine Withdrawing From	Alprazolam (N=19)	Alprazolam (N=9)
Treated with Benzo	88% (n=30)	76% (N=19)
Most Common Type Benzodiazepine Given	Lorazepam (N=19)	Lorazepam (N=13)

192. An anticlimactic phosphodiesterase inhibitor ingestion

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Background: Phosphodiesterdase 4 (PDE4) inhibitors are a class of medications with increasing use. Roflumilast and apremilast are currently the two FDA approved PDE4 inhibitors, used in COPD and psoriasis respectively. There are others in research stages. PDE4 is present throughout the body, and is the major enzyme class responsible for the hydrolyses of cyclic adenosine monophosphate (cAMP), an intracellular messenger that helps to control pro-inflammatory and anti-inflammatory mediators, and decreases expression of nitric oxide synthase, TNF-α, interleukin (IL)-23 and IL-10. In contrast, PDE5 is the enzyme that hydrolyzes cyclic guanosine monophosphate (cGMP) in smooth muscle, thus PDE5 inhibitors lead to vasodilation. Apremilast was approved in the US in 2014. It is a selective PDE4 inhibitor used to treat psoriasis and psoriatic arthritis. Apremilast is well absorbed with a bioavailability of approximately 73%. Peak plasma levels occur around 2.5 h and the half-life is 6–9 h. Adult dosage is 30 mg twice a day, with no recommended dose in children. Common side effects are diarrhea, nausea, and headache. However, there is no information about overdose available in toxicology literature or databases. We report the case of a child with an overdose of 120 mg of apremilast.

Case report: The mother of a 4-year-old, 20 kg girl called the poison center minutes after she ate 120 mg from an initial dose pack of Otezla (apremilast). There were three 30 mg tablets, one 20 mg tablet, and one 10 mg tablets punched out from the pack. The girl thought it was a candy product and admitted to eating them. She was observed in the emergency department for 3 h. During this time, she reported nausea that resolved without intervention. Her initial blood pressure was 117/78 mmHg with a nadir of 90/66 mmHg, which was normal for her age. The rest of her vital signs remained within normal limits. The patient was discharged home with no sequelae.

Discussion: Roflumilast is another PDE4 inhibitor that was approved in 2011 for use in COPD. During Phase I trials, larger doses were reported to cause headache, dizziness, palpitations, hypotension, and gastrointestinal effects. Apremilast has no published information about the effects of overdose in either children or adults. Gastrointestinal side effects are common, and the medication is normally titrated up over 6 d to make these effects more tolerable. This patient ingested four times a normal therapeutic adult dose with minor effects. She had nausea with no vomiting, and demonstrated no effects to any other organ system. Given the wide distribution of PDE4 in the body, and the beneficial effects PDE4 inhibitors have on inflammation, an increased use of apremilast and other PDE4 inhibitors can be expected in coming years.

Conclusions: Apremilast is a PDE4 inhibitor with no current published information regarding the effects of pediatric overdose available to toxicologists or poison centers. We report an ingestion that was well tolerated in a pediatric patient who ingested four times the normal adult dose.

KEYWORDS Pediatric; ingestion; new drug

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193. Could early dialysis have prevented a death from acetaminophen treated with timely NAC?

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Background: Acetaminophen (APAP) toxicity is common, accounting for nearly 10% of all poison center fatalities and more than 65,000 exposures annually when considered alone or in combination products. Severe acetaminophen toxicity refractory to standardized therapy, however, is rare. *N*-Acetylcysteine (NAC) effectively prevents and treats APAP-induced hepatotoxicity. Clinical guidelines based on low-grade evidence describing the use of hemodialysis in acetaminophen poisonings have recently

been published by the Extracorporeal Treatments in Poisoning Workgroup (EXTRIP); however, it is unclear if these guidelines are properly inclusive.
Case report: A 38-year-old man presented by ambulance 2 h after reportedly ingesting Tylenol® PM (APAP 500mg/diphenhydramine 25mg), with 450 tablets unaccounted for from bottles found on scene. On arrival to the emergency department, he was minimally responsive. Naloxone was ineffective. Initial blood pressure was 93/53mmHg, pulse 105 beats/min and temperature 34 °C. Initial labs included 3-h serum acetaminophen concentration [APAP] 561 mcg/mL, ALT 17 IU/L, AST 25 IU/L, and INR 1.2. He was intubated and given 140 mg/kg of oral NAC. The patient was then transferred to a higher level of care where intravenous NAC (Prescott Protocol) was initiated. Refractory hypotension was treated with a norepinephrine infusion. Labs at the receiving hospital were as follows: lactate 5.3 mmol/L, glucose >400 mg/dL, serum creatinine 0.6 mg/dL, bicarbonate 16 mEq/L, and 7-h [APAP] 522 mcg/mL. AST, ALT, and INR were normal. The following morning, labs were as follows: [APAP] 521 mcg/mL, AST 47 IU/L, ALT 167 IU/L, and INR 1.6. NAC therapy continued via oral and intravenous routes, but progressive metabolic acidosis and transaminase derangement developed over the following 24 h. By 48 h post-ingestion, the patient was critically ill and spontaneously bleeding. He became agitated with decreased sedation. AST was 13,776 IU/L, ALT 8,755 IU/L, INR 6.9, lactate 8.8 mmol/L, pH 7.17, bicarbonate 7 mEq/L, serum creatinine 2.0 mg/dL, glucose 122 mg/dL, and [APAP] 545.2mcg/mL. Fifty-four hours following ingestion, the patient was transferred to a liver transplant center. Arterial blood gas at that time revealed a pH <6.8. He received continuous dialysis supported by three vasopressors, and was unresponsive without sedation. Liver transplant was scheduled for hospital day 4; however, he sustained an arrest from which he could not be resuscitated just prior to transplantation.
Discussion: NAC dosing for APAP toxicity is standardized, regardless of presenting [APAP] level or other details of patient presentation. Higher NAC dosing may be of increased benefit in patients with an extremely high APAP burden. This patient did not meet criteria for hemodialysis based on EXTRIP guidelines; subsequently he was not dialyzed until he was critically ill. Early onset of toxicity and persistently elevated [APAP] – likely secondary to decreased GI motility and persistent absorption in the setting of antimuscarinic co-ingestion – support the notion that early dialysis may have improved his outcome in this setting of NAC failure.
Conclusions: Early dialysis should be considered in massive APAP ingestions with evidence of coma and mitochondrial dysfunction. This case supports expansion of the EXTRIP guidelines for hemodialysis in acetaminophen toxicity.

KEYWORDS Acetaminophen; dialysis; *N*-acetylcysteine

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	3 Hours Post Ingestion	7 Hours Post Ingestion	Day 2	Day 3
APAP (mcg/ml)	561	522	521	545.2
AST (IU/L)	25	not reported	47	13,776
ALT (IU/L)	17	not reported	167	8,755
INR	1.2	not reported	1.6	6.9

194. Drilling down on teething product ingestions from 2000 to 2016

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Background: Hyland's homeopathic teething tablets have been concerning people across the country after finding that the products contain varying amounts of belladonna. Last year, the FDA issued a warning to parents about using the homeopathic teething tablets, and as of April 2017, the tablets were officially recalled. This study aimed to examine the impact of variables associated with teething product ingestions reported to a state poison center network from 2000 to 2016.
Methods: All cases involving Hyland's homeopathic teething products were obtained from a state poison center network from 2000 to 2016. Demographic information was obtained for age group and patient gender. Data gathered included year, exposure site, exposure reason, management site, clinical effects, treatments, and medical outcome. We analyzed the data using descriptive statistics.
Results: A total of 4937 exposures were reported over a 17-year period. During a six-year stretch between 2005 and 2010, 56% (2767) were reported. Of total teething product ingestions, 54% overall were female. Amongst children 0–5 years of age, 8% were under the age of 1 year, 22% were 1-year old, 47% were 2, 17% were 3%, 5% were 4, 0.5% were 5, and 0.5% were unknown. Out of 4937 cases reported, 98% (4,846) included only teething tablets ingested, and 2% (91) involved teething tablets and other coingestants. The reason for the exposure was 99% unintentional, 0.7% adverse reaction, 0.1% intentional, and 0.2% other unknown. About 97% of the exposures occurred in the patient's own residence, and 96% of exposures were managed on site. The poison center referred only 20 cases to a healthcare facility. The two most common clinical effects reported were drowsiness 0.9% (46) and vomiting 0.9% (42), and the two most common treatments were dilute/irrigate/wash 60% (2954) and food/snack 18% (866). One case required intubation and a ventilator, but that patient had ingested teething tablets and Balamine DM®. Medical outcomes reported included 68.7% not followed/minimal or nontoxic, 28.6% no effect, 1% minor effect, 0.1% moderate effects, 1.1% unrelated effects, and 0.5% unable to follow. There were no deaths.
Conclusions: In general, teething tablet ingestions could safely be managed at home. The one case reported that required extensive treatment included a coingestant.

KEYWORDS Teething product; uninetentional; product recall

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195. Criminal conviction histories in heroin verses prescription overdose fatalities

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Background: Opioid-related fatalities are at an all-time high in the US and the rate is rising. Crime has been associated with drug activity for decades. The association between criminal activity, and heroin and prescription opioid-related fatalities is unclear. We hypothesize that opioid fatalities involving heroin are more likely to have criminal convictions than prescription opioid-related fatalities.
Methods: We performed a case–control study of opioid fatalities statewide. We identified cases using the state's Office of Medical Investigator database for the primary cause of death related to an opioid between 1 January 2010 and 31 December 2015. We matched fatalities to criminal convictions using the state's

Sentencing Commission records. Frequencies of fatalities were calculated for the variables of sex, race/ethnicity, and conviction history. Since sentencing data are available for those 18 years or older, we restricted analyses to age 19 years and older to allow them to have at least one year of potential criminal conviction history as adults. Fatalities involving both heroin and prescription opioids were classified as heroin fatalities. We used Chi-square tests and logistic regression to assess categorical variables.
Results: We identified 1735 opioid fatalities in the study period with 37.0% heroin, 55.7% prescription opioids, and 7.3% as both. No novel synthetic opioids were identified in the study population. Men represented 63.8% and women 36.2% of the fatalities. By race, fatalities were White 51.4%, Hispanic 42.6%, Native American 4.4%, and African American 1.3%. Heroin fatalities were younger (39.2 versus 45.8 year; $p<.001$). At least one criminal conviction was reported in 480 fatalities, corresponding to 880 discrete court cases. Fatalities involving heroin were more likely than prescription opioid fatalities to have a conviction (40.8% versus 17.3%; $p<.001$). Men were more likely to have convictions than women (35.0% versus 14.8%; $p<.001$). Fatalities by opioid and conviction type are listed in the Table.
Discussion: Heroin-related fatalities are associated with more criminal convictions than prescription-opioid fatalities. Additionally heroin-related fatalities are more likely to be male, White or Hispanic, and die at a younger age. Limitations of the study include the use of data from only one state. By excluding fatalities in which opioids were contributing but not primarily responsible, we may have some selection bias.
Conclusions: Based on the results of our study, heroin-related fatalities appear to have more criminal convictions than prescription-related fatalities, especially in the areas of drug possession, property theft, public order, and violent crimes.

KEYWORDS Convictions; fatalities; opioid

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Table. Fatalities by opioid- and conviction type.

	Drug-related fatality type (%)		
Conviction Types	Heroin	Prescription opioids	P value
Drug possession	9.1	3.3	< .001
Drug trafficking	3.4	1.6	0.013
Domestic violence	2.5	1.8	0.3
DWI	5.9	3.4	0.015
Property theft	18.5	4.1	< .001
Public order	6.5	1.9	< .001
Violent crimes	10.4	3.9	< .001
Vehicular traffic	6.1	4.3	0.1

196. High rates of recreational abuse in patients hospitalized after dextromethorphan ingestion

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Background: Dextromethorphan (DXM) is an over-the-counter antitussive that has gained popularity as a drug of abuse. DXM has a complex pharmacology. It is an optical isomer of levorphanol and it is structurally an opioid itself, although unlike levorphanol it lacks any analgesic effect. It undergoes primary metabolism by the CYP450 system as a 2D6 substrate with dextrorphan as the primary metabolite. At supratherapeutic dosing, patients experience a mixture of serotonergic and dissociative effects varying primarily by an individual's metabolic profile. DXM enhances serotonin release and inhibits its reuptake whereas the primary metabolite of DXM; dextrophan, is a potent NMDA receptor antagonist. It is reported that extensive metabolizers experience more psychoactive effects and those with low levels of 2D6 may have more risk for serotonin syndrome.
Objectives: To describe the epidemiology, clinical findings and treatments associated with patients hospitalized related to DXM ingestion.
Methods: Retrospective review of an academic, tertiary-care bedside medical toxicology consultation service records (single provider coverage) 1/1/2011 to 12/30/2016. Data were extracted from site bedside toxicology case registry data (ToxIC site records) and entered into spreadsheet format where a medical statistician analyzed them.
Results: One hundred and one cases were identified. 41 (41%) involved individuals aged 13–18, 55 (55%) involved 19–65 year-olds, three (3%) were in children aged 2–6, and one was > 65 years old. The mean age was 23.7. 61% of ingestions occurred in males. The primary reason for ingestion was related to abuse in 77 (76%) followed by self-harm in 21. ADE/ADR or accidental ingestion accounted for a small number of cases (4%). While DXM was the primary agent ingested in all of the cases other agents were reported in 70% with 30% having more than three agents involved. Most commonly reported were other psychoactives including alcohol, sedative-hypnotics, illicit drugs of abuse and co-formulated medications such as chlorpheniramine and acetaminophen. Antidotes were administered in 10 (NAC) with two cases treated with physostigmine (co-ingestion with chlorpheniramine). Serotonin syndrome was diagnosed in 30% and anticholinergic toxidrome occurred concomitantly in 13 cases. Benzodiazepines were administered in 48% and neuroleptics in 8%. Hyperreflexia or clonus was found in 49% with 25% experiencing agitation, 19% toxic psychosis or delirium and 30% CNS depression as a primary finding. About 18% of patients required > 2 treatments or supportive cares.
Conclusions: For patients hospitalized after DXM ingestion, abuse is a frequent reason for ingestion. Its OTC availability makes it generally accessible and readily available to a large population including teens and adolescents. Ingestion is generally associated with other psychoactive agents and drugs of abuse and it can cause significant clinical impairment with primarily neurologic symptoms, which requires substantial clinical resources and interventions. DXM availability as an OTC antitussive should be reconsidered given high rates of hospitalization from abuse.

KEYWORDS Dextromethorphan; DXM; drug abuse

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197. Man succumbs to bite from severed snake head

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Background: Venomous snake heads may reflexively bite after being severed from the body resulting in envenomation. We report, to our knowledge, the first fatality in the medical literature after envenomation by a severed snake head.
Case report: A 53-year-old man reported he had killed a wild rattlesnake in a region endemic for the prairie rattlesnake (*Crotalus viridis*). He reported holding the severed head when he

was bitten on the hand. Upon EMS arrival, he was bradycardic and had difficulty breathing. Aeromedical EMS was subsequently activated. In flight, he experienced cardiac arrest. After 15 min of cardiopulmonary resuscitation, spontaneous circulation was achieved. Upon arrival to the hospital, he was bleeding from multiple sites, was tremulous, and had swelling at the bite site. His initial prothrombin time (PT) was 30.9 s (INR 2.9), partial thromboplastin time (PTT) 147 s, fibrinogen 32 mg/dL, d-dimer >20 μg/mL FEU, and platelets 31,000/μL. Initial control was achieved with 18 vials of crotalidae polyvalent immune fab (CroFab®) and blood products including cryoprecipitate, plasma, and platelets. He had improvement in coagulation parameters and bite site swelling. He remained critically ill with neurologic compromise and myoclonus; anoxic brain injury was suspected. During his 4-day hospital course, he received at total of 23 vials of crotalidae polyvalent immune fab. He never improved neurologically and care was withdrawn. He died on hospital day 4.
Case discussion: Snakes retain the bite reflex after death. Envenomation by severed snake heads within hours of decapitation are well reported in the literature. One case report describes a significant envenomation from a preserved rattlesnake head. In this particular case, the rapid decline after likely *Crotalus viridis* envenomation suggests intravascular envenomation. In general, live pit vipers can regulate venom dose. It is not known how venom dose is affected when the head is severed; however, to our knowledge no fatalities have previously been reported.
Conclusions: Death is possible following envenomation from a severed rattlesnake head.

KEYWORDS Snake; envenomation; crofab

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198. The use of Sustained Low Efficiency Dialysis (SLED) in massive acetaminophen overdose

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Background: Massive acetaminophen ingestion causing mitochondrial dysfunction (hypothermia, coma, hyperglycemia, and lactic acidosis) is uncommon. The use of SLED to improve acidaemia and enhance paracetamol elimination has not been previously described in this scenario.
Case summary: A 44-year-old male presented to the Emergency Department 2.5-h post-overdose of 200-g (2.5 g/kg) of immediate-release acetaminophen. On arrival, examination revealed BP 85/60 mmHg, pulse 112bpm, temperature 33.9 °C, and BSL 13.9mmol/L. He was unconscious (GCS =3), respiratory rate of 14/min, oxygen saturations 91% (room-air) and was intubated on arrival. Venous blood gas 5.5-h post-ingestion showed pH 6.9, pCO2 58mmHg, HCO3 13mmol/L, and lactate 14mmol/L. Fifty grams of activated-charcoal were administered via nasogastric tube. A loading-dose of acetylcysteine (200 mg/kg over 4-h) was given. The second infusion dose was doubled initially (200 mg/kg over 16-h). Acetaminophen concentration peaked at 637 mg/L (4207 μmol/L), 6-h post-ingestion. In view of severe acidaemia and a high serum paracetamol concentration, SLED was commenced 9-h post-ingestion in ICU (18-h duration). During dialysis, acetylcysteine infusion dose was increased to 400mg/kg/16-h. Plasma pyroglutamic acid concentration was undetectable. Acidaemia improved and lactate fell to normal range during the course of SLED. Apparent paracetamol half-life during SLED and post-dialysis was 6 and 10-h, respectively. Extraction ratio was 47–52%. Plasma acetaminophen clearance was steady throughout SLED (53–58 mL/min). There was no evidence of significant hepatotoxicity with a peak ALT of 76 IU/L on day 3 and peak INR of 1.9 on day 2 post-ingestion. Acetylcysteine was ceased 3 d post-initial overdose. The patient was extubated on day 4 and made a full recovery.
Discussion: SLED was performed primarily to improve acid-base status and clear lactate but also may have reduced apparent acetaminophen elimination half-life. Endogenous plasma clearance of paracetamol is reported as 200-300ml/min. Intermittent hemodialysis is considered more efficient than SLED or CRRT in terms of increasing paracetamol elimination, and clearance (IHD plasma clearance reports range from 36 to 215mL/min, extraction ratios 47–87%). While IHD sessions are usually shorter, it requires haemodynamic stability and a separate dialysis nurse dedicated to the machine.
Conclusions: In our patient, SLED was effective in improving acidaemia but resulted in only moderate plasma clearance of acetaminophen.

KEYWORDS Paracetamol; mitochondrial; massive

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199. Methanol poisoning from inhalation: a case series

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Background: Methanol intoxication is a well-recognized toxicological emergency. While most cases of significant methanol poisoning occur via ingestion, there are reports in the literature of poisoning resulting from the inhalational route. We report a series of methanol intoxications secondary to inhalational abuse of a methanol containing lacquer thinner presenting to an inner city Emergency Department.
Case reports: A laboratory database was searched for methanol levels >5 mmol/L. (16mg/dL). From 1 January 2010 to 31 December 2015. We found 35 patients who made a total of 83 emergency department (ED) visits with a methanol level >5 mmol/L (16mg/dL). The methanol levels ranged from 5.3 to 39.6 mmol/L (16.96–126.72 mg/dL). Of these, 73% of poisonings were secondary to inhalation of a methanol-containing lacquer thinner. The median age of these patients was 43 years, and 49% were male. The majority of patients (96%) resided in the core area. The most frequent chief complaints were substance abuse/intoxication, gastrointestinal complaints, and chest pain. About 18% of patients described visual symptoms. Treatments were fomepizole only (59%), fomepizole plus hemodialysis (26%), and hemodialysis alone (2%). About 49% of patients were discharged from the ED, while 28% and 23% were admitted to an intensive care unit (ICU) and an internal medicine ward, respectively. There were no cases of blindness.
Case discussion: We describe a cohort of patients who developed methanol poisoning from inhalation of a methanol containing lacquer thinner that required treatment with fomepizole and hemodialysis. While almost 1/3 of these patients were admitted to ICU, 49% were discharged from the emergency department after a course of fomepizole. The etiology of this outbreak was found to be a change in the formulation of the lacquer thinner,

substituting a higher concentration of methanol for toluene. The manufacturer and a number of local retail outlets were contacted. This resulted in the product being taken off the shelves by the retail outlets, and eventually, a change in the product formulation by the manufacturer, with a resultant decrease in the methanol content. After these actions, we have not seen any additional presentations of inhalational methanol intoxication.
Conclusions: We report the largest case series to date of patients who presented with methanol intoxication, requiring fomepizole and/or hemodialysis, secondary to inhalation of a methanol containing lacquer thinner. Physician advocacy regarding the etiology of this outbreak resulted in collaboration with retail outlets and subsequent action by the manufacturer. This ended the outbreak.

KEYWORDS Methanol; inhalation; poisoning

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200. Deaths associated with carfentanil in Hamilton County, OH

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Background: Carfentanil is a synthetic fentanyl analog that is used as a veterinary sedative for large animals. It is considered to be approximately 100 times more potent than fentanyl. It was identified as a heroin adulterant/substitute in 2016 and was believed to be responsible for a surge in overdoses and deaths in Ohio during August and September of 2016. Very little data on carfentanil exposures in humans exists. The purpose of this study is to describe deaths associated with carfentanil in Hamilton County, Ohio.
Methods: This was a retrospective study of post-mortem examinations in Hamilton County from July 2016 to January 2017. Hamilton County is in southwestern Ohio and has a population of approximately 800,000. Cincinnati is the largest city in the county with an approximate population of 300,000. Hamilton County Coroner data was searched for cases where carfentanil was assigned as the cause of death. At present, carfentanil is only tested on deaths from suspected overdoses. All postmortem bloods samples were done on peripheral blood. Qualitative carfentanil testing was done by Axis Forensic Toxicology, Indianopolis, IN and NMS Labs, Willow Grove, PA.
Results: There were a total of 49 deaths. The mean age was 42 (range 21–63). Gender breakdown was males 35 (71.4%), female 14 (28.6%). Race makeup was white 43 (88%), black 4 (8%), and Hispanic 2 (2%). Deaths peaked in the month of September with 22. 32 of the 49 cases had known quantitative carfentanil levels which ranged from 0.013 to 1.3 ng/mL. The mean carfentanil level was 0.259 ng/mL. Fentanyl, fentanyl analogues, or morphine/6-monoacetylmorphine (6-MAM) were found in 33 of the cases. Eleven cases with quantitative levels did not have another opioid identified. The mean carfentanil level for those 11 cases was 0.350 ng/mL. There were two cases with levels where the sample was antemortem. In these two cases, the levels were 0.055 ng/mL (also identified with acetyl fentanyl and furanyl fentanyl) and 0.370 ng/mL (also identified with alprazolam and clonazepam). The most common other agents were fentanyl (15), morphine/6-MAM (30), ethanol (14), and cocaine (11). Acetyl fentanyl and furanyl fentanyl were the only other fentanyl analogs identified.
Conclusions: This study provides a starting point for interpretation of postmortem carfentanil levels in forensic casework. The study is limited by the lack of incidental carfentanil levels in deaths from other causes other than overdose as well as levels in patients surviving overdoses. In addition, it is unknown whether carfentanil undergoes significant postmortem redistribution.

KEYWORDS Carfentanil; heroin; fentanyl

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201. Fibrillating to sleep, trazodone-induced atrial fibrillation

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Introduction: We present a case of a 22-year-old male presenting with atrial fibrillation following therapeutic Trazodone use. While atrial fibrillation has been reported previously in patients with cardiovascular disease it has not been reported in an otherwise healthy male.
Case description: A 22-year-old male without past medical history presented to the emergency department (ED) with complaints of palpitations. The patient had ingested 100mg of Trazodone approximately 0.5 h prior to arrival in an attempt to sleep. He then developed symptoms of palpitations and orthostasis. He reported that this had occured twice before when taking Trazodone for sleep and resolved spontaneously.Initial EKG revealed atrial fibrillation with a ventricular rate of 134 beats per minute, with ST depression in leads V2–V4. Normal saline bolus, basic metabolic panel and complete blood count were ordered. No electrolyte abnormalities were noted and blood count was unremarkable. Comprehensive urine drug screen was negative. After 1.5 h of observation the patient's symptoms resolved. Repeat EKG revealed normal sinus rhythm with a rate of 86, with a QTc of 431. A sample was sent to NMS for serum Trazodone concentration. Trazodone concentration of 0.50mcg/mL this correlates with approximately 2 h post-ingestion.
Discussion: Therapeutic range for Trazodone is 0.30–1.5 mcg/mL. It is possible that symptoms may be related to the drugs metabolite meta-Chlorophenylpiperazine (mCPP). Unfortunately concentrations of mCPP were not obtained. While non-fatal and without lasting harm, this case illustrates the potentially disastrous effects that therapeutic Trazodone may have on individuals with excitable atrial tissues. To our knowledge, this is the first case with quantitated Trazodones levels, the absence of other cardioactive coingestants and without cardiac history. Great care should be taken before starting any patient on trazodone and a thorough evaluation for underlying arrhythmia should be undertaken.

KEYWORDS Arrhythmia; Trazodone; cardiovascular

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202. Retrospective review of methotrexate overdoses reported to the California Poison Control System: a 17 year review

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Background: Methotrexate is an antimetabolite antineoplastic that may result in significant adverse effects in overdose including gastrointestinal effects, mucositis, bone marrow suppression, renal and liver failure. However, it is difficult to predict which patients are likely to go on to experience significant adverse effects after overdose.
Objectives: To describe adverse events, therapies, and outcomes of patients of all ages with methotrexate overdoses reported to the California Poison Control System over a 17-year period.
Methods: This is a retrospective review of methotrexate exposures reported to the California Poison Control System (CPCS) from 1 January 1997 to 31 December 2013. Patients were excluded if there was no exposure to methotrexate, duplicate cases, not treated at a health care facility, or if lost to follow-up. Individual CPCS case notes were reviewed by two independent reviewers to verify inclusion and exclusion criteria, demographics, clinical and treatment data. Clinical data include reason for exposure, acuity of exposure, route of exposure, serum methotrexate concentration values, adverse events (gastrointestinal (GI) effects, central nervous system (CNS) effects, mucositis, bone marrow suppression, renal injury defined as creatinine elevated above normal, and liver injury defined as AST or ALT above reference ranges), outcome, and disposition. Treatment data include decontamination, type of supportive care, and administration of leucovorin, bicarbonate, and glucarpidase.
Results: Of the initial 369 cases identified, 134 patients met inclusion criteria, including 83 (61.5%) females, and 51 (37.8%) males with an average age of 38.7 years (range 0.83–89). Acuity of ingestion was determined to be acute in 44 (23.8%) patients, acute on chronic in 42 (31.3%) patients, chronic in 44 (23.8%) patients. Of the included patients, 53 (39.6%) patients experienced GI symptoms (including nausea, vomiting, diarrhea, abdominal pain, or other GI symptoms), 5 (3.7%) patients were noted to have elevated AST/ALT, 9 (6.7%) patients were noted to have CNS abnormalities (including drowsiness and ataxia), 17 (12.7%) patients developed mucositis, 17 (12.7%) patients developed bone marrow suppression, and 10 (7.5%) patients developed renal failure. Most patients with moderate or major outcomes were the result of chronic exposures ($n = 17/20$; 85%), including a single identified death. No major clinical effects or deaths were identified in patients after acute ingestion; no bone marrow suppression, renal failure, or mucositis was noted in these patients. A single patient (1/44; 2.3%) was noted to have AST and/or ALT elevation after acute ingestion. Of the acute pediatric ingestions ($n = 37$), the median amount of methotrexate ingested was 10mg (range 2.5–55mg); however, no adverse events were noted. Twelve (12/37; 32.4%) of the pediatric patients received leucovorin rescue, two (2/37; 5.4%) patients were treated with sodium bicarbonate, and one (1/37; 2.7%) patient received folate.
Conclusions: In this review of methotrexate exposures reported to the California Poison Control System over a 17-year study period, most patients (79.1%) experienced minor or no adverse events. Patients with chronic exposures experienced more significant adverse events than any other ingestions, while no acute pediatric ingestions resulted in significant adverse outcomes.

KEYWORDS Methotrexate; poison control; adverse effect

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203. Multiple seizures in a pediatric patient following marijuana ingestion

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Background: Recent legalization of recreational marijuana in several states has led to an increased incidence of pediatric exposure, often through the ingestion of edibles containing tetrahydrocannabinol (THC). Case reports of seizure after marijuana exposure are uncommon. We report the first case of multiple seizures in a pediatric patient following an unintentional THC ingestion.
Case report: The patient is a 12-month-old male who presented to the emergency department for evaluation of decreased responsiveness. His mother stated that he was in his usual state of health until 1 h prior to arrival, at which time he was noted to be somnolent. He had one episode of "staring" with unresponsiveness while at home lasting an unknown amount of time. On initial evaluation, the patient was somnolent, occasionally opening his eyes. He also demonstrated hypotonia in all extremities. There were no external signs of trauma. Vital signs were normal except for a heart rate of 120 and blood pressure of 70/40. He suddenly became unresponsive with fixed left gaze deviation, jaw clenching, and increased tonicity in all extremities. This lasted 45 s and resolved spontaneously after which he cried inconsolably. He then had a second similar episode lasting 1–2 min which resolved after administration of intravenous lorazepam. The patient then had a third similar episode lasting 45 s which resolved after further administration of intravenous lorazepam. These events were felt to be consistent with seizures. Urine drug screen was positive for THC. Other laboratory tests including CBC, CMP and lactate were unremarkable. CT Head was negative. Blood was sent for serum THC concentration analysis. He was admitted to the pediatric ICU and improved overnight, returning to baseline mental status without further intervention. He was discharged to the care of extended family.
Case discussion: The patient's family reported having marijuana "cigarettes and buds" in the home. They admit he may have ingested marijuana cigarette butts from an ash tray. After discharge, the serum 11-Nor-9-carboxy-THC (TCH-COOH) concentration resulted at 186 ng/mL. Although there are reports of serum TCH-COOH concentrations of this magnitude in chronic heavy daily marijuana users, to our knowledge, this is the highest reported concentration after acute THC ingestion. The patient did not return to baseline between seizures, implying status epilepticus.
Conclusions: Children who ingest THC are at risk of numerous adverse events including seizure. This case demonstrates the possibility of multiple seizures and status epilepticus with very high serum marijuana metabolite concentrations. Families and clinicians should be aware of this risk.

KEYWORDS Marijuana; THC; seizure

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204. Sex differences in intentional exposures among adolescents and adults: a retrospective review of National Poison Data System (NPDS) pharmaceutical exposures 2007–2016

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Background: The available sex and gender-based data in suicide attempts suggests that male patients are more likely to complete a suicide attempt, and that female patients are more likely than male patients to attempt suicide by poisoning. However, little is known about overall sex differences among intentional ingestions of all kinds.
Methods: National Poison Data System (NPDS) data were extracted for intentional exposures to pharmaceuticals, both single and multiple substance ingestions, with reasons for exposure including "intentional – abuse", "intentional – misuse", "intentional – suspected suicide", and "intentional – unknown reason", among patients aged 13–19 and aged 20–65. Exposures were included if categorized as more serious (outcome = moderate, major, or death) and reported to NPDS between 1 January 2007 and 31 December 2016. Descriptive statistics, graphical displays, linear regression, and multivariate analysis of variance were performed for exposure year and sex (male versus female) using SAS JMP version 12.0.1 (SAS Inc., Cary, NC).
Results: From 2007–2016, NPDS reported 206,306 intentional exposures with more serious outcomes for age 13–19 years old; of which 65.1% were suspected suicide, 25.4% abuse, 5.62% misuse, and 3.97% unknown. NPDS likewise reported 795,989 for age 20–65 years old; of which 72.8% were suspected suicide, 15.2% abuse, 6.84% misuse, and 5.18% unknown. Exposures were consistently increasing over this decade at a rate of 1–8% per year ($p<.0001$). From the multivariate analysis for age 13–19 years old, R^2 was 0.988, LogWorth for sex was 11.5 and for year 10.8 ($p < .0001$) with a female:male ratio of 1.43. From the multivariate analysis for age 20–65 years old, R^2 was 0.952, LogWorth for sex was 10.7, and for year 7.65 ($p < .0001$) with a female:male ratio of 1.17.
Conclusions: Females were more likely to have an intentional ingestion with serious outcomes reported to the NPDS during the time period 2007–2016. Identifying sex-based differences in intentional toxicological exposures may help inform sex-specific approaches to the care of the poisoned patient, as well as to poisoning prevention efforts.

KEYWORDS Intentional ingestions; National Poison Data System; adolescent and adult

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Adverse Drug Events over time	ADEs Mean/year	Slope and 95% Confidence Interval %/year	#/year	95% CI	Rsquare
Females	2,001	3.47%	69.4	[54.8, 83.9]	0.938
Males	1,303	3.88%	50.5	[38.7, 62.3]	0.924
Males+Females	3,304	3.63%	119.9	[97.2, 143]	0.949

205. Sex differences in adverse drug events in older adults: a retrospective review of National Poison Data System cases 2007–2016

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Background: Physiological, hormonal, and genetic differences between male and female patients may affect the rate of adverse drug events (ADE), with female patients experiencing higher drug concentrations and more ADEs, even after accounting for weight differences.
Methods: National Poison Data System (NPDS) data were extracted for ADEs to single substance exposures in adults age 60 years and older, categorized as more serious (outcome = moderate, major, or death), between 1 January 2007 and 31 December 2016. Descriptive statistics, graphical displays, linear regression, and multivariate analysis of variance were performed for exposure year and sex (male versus female) using SAS JMP version 12.0.1 (SAS Inc., Cary, NC).
Results: From 2007 to 2016, NPDS reported 105,548 single exposures with more serious outcomes among those age 60 years and over, including 59,410 females, 46,092 males, and 46 of unknown sex. Of the males and females, 17,034 were ADEs, of which 89.8% were associated with a drug, 2.9% with a food, and 7.3% with other. ADEs were consistently ($p<.0001$) increasing over this decade at a rate of 3.5–4% per year. From the multivariate analysis, R^2 was 0.981, LogWorth for sex was 14.6 and year 9.61 ($p<.0001$) with a female:male ratio of 1.53.
Conclusions: Among patients age 60 years and over with ADEs reported to the NPDS for 2007–2016, ADEs occurred in more females than males and increased over time for both. These results may guide both provider awareness, and efforts to prevent adverse drug events. More research is needed to determine the underlying reasons for increased ADEs in females versus males, with possible etiologies including lack of pharmaceutical research in female patients, increased susceptibility to ADEs, increased exposure to pharmaceuticals, and polypharmacy.

KEYWORDS Adverse drug event; National Poison Data System; geriatric

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Age Group	All Exposures over time	Exposures mean/year	Slope and 95% Confidence Interval %/year	#/year	95% CI	Rsquare
13-19 y/o	Females	12,115	8.08%	979	[741, 1,218]	0.918
	Males	8,489	1.65%	140	[-1.79, 282]	0.393
	Males+Females	20,603	5.43%	1,119	[937, 1,302]	0.961
20-65 y/o	Females	42,911	4.36%	1,870	[1,520, 2,220]	0.950
	Males	36,572	4.48%	1,637	[1,251, 2.023]	0.923
	Males+Females	79,483	4.41%	3,507	[2,777, 4,237]	0.939

206. The Vulcan Cleanse: an attempt at a "Natural Colon Cleanse" leads to the *in vivo* execution of a classic elementary school science project

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Background: Home and naturopathic remedies are generally benign until they are not. The combination of vinegar (acetic acid) with baking soda (sodium bicarbonate) is an endothermic reaction that releases carbon dioxide. We describe a patient that ingested vinegar and baking soda that caused substantial gastric injury and perforation.
Case report: A 52-year-old man presented to the ED complaining of generalized abdominal pain after "doing a colon cleanse" with apple vinegar, cayenne pepper, and two tablespoons of baking soda in a glass of water. He drank the vinegar and cayenne pepper first and subsequently drank the baking soda solution. The patient stated he heard a "pop" and "felt like his stomach suddenly got really big." He had immediate pain and vomited red material. Upon hospital arrival, his vital signs were normal and his complete blood count and electrolytes were likewise normal with the exception of hyperglycemia to 432 mg/dL. Exam revealed diffuse abdominal pain to palpation with signs of peritonitis. CT scan of the abdomen demonstrated perforation of the stomach at the lesser curvature with pneumoperitoneum and a moderate amount of heterogeneous free fluid. General surgery was consulted who took him to the operating room. Intraoperatively, he was found to have over 2 L of gastric contents in the abdominal cavity. Inspection of the stomach noted a large perforation along the lesser curvature. Extensive necrosis was also noted. A subtotal gastrectomy and Roux en Y gastrojejunostomy was performed. Pathology report demonstrated severe erosive changes and transmural hemorrhage. His hospital course was complicated by a collection of intraabdominal fluid requiring IR drainage but otherwise unremarkable. He was discharged post-operative day 19.
Case discussion: Ingestion of vinegar, combined with intrinsic stomach acid and baking soda causes the well-known endothermic reaction and release of carbon dioxide. Two tablespoons of baking soda could theoretically form 2.5 L of carbon dioxide under ideal conditions. The pathology report described changes consistent with caustic injury. It was likely a combination of caustic injury with a rapid increase in gastric pressure that resulted in gastric perforation.
Conclusions: Mimicry of grade school science fair volcanic simulations within the gastrointestinal tract is ill advised and should be avoided.

KEYWORDS Caustic injury; adverse drug event; naturopathic

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207. A video-based emergency department education program for opioid overdose recognition and response

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Background: As bystander naloxone becomes more readily available in the community, educating citizens to respond to an opioid overdose has become a vital component of combating the opioid epidemic. The Emergency Department is a potential site for education, given that it is the primary site of care for opioid overdose patients. However, ED staff and resources are limited. We performed a small pilot study to assess the efficacy of video education for teaching overdose first aid and use of rescue naloxone in an emergency department.
Methods: We conducted a pilot survey study of participants considered at risk for opioid overdose presenting to a single emergency department. We included English-speaking adults at risk of future opioid overdose based on history of opioid abuse, prior care for an opioid overdose, or voluntary participant request. Participants were shown an educational video on the recognition and treatment of an opioid overdose publicly available at www.prescribetoprevent.org. Participants were ensured a private area to view the video and were provided with a tablet computer and headphones. A survey and semistructured interview assessing knowledge, attitudes and practices of overdose response and naloxone use was administered before and after showing the video. Participants were assessed on their ability to identify the steps required in responding to an opioid overdose and using rescue naloxone. They were also asked about their access to naloxone, opioid use habits, and willingness to educate friends and family regarding the use of naloxone. Study participants were contacted at 30 d after intervention to assess retention of the information presented in the video.
Results: Participants ($n = 11$) were predominantly white (72.7%) and male (63.6%). Prior to the delivery of the educational module, participants correctly identified an average of two steps (median = 2) of the 11-step overdose response process; post-educational module participants identified an average of 6.8 steps (median = 8.5, $p < 0.05$). All 11 participants expressed willingness to speak to friends and family about naloxone, educate those with whom they use on the correct use of naloxone, and go to a pharmacy with a standing order to obtain naloxone. We were able to contact only three participants at 30 d after enrollment. These participants had low retention of the video educational content, recalling an average of only 1.7 steps (median =2) of the 11 steps of naloxone use.
Conclusions: Viewing an educational video in the emergency department improved participants' knowledge of first aid and use of rescue naloxone. With limited follow up in this challenging population, we were unable to adequately assess knowledge retention over time.

KEYWORDS Naloxone; opioid; prevention

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208. The effect of a toxicology standardized curriculum on toxicology section In-Training Examination scores of emergency medicine residents

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Background: Anecdotally it is believed that exposure to toxicology fellowships improve emergency medicine medical education, yet this has never been demonstrated empirically. Multiple studies have shown that formalized curriculum leads to increase pass rates among residents on the in-training examination, which is predictive of success on the board qualifying examination. Toxicology is one of the 20 major systems tested and accounts for approximately 5% of the total examination score. It is currently unknown if the development of a structured toxicology rotation has been effective in increasing resident success on the toxicology section of the in-training examination. To our knowledge, no prior study has evaluated the effect of toxicology curriculum development has on emergency medicine resident testing outcomes. In 2009, our program restructured the toxicology curriculum and hired our first board certified medical toxicologists. Over the next several years a structured curriculum of toxicology education was formalized. During this rotation the residents would:
•Have one-on-one case based teaching with a board certified toxicologist,
• Attend statewide grand rounds,
• Take toxicology consultation call,
• Treat adult and pediatric patients in the ED, floor, and ICU,
• Attend daily rounds on admitted patients,
• Evaluate chronically poisoned patients in outpatient clinic, and
• Teach colleagues and students about the toxins they encountered.
Purpose: To determine if the institution of a toxicology curriculum and consultation service improved the toxicology section scores of the Emergency Medicine In-Training examination for third year residents.
Methods: Exam scores for third year residents were collected for all residents taking the in-training examination 3 years prior to the toxicology curriculum change (2007–2009) and three years after (2013–2015). Available national average scores and toxicology section scores for the same time periods were collected. Scores for 2010–2012 were excluded as this was during the transition period.
Results: A total of 30 scores were collected prior to the curriculum change and 36 after for both the total in-training examination and the toxicology section scores. Available matched year national scores were collected for comparison. Our average total scores for the pre intervention years were 76%, 73%, and 74%. The toxicology scores for these years were 78%, 76%, and 78%. The total scores post-intervention were 78%, 76%, and 77%. The tox section scores of these years were 85%, 85%, and 89%. National average scores for the pre-intervention years were 82%, 81%, and 80% National average for the post-intervention years were 80%, 79%, and 80%. Toxicology section scores for the post-intervention years were 82%, 85%, and 85%.
Conclusions: From 2007 to 2015, our resident scores on the in-training exam and the toxicology section have increased, national scores have remained largely unchanged; however, our tox section scores have outpaced total score improvement and currently tox section scores are at or above the national average. This trend suggests that the development of a focused toxicology curriculum has had a positive impact on toxicology section scores on the national emergency medicine in-training examination. While more studies are needed, this suggests that similar programs might improve the toxicology scores of residents nationally.

KEYWORDS Resident education; curriculum development; In-training examination

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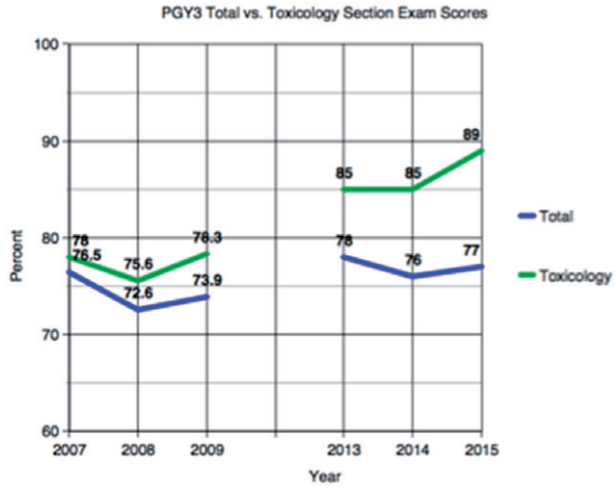

209. Self-reporting of medications in sexual assault patients across time

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Background: To date, a paucity of literature exists describing the self-reporting of medications used by sexual assault patients prior to assault, 1 week after, and at 6-week follow-up. We aim to provide descriptive data from an on-going NIH-funded study to examine the medications used by sexual assault patients across time.
Methods: This is a secondary analysis of data collected from June 2015 to March 2017 as part of an on-going NIH-funded trial evaluating the mechanisms of chronic musculoskeletal pain following sexual assault among females presenting to 13 emergency department and clinical-based sexual assault programs across the US. Female survivors ≥18 who presented to a sexual assault program within 72 h of assault, received a SANE exam, and who meet other inclusion criteria were eligible to participate. Subjects completed a short self-report assessment at time of exam, followed by self-report assessments at 1 week, 6 week, 6 month, and 12 month time periods. Self-reported data related to medication use prior to assault, 1 week post-assault and weeks 6 post-assault were used in this analysis. Data are reported as frequencies and percentages with corresponding *p*-values.
Results: There were 344 instances of medication use prior to the assault, 429 instances of medication use at 1 week follow-up, and 277 instances of medication use at 6 weeks post-assault. The instances of over-the-counter (OTC) medication use prior to the assault significantly increased compared with the use at 6 weeks (25% & 37%, respectively; $p=.001$), and OTC use at 1 week

compared with 6 weeks approached significance (30% & 37%, respectively; p=.053). There were no significant findings for benzodiazepines, non-benzodiazepine-like, opioids, and centrally acting muscle relaxants at any time point. There was a significant decrease in psychotropic use prior to the assault compared with 1 week use (22% & 15%, respectively; p=.012) and an increase in 1 week compared with the 6 week use (15% & 22%, respectively; p=.018). There was a significant decrease in prescription medication use prior to assault compared with 1 week (31% & 24%, respectively; p=.03), prior to assault compared with 6 weeks (31% & 24%, respectively; p=.0001), and 1 week compared with 6 weeks (24% & 15%, respectively; p=.0038).

Conclusions: Limitations include the self-reporting nature of this study, lack of validation of agents by conformational screening, limited follow-up and exclusion on non-English speaking patients. This is the first multi-site comparison of medication use prior to and following sexual assault. OTC medication use increased in the weeks following sexual assault. Benzodiazepine, non-benzodiazepine-like, opioids, and centrally acting muscle relaxant use did not significantly change. Psychotropic agents significantly increased and decreased at the 1 week versus 6 week time periods and prior to assault versus 1 week time period respectively. Prescription medication use decreased at all time points, likely related to lack of follow-up. It is notable that OTC medication use significantly changed from pre- to post-assault and significantly increased over time after the assault. These results suggest that the medication needs of sexual assault survivors evolve in the subsequent weeks after an assault.

KEYWORDS Sexual assault; medication; over-the-counter

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210. Analysis of medical marijuana laws in states transitioning to recreational marijuana – a gateway drug policy?

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Introduction: Every state that has recreational marijuana initially had a medical-based marijuana or cannabinoid law. Some of these laws have specific language regarding the poorly-psychoactive cannabidiol (CBD) and the highly-psychoactive tetrahydrocannabinol (THC). We analyzed these medical-based marijuana and cannabinoid laws to determine if there were patterns within these statutes that could predict which states would progress to recreational marijuana.

Methods: Every current medical marijuana or cannabinoid state law (as of March, 2016) was analyzed as to the substance of the individual acts. Particular attention was directed toward language relating to individual cannabinoids, such as CBD and THC, and if there are any limits to the THC content specified in the acts. Association between states with CBD-specific laws and non-CBD laws and their eventual passage of recreational marijuana laws was performed using Fisher's exact test.

Results: Since 1996, 42 of 50 states, and Washington, DC, have some law regarding the medical use of marijuana or cannabinoids. There are 16 states (Alabama, Delaware, Florida, Georgia, Iowa, Kentucky, Mississippi, Missouri, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Utah, Virginia, and Wisconsin) that have medical cannabinoid laws which focus on CBD and limit THC concentraion. All of these except Delaware, Georgia, Virginia, and Wisconsin specify a THC composition of <1%. None of these states have yet passed a recreational marijuana law (0/16, 0%). There are 28 states, and Washington D.C., that have medical marijuana laws without a focus on CBD. Eight of these (Alaska, California, Colorado, Maine, Massachusetts, Nevada, Washington, and Washington, DC) have since passed recreational marijuana laws (8/29, 27.9%). Delaware and Florida have laws pertaining to both medical marijuana plant use and CBD-specific use. Comparison of states with these laws shows that states with CBD-based laws have a decreased association with eventual passage of recreational marijuana laws compared with states without CBD-based laws (p=.037).

Conclusions: States with medical marijuana laws that are not CBD specific and do not limit the concentration of THC are associated with an increased likelihood of eventual passage of recreational marijuana statutes. Since no state has ever legalized recreational marijuana use without first legalizing medical marijuana use, these laws may predict which states are likely to progress to legalized recreational marijuana statutes. It appears that the medical establishment is being utilized to legitimize medical THC and this may herald a transition to recreational use. Whether this is a two-step legislative plan (to legitimize THC use) or due to coincidence needs to be determined.

KEYWORDS Medical marijuana; tetrahydrocannabinol; cannabidiol

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211. Development of an emergency department opioid treatment and prescribing guideline uing a Modified Delphi method

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Background: The emergency department (ED) treatment of pain has come under increased scrutiny in recent years due to the prescription opioid epidemic in the United States. Efforts to curtail the prescribing of opioid analgesics have led to guidelines published by groups such as the Centers for Disease Control (CDC) and the American College of Emergency Physicians (ACEP). Additionally, prescribing guidelines derived from expert opinion have been developed for individual hospitals and hospital systems. We describe the multidisciplinary development of an Emergency Department Opioid Treatment and Prescribing Guideline for Non-Oncologic or Hematologic Pain developed at one institution using a Modified Delphi Method.

Methods: An Opioid Treatment Workgroup (OTW) was established in the ED of a large public academic hospital. The OTW consisted of ED attending physicians, medical toxicology fellows, clinical pharmacists, and resident physicians in emergency medicine. Relevant literature and external opioid guidelines were reviewed by the OTW. A set of guidelines was developed and evaluated by three external reviewers with expertise in opioid prescribing, addiction medicine, and medical toxicology. After modifying the guideline based on that initial feedback, a Delphi survey was sent to a panel of internal experts consisting of six ED attending physicians and 3 ED residents each from the PGY1 through PGY4 training levels (18 total experts). The Delphi Method involves the anonymous surveying of experts to achieve consensus on content. A predefined agreement level of 70% was

deemed necessary (agree or strongly agree on a standard 5-point Likert scale) for eventual inclusion in the final guideline along with a minimum of two rounds of voting.
Results: After initial literature review by the OTW and external reviewer suggestions, a 14-point guideline was developed. In the first round of Delphi expert voting, 13/14 points achieved greater than 70% agreement. Edits by the OTW were based on voting and supplemental comments. In the second round of expert voting, 13/14 points achieved greater than 70% agreement. The same guideline element achieved less than 70% agreement in each round and was subsequently eliminated from the final guideline. This element discouraged administration of intravenous or intramuscular opioid analgesics for the initial relief of acute exacerbations of chronic pain. Each round of voting achieved a 100% response rate.
Conclusions: An ED Opioid Treatment and Prescribing Guideline can be developed utilizing a multidisciplinary approach, external feedback, and a Modified Delphi Method incorporating internal experts. Institutions should consider this approach when developing individualized guidelines.

KEYWORDS Opioid Guideline; emergency department; prescription opioid

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212. Massive hearing aid battery ingestion: toxic or tame?

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Background: Despite hearing aid battery ingestions being common occurrences due to their small size and ease of swallowing, there is a paucity of literature specifically describing management and potential complications of intentional ingestions of multiple hearing aid batteries in an adult. Concerns from these ingestions are due to local tissue damage and from potential exposure to toxic components of the batteries such as the inorganic mercury molecule, mercuric oxide. The majority of these ingestions are accidental and involve a single battery. We report the case of a young male who ingested a large number of hearing aid batteries and was treated conservatively without acute systemic complications.
Case report: A 33-year-old male presented to the emergency department after an intentional ingestion of 16 hearing aid batteries he had purchased earlier that day. He had a past medical history of HIV infection, peptic ulcer disease, depression, borderline personality disorder, and chronic abdominal pain. He ingested the batteries so the Emergency Department would take his "abdominal pain seriously." He had done this in the past with AAA batteries and pens. Initial radiography showed 16 radiopaque foreign bodies in the proximal small bowel and several in the stomach. Endoscopy was performed which showed a large amount of food content in the stomach but no visualized batteries. Medical Toxicology consultation was obtained to evaluate for systemic toxicity from ingestion of the batteries. The patient never developed gastrointestinal, dermatologic, or renal symptoms during his course and serial radiographs were obtained. The batteries were at the ileocecal valve at approximately 38 h, and the patient was ultimately able to pass all the batteries within 72 h post-ingestion without further medical intervention.
Case discussion: The patient had an uneventful recovery and passage of the 16 batteries over 3 days without intervention. At presentation, all batteries were located past the gastroesophageal junction. Based on the locations of the batteries during serial radiographs, the transit time of the batteries from the stomach and proximal small bowel to the colon was 38 h with subsequent complete passage of batteries 24 h later. Button battery ingestions are commonly reported, especially in the pediatric population. Severe tissue damage to the esophagus can occur in as little as 2 h. Delayed complications include esophageal perforation, tacheoesophageal fistula formation, strictures, and bleeding. Hearing aid batteries account for over 36% of all battery ingestions and are more common in the pediatric and elderly populations. Mercuric oxide previously comprised greater than 50% of the weight of hearing aid batteries prior to the advent of zinc air batteries in the late 1970s. Despite this, mercuric oxide still comprised about 1% of zinc batteries. In the acidic gastric environment, corrosion and release of mercury is increased as compared with zinc batteries. Since 2011, some states have banned the sales of batteries with any mercury content and mercury-free batteries were subsequently developed and marketed.
Conclusions: Hearing aid battery ingestion caused no acute complications in our patient. Conservative management is advised if batteries have already passed the gastroesophageal junction.

KEYWORDS Hearing aid battery; endoscopy; button battery

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213. Flecainide toxicity in an infant

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Background: Flecainide acetate is a IC antiarrhythmic used to treat tachydysrhythmias of atrial origin. It blocks sodium and potassium channels, thereby slowing the upstroke of the cardiac action potential and delaying repolarization, respectively. The drug exerts its greatest effect at the His-Purkinje system and ventricular myocardium. Flecainide is also known to be arrhythmogenic and can induce QRS widening, as well as prolongation of the PR and QT intervals. We present a case of an infant who presented to the ED with cardiac conduction abnormalities secondary to flecainide toxicity after a routine dosing change.
Case: A 49-day-old male born at 36 weeks gestation, with a medical history of WPW and SVT, was brought to the ED because his at-home telemetry monitor indicated a heart rate in excess of 200 BPM. One week prior to the current visit, his flecainide dose was increased from 150 mg/kg/mm^2 to 200 mg/kg/mm^2 BID. His vital signs on arrival to the ED were Temp 98.2 °C, HR 113, BP 86/44,and O2 Sat. 98% on RA. Physical exam was unremarkable. His initial ECG demonstrated a QRS of 168 ms, prolonged from a baseline of 82 ms. The patient received 1–2 meq/kg boluses of sodium bicarbonate with narrowing his QRS to 138 ms. He was subsequently placed on a drip which seemed to stabilize the conduction abnormalities. Four hours after the sodium bicarbonate infusion was initiated, the patient's QRS returned to baseline with a heart rate of 117. The infusion was discontinued without recurrent prolongation. He had no further wide complex rhythms and no episodes of SVT. He was successfully discharged home on hospital day 3. Post-discharge lab results revealed an initial flecainide level of 2.10 mcg/mL (reference 0.20–1.00 mcg/mL); 15 h later the level was 1.60 mcg/mL.
Discussion: Flecainide is an antiarrhythmic known for its narrow therapeutic window and its propensity to cause conduction disturbances, predominantly QRS widening due to sodium channel blockade. Even after initiating flecainide at 100 mg/kg/mm^2 bid the patient experienced recurrent episodes of SVT and so his dose was increased to a higher dose which is still in the therapeutic range. Although our patient's outcome was favorable,

toxicity from IC anti-arrhythmics carries a higher mortality when compared with other sodium channel blockers.
Conclusions: Our infant's conduction abnormalities presented as QRS prolongation without rhythm disturbance in the setting of a routine dosing change. This abstract reemphasizes the narrow therapeutic window of flecainide and how even routine changes in dosing that are still within the therapeutic dosing range can lead to clinical signs of flecainide toxicity.

KEYWORDS Flecainide; infant; pediatric

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214. More than just orange urine! A case of rifampin-induced aplastic anemia

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Background: Rifampicin is a drug commonly used to treat active or latent tuberculosis (TB) infection. It is often used to this purpose for extended periods of time and patients are usually monitored for hepatotoxicity, its most common side effect. We present the case of a patient treated with rifampicin for latent TB who presented with pancytopenia.
Case: A 56-year-old male with a history of diabetes, hypertension and latent TB on rifampicin monotherapy presented to the ED for bleeding gums and fatigue. The patient had been sent in by a hematologist after he had been found to have persistently abnormal bloodwork in the office. He had taken three weeks of rifampicin and had been off it for a week per the hematologist. Upon arrival to the ED, he was found to have vital signs only significant for mild tachycardia (102). Labs were significant for decreased cell counts in all lines: WBC 3000 (ANC 1600), hemoglobin 7.5, and platelet count 7000. His electrolytes, creatinine, liver function tests, and coagulation panel were all normal. He was admitted for packed red blood cell (PRBC) and platelet transfusion and had full malignancy workup including bone marrow aspirate which was consistent with aplasia but no evidence of dysplasia. Additionally, he had negative heavy metal screening, CMV/EBV IgM, and HIV screens. He was discharged the next day but returned 1 week later with petechial rash and worsening fatigue. At that time, he had a WBC of 2500, a hemoglobin of 6.6, and a platelet count of 4000. He was transfused both platelets and PRBC's again and was discharged a second time.
Discussion: Rifampicin is often used as an alternative to isoniazid in the treatment of latent TB infection. The most common side effects requiring close monitoring include gastrointestinal side effects or elevated liver function tests. There are very few reports in the literature of hematologic abnormalities secondary to rifampicin use, and they all describe thrombocytopenia following high-dose, long-term use of the medication prior to hematologic aberrations. We believe this is the first report of aplastic anemia following rifampin use. The patient required multiple transfusions and two admissions for continued leukopenia, anemia and profound thrombocytopenia despite discontinuation of medication.
Conclusions: This is an important, albeit rare, side effect of a commonly used drug that patients often use for extended periods of time, and they should be monitored carefully for the development of hematologic abnormalities.

KEYWORDS Rifampin; pancytopenia; aplastic anemia

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215. Acute fatal nitrofurantoin-induced liver failure: a case report

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Background: Nitrofurantoin is recommended as a first-line treatment of uncomplicated urinary tract infection by some guidelines. It has been implicated in hypersensitivity-type pulmonary and hepatic drug reactions. We report a fatal case of nitrofurantoin-induced liver failure in a patient with repeat nitrofurantoin exposure.
Case report: A 68-year-old lady presented to hospital with new onset jaundice, anorexia, and malaise. Past medical history was significant for hypertension, dyslipidemia, GERD, and recurrent cystitis. She had recently been started on nitrofurantoin for recurrent cystitis. On admission, she had stable vital signs. Initial investigations revealed a bilirubin 292 μmol/L (0–24 μmol/L), AST of 861 U/L (8–32 U/L), alkaline phosphatase 307 U/L (30–145 U/L), LDH 1396 U/L (100–235 U/L), GGT 1059 U/L (8–35 U/L), and ALT 686 U/L (1–40 U/L). Lipase, urea, creatinine, and electrolytes were within normal ranges. Imaging and immune assays did not reveal an etiology of her liver failure. Subsequent liver biopsy showed chronic hepatitis with mixed cellularity, with foci of bile duct epithelial injury and cholestasis, thought to favor the diagnosis of drug induced liver injury. The patient was started on prednisone and showed some improvement initially. She was discharged with hepatology follow-up, but re-presented 6 d after discharge home with worsening cholestasis and developed multi-organ system failure, including respiratory failure requiring intubation. Despite aggressive supportive measures such as IV fluids, antibiotics, and vasopressors, she continued to deteriorate and died 30 days after initial presentation.
Discussion: Drug-induced liver injury is recognized to occur rarely in response to nitrofurantoin exposure. A recent study suggests that this phenomenon may be underestimated, and reported an incidence of 73 cases per 100,000. Mortality in these patients is estimated at 8–10%. Nitrofurantoin induced liver injury may be acute or chronic. The mechanism of this reaction is not fully understood but it is thought to be an immune hypersensitivity reaction partially mediated by CD8+ cells. Specific risk factors include the geriatric population and female sex. However, these may be confounding factors given that recurrent urinary tract infections are found predominantly in the same population. The type of nitrofurantoin-induced liver injury tends to be predominantly a hepatocellular (32%) or mixed cholestatic-hepatocellular pattern (4%). The cornerstone of treatment of nitrofurantoin-induced hepatotoxicity is withdrawal of the medication and avoidance of nitrofurantoin in the future. Clear documentation should be established. Corticosteroids have been shown to have some mortality benefits if there are features of autoimmune hepatitis; however, they have not specifically demonstrated effect in nitrofurantoin induced liver injury. Early referral for consideration of liver transplant is recommended.
Conclusions: Nitrofurantoin is commonly prescribed and has been implicated in both acute and chronic liver injury. If the agent is withdrawn early, prognosis is generally good. Treatment of recurrent cystitis may prove difficult if the patient has previously experienced a drug induced liver injury, given that many other antimicrobials have been implicated in previous studies. Nitrofurantoin toxicity should be suspected in all patients exposed to this medication who present with signs of hepatotoxicity or cholestasis.

KEYWORDS Nitrofurantoin; hepatotoxicity; death

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216. The relationship between health insurance type and choice of non-poison center alternative care by callers of a poison center: results from 2016 survey data

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Background: Multiple studies have documented that if the poison center were not available, people with potential poison exposures would seek medical care. This would result in unnecessary healthcare utilization. These data have been reported as aggregate results, and it remains unknown if the caller's chosen alternative action differs based on their insurance type. The objective of this study was to determine if there is a difference in the chosen alternative actions by caller insurance type.
Methods: A regional poison control center (PCC) conducts ongoing customer satisfaction surveys (CSS) for a portion of PCC cases that are managed on-site. The two survey questions of interest for this study were (1) "If the poison center was not available, what would you do first in solving poison related emergencies?" and (2) "Does the person you called about have health insurance?" Alternative action responses were defined as call 911; call/visit ED; call/visit urgent care; call/visit physician; search online; other. Insurance type was defined as government (state/federal); commercial; self-pay; other/unknown/refused. Data were obtained from surveys on 2016 cases. Alternative actions and insurance type were cross tabulated for analysis.
Results: A total of 995 surveys were completed in 2016. The majority of respondents had commercial insurance (635; 63.8%), followed by government (265; 26.6%). The majority of callers (775; 77.9%) would seek medical care if the poison center had not been available. Call/visit ED was the most common alternative action (255; 25.6%) followed by call/visit physician (250; 25.1%) and call 911 (224; 22.5%). For callers with government insurance, the most common alternative action response was visit ED (85; 32.1%); for callers with commercial insurance, the most common response was call/visit physician (185; 29.1%); for self-pay callers, the most common response was visit ED (12; 34.3%). See Table 1 for further characterization of results.
Conclusions: Most callers would seek medical care if the poison center were not available. Visit ED and call physician appear to be substitute options depending on the insurance type.

KEYWORDS Insurance; poison center utilization; poison exposure management

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217. Autopsy reports improve assessment of relatedness in pediatric fatalities involving cough/cold medications

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Background: Over-the-counter cough/cold medications (CCMs) are commonly used in children, but misuse of CCMs has been linked to severe toxicity and death. A surveillance study was initiated in 2008 to understand the relationship between toxicity and CCM exposure. This analysis describes the utility of autopsy reports (ARs) in assessing relatedness of pediatric fatalities to CCMs exposures.
Methods: *Case sources*: NPDS, FDA Adverse Event Reporting System, medical literature, news/media reports, manufacturer internal safety reports. Case criteria: fatality, child aged <12 years, ≥1 CCM ingredient exposure (brompheniramine, chlorpheniramine, dextromethorphan, diphenhydramine, doxylamine, guaifenesin, phenylephrine, and pseudoephedrine), detected between 2008 and 2016. ARs were requested when identifiable information was provided. The Pediatric CCM Safety Surveillance Expert Panel evaluated causality between the exposure and fatality. For cases at least potentially related to the CCM, the Panel determined whether the CCM dose category was therapeutic, supratherapeutic or unknown and assessed intent of administration (e.g., for a labeled indication).
Results: Of 178 eligible fatalities requested, 82 (46.1%) ARs were received. An AR was not received ($n = 96$; 53.9%) due to insufficient identifiable information ($n = 71$; 74.0%), AR only released to next of kin ($n = 16$; 16.7%), AR pending ($n = 6$; 6.3%), or other reason ($n = 3$; 3.1%). Table 1 shows causal relationship was evaluable in 81.7% of cases with and 43.8% without an AR. Of evaluable fatalities, 77.6% with and 59.5% without an AR were determined to be at least potentially related to a CCM. The dose category and intent were both more likely to be determined in cases without an AR. In 20 cases, the Panel reviewed the fatality for causality before and after receipt of the AR (Table 1). Causal relationship was evaluable in 55.0% of cases initially, compared with 95.0% after AR receipt. While intent was equally evaluable before and after AR receipt, dose category was less likely to be determined after AR receipt.

Table 1. Alternative action in solving poison related emergencies by caller insurance type

Insurance Type, n	Alternative Actions, n (%)											
	Call 911		Call/Visit ED		Call/Visit Urgent Care		Call/Visit Physician		Search Online		Other	
Government, 274	674	(24.5)	88	(32.1)	16	(5.8)	52	(19.0)	21	(7.7)	30	(11.0)
Commercial, 626	140	(22.4)	141	(22.5)	26	(4.2)	182	(29.1)	69	(11.0)	68	(10.9)
Self-pay, 35	8	(22.8)	12	(34.3)	2	(5.7)	5	(14.3)	3	(8.6)	5	(14.3)
Other/Unknown/Refused, 60	9	(15.0)	14	(23.3)	2	(3.3)	11	(18.3)	6	(10.0)	18	(30.0)

Table 1. Case Evaluation With and Without an AR and Before and After receipt of AR

	Cases with AR (n=82)	Cases without AR (n=96)	All Cases (n=178)	Initial Assessment (n=20)	Follow-Up Assessment (n=20)
Unable to Determine	15 (18.3%)	54 (56.3%)	69 (38.8%)	9 (45.0%)	1 (5.0%)
Evaluable	67 (81.7%)	42 (43.8%)	109 (61.2%)	11 (55.0%)	19 (95.0%)
Unlikely Related	15 (22.4%)	17 (40.5%)	32 (29.4%)	0 (0.0%)	4 (21.1%)
=Potentially Related	52 (77.6%)	25 (59.5%)	77 (70.6%)	11 (100.0%)	15 (78.9%)
Known Intent	37 (71.2%)	20 (80.0%)	57 (74.0%)	9 (81.8%)	12 (80.0%)
Known Dose Category	18 (34.6%)	13 (52.0%)	31 (40.3%)	7 (63.6%)	2 (13.3%)

Conclusions: ARs are valuable drug safety data sources as they contain additional history details surrounding exposure and clinical course, which may not be routinely collected as part of the original case documentation. These factors improved the ability to determine causal relationship between CCM exposure and fatal outcome in this study. Assessment of estimated dose did not improve because of the lack of reliability in interpreting postmortem drug concentrations, which is an important consideration when using ARs for relatedness assessments.

KEYWORDS Autopsy reports; pediatric cough/cold product exposures; adverse event surveillance

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218. Suicidal poisonings for patients age 6–19 as reported to one Regional Poison Center

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Background: Pediatric mental health is a growing public health concern. According to the CDC, suicide is the second leading cause of death among young people age 10–24. The aim of this study is to report one statewide Regional Poison Center's (RPC) experience with poisoning by suicidal intent in young patients aged 6–19.

Methods: RPC records were queried for all exposures with an NPDS reason code of Intentional Suspected Suicide for the period 1/1/2007–12/31/2016. Number of exposures, detail on generic substance code involved, and outcome were analyzed for age groups 6–12 years and 13–19 years.

Results: Among patients aged 6–19, suicidal exposures reported to this RPC increased 92% over the study period (see Table 1). In addition to greater total number of suicidal exposures, the proportion of cases with a serious outcome (defined as death, major effect, or moderate effect) increased from 16.4% of cases in 2007 to 26.6% of cases in 2016 for patients aged 6–19 (see Table 1). The substance categories associated with the highest number of exposures are detailed in Table 2. Non-opioid analgesic was consistently the substance category with the most suicidal exposures in this age group, accounting for roughly one-third of all exposures in each year.

Conclusions: Suicidal exposures reported to this RPC in patients age 6–19 have nearly doubled in the past 10 years. Additionally, the severity of suicidal overdoses increased during this time period. A review of RPC data indicates that an increasing number of children and adolescents are utilizing poison overdose as a means of self-harm.

KEYWORDS Suicide; poison center; adolescent

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Table 1	Total Exposures	Death	Major	Mode	death/maj/mod
2007	3,143	1	29	485	**16.4%**
2008	3,442	4	36	563	**17.5%**
2009	3,554	1	26	563	**16.6%**
2010	3,659	1	42	616	**18.0%**
2011	3,610	0	52	648	**19.4%**
2012	4,031	3	57	847	**22.5%**
2013	4,634	10	25	1080	**24.1%**
2014	5,284	2	81	1209	**24.5%**
2015	5,875	2	68	1517	**27.0%**
2016	6,038	7	92	1510	**26.6%**

Table 2	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Analgesics (non-opioid)	1,065	1,199	1,228	1,205	1,095	1,239	1,371	1,677	1,764	1,779
Analgesics (opioid)	125	160	150	157	166	194	189	126	194	209
Anticonvulsants	139	123	139	143	141	143	187	188	238	225
Antidepressants	403	402	413	572	505	572	706	788	924	1,012
Antihistamines	138	129	196	195	184	195	265	310	354	372
Sedative hypnotic/ antipsychotic	391	458	510	548	464	548	571	668	702	758

219. Web-based information and NPDS: lack of clear correlation between page views and drop in NPDS call volume of non-toxic exposures

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Background: The advent of the internet and mobile platforms such as tablets and smartphones have revolutionized how people obtain health-related information. From 2008 to today, there has been an increasing adoption of smartphone technology; in the same time period there has also been a steady drop in exposure calls to the US poison center network. Some poison centers have hypothesized that consumers are seeking information from the internet and once found and reassured, no longer contact poison centers. An observational study looking at high volume web page views for non-toxic exposures and comparing exposure volume decrease for those exposures was undertaken.
Methods: Number of page views from 10 high-volume non-toxic substance webpages from three regional poison centers (RPC) were compared with the NPDS exposure volume drop for corresponding substances from 2008 to 2016 (silica gel, diaper cream, craft writing supplies, deodorant, toothpaste, soap, creams-lotions-makeup, sunblock, glow stick and feces).
Results: The 10 categories collectively had 455,113 web page views from United States consumers in 2016. The NPDS exposure volume drop from 2008 to 2016 in the 10 categories totaled 89,930. The exposure volume drop per substance ranged from 11.9% (feces) to 52.7% (silica gel). The page view volume ranged from a low of 19,251(deodorant) to 111,262 (glow sticks) – see Table 1. A regression analysis of drop in call volume versus web page views was completed with $R2 = 0.0539$ – see Chart 1. As constructed, the study did not show a correlation between high volume page views of RPC clinical information and a corresponding decrease in NPDS volume. Some potential pitfalls in the analysis include (1) the three RPC websites used may be a small portion of the overall web presence for poison information and (2) the study was set up to look at correlation of page view volume and the effect on NPDS volume. A study that looked at many more minimally toxic substances, whether associated with high or low web page views, may yield a different result.
Conclusions: No correlation was found in a comparison of high volume web page views for non-toxic substances from three RPC and NPDS case volume drop from 2008 to 2016.

KEYWORDS Poison center; NPDS; Internet

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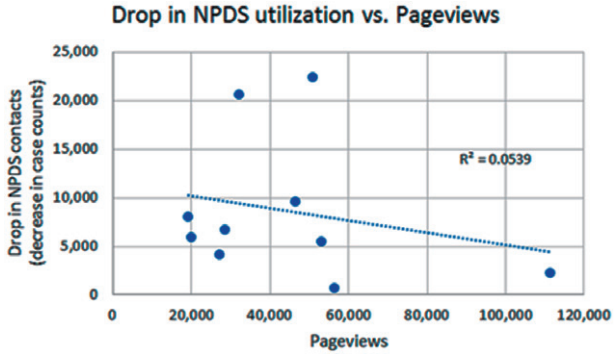

Substance	2008 NPDS	2016 NPDS	Total Decrease	% Decrease	Page Views	Page View Rank
Diaper Cream	45,196	24,509	20,687	45.8%	32,062	6
Silica Gel	42,592	20,158	22,434	52.7%	50,932	4
Creams, lotions, make up	34,005	28,480	5,525	16.2%	53,142	3
Toothpaste	25,777	19,061	6,716	26.1%	28,598	7
Deodorant	24,682	16,589	8,093	32.8%	19,251	10
Craft writing	23,326	13,643	9,683	41.5%	46,322	5
Soap	19,475	13,481	5,994	30.8%	20,045	9
Glow Stick	19,213	16,902	2,311	12.0%	111,262	1
Sunscreen	13,106	8,953	4,153	31.7%	27,233	8
Feces	6,386	5,627	759	11.9%	56,266	2

220. Applying the poison center model to an occupational and patient safety support line

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Background: Numerous studies have demonstrated that poison control centers (PCC) reduce healthcare spending and harm tied to poisoning injury. This report looks at the parallel success of one PCC after applying its operating model to patient and occupational safety in the hospital setting. The healthcare sector is attributed with some of the highest incidence of work related injuries and illnesses. The Safety Hotline was established as a 24/7 telemedicine service for reporting and mitigating occupational and patient-related incidents and safety concerns. The Hotline represents a collaborative between the PCC and parent medical center. Early intervention, process control, and continuous improvement are key design features of the program.
Goals: The program was designed to

- strengthen the PCC role within the parent institution by directly supporting its safety related goals and outcomes.
- Improve employee participation in reporting of safety incidents to promote a prevention-based model for reducing OSHA recordable and serious harm events.
- Reduce unnecessary healthcare spending and lost time due to preventable illness and injury.

Discussion: The Safety Hotline has demonstrated unprecedented reductions in injury rates and spending associated with workers compensation and lost productivity claims.The "Worker's Compensation (WC) Benchmarking Report", released annually by the state hospital association, outlines year on year reductions for the medical center over a 5-year period (2010–2014):

- WC claims per 100 FTE decreased by 46.6% (1.03–0.55), which is 5–7 lower than the aggregate mean (4.53) for hospitals within the state (regardless of hospital size).
- Although employment levels increased, annual WC spending consistently declined each year by $500,000, representing a 57% decrease in the average cost per claim, and 26.2% decrease in claim severity.
- Estimated cost savings exceeded 12 million dollars.

PCCs and the Safety Hotline rely on utilization of services to make an impact. Calls to the Safety Hotline have increased 5-fold since initial launch (2008). Participation is influenced by ease of use and perception of value among its users. The PCC design principles are well suited for this diversification of services. Additionally, given the complexities of healthcare, staff are often skeptical that individual action can impart meaningful change. Investing time to build relationships, seek feedback, and routinely follow-up is critical to sustained participation and personal accountability.
Conclusions: In addition to the PCC community health mission, the Safety Hotline collaboration has strengthened the PCC's relationship with the parent institution and shown an alternative way a PCC can add value by directly supporting the institution's safety related objectives, goals and measures. Efforts to raise awareness, improve participation, and specialize services for high-risk target populations remains ongoing, including broadening scope to directly support patients and families.

KEYWORDS Safety; hotine; model

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221. Emergency room visits related to laundry product exposures – a temporal analysis

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Objective: National Electronic Injury Surveillance System (NEISS) data represents a probabilistic sampling of emergency department (ER) visits in the United States and its territories. The purpose of this report is to assess temporal trends of weighted estimates of ER visits and subsequent hospital admissions for Laundry Pacs (LP) and Non-LP laundry Detergents.
Methods: This study used all observations with injuries involving laundry detergent (Code 0949) from the NEISS from 2012 to 2015. LP Laundry products were identified by reviewing case narratives looking for key terms. Weighted estimates were obtained using SAS version 9.4 proc surveyfreq and proc surveymeans (SAS Inc., Cary, NC). Simple descriptive statistics for demographics were performed, as well as 2×2 analyses of covariates. Weighted estimates were normalized per MMSU (million statistical unit) for all Laundry products and per MU (million units) for LP Laundry products.
Results: Weighted trends for LP related ER visits increased from an estimated 2462 (95% CI 1900–3025) in 2012 to an estimated 5763 (95% CI 4847–6680) in 2014. A decrease in weighted cases to an estimated 5583 (95% CI 4630–6536) was observed in 2015. Hospitalization subsequent to LP related ER visits increased from 208 (95% CI 0–422) in 2012 to 569 (95% CI 275–901) in 2013, followed by decreases in weighted reports in 2014 and 2015, estimated 560 (95% CI 275–846) and 433 (95% CI 159–727), respectively. Similarly, weighted trends for all Laundry product ER visits increased from 2012 to 2014 and a decrease in weighted cases was observed in 2015. Hospitalization subsequent to laundry detergent (all forms) related ER visits increased in 2013 as compared with 2012 followed by a decrease in 2014 and 2015. Weighted estimates for Laundry products (all forms) normalized per MMSU increased from 22.4 reports per MMSU in 2012 to 26.0 reports per MMSU in 2015. For subsequent hospitalization of Laundry products (all forms) related ER visits weighted estimates decreased from 1.31 per MMSU in 2012 to 1.14 per MMSU in 2015. Weighted estimates for LP normalized per MU decreased from 1.46 reports per MU in 2012 to 1.31 reports per MU in 2015. For subsequent hospitalization of LP normalized per MU there was a decrease from 0.12 reports per MU in 2012 to 0.10 reports per MU in 2015.
Conclusions: Analysis of probabilistic Emergency Room visit data obtained from the NEISS database indicates the beginning of a decreasing trend in LP related visits, as well as in hospitalization. This is tempered for hospitalization given that weighted estimates are low and are considered to be unstable and potentially unreliable. Aside from Laundry detergent (all forms), trends were sustained when normalizing weighted estimates per shipping unit (MMSU/MU).

KEYWORDS Emergency room; laundry pacs; NEISS

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222. Utilization of an automated phone survey to evaluate caller satisfaction

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Background: Patient satisfaction is widely recognized by organizations and funding agencies as a key measure of quality, patient centered care. The American Association of Poison Control Centers has incorporated customer satisfaction as an essential component of the Quality Management and Improvement program for all accredited Poison Centers (PC). Evaluating PC caller satisfaction poses difficulties due to changes in technology and public perception of the time, convenience and confidentiality of providing feedback. Our PC conducted a caller satisfaction survey annually, utilizing pharmacy students as ''independent'' surveyors to conduct a phone survey of previous PC callers several days after the original call. Response rates have decreased in recent years, due to increased difficulty contacting callers and having them call back if unavailable. A web-based survey tool was used in subsequent years, with the staff requesting the caller's email at the time of the final call and sending a link to the survey website. Obtaining the email and ensuring timely communication of the survey web link continued to be problematic. The PC sought a new methodology of obtaining feedback using call technology through automated phone prompts and touch tone phone screen responses.
Method: A telecommunications analysist (TA) collaborated with PC staff to build a phone survey algorithm utilizing the infrastructure of the Cisco phone system. A soft extension served as the platform for phone messaging introducing the survey and instructions for completion. Five questions used a Likert scale range of numbered responses. At each recorded question the caller used the phone keyboard to indicate their response. Phone data reports were able to identify the number and type of response for each question. At the conclusion of the survey, callers was able to leave comments in a voice mail box. PC staff asked callers for home management cases to participate in a brief 5-question survey regarding the poison center service. Callers were transferred to an internal phone extension to initiate the survey.
Results: The survey was conducted during a 2-month period with 289 callers participating. Satisfaction rates for the five questions ranged from 97% to 99.6%. Caller comments were transcribed and posted with the results for staff review. This response rate represented a 20-fold increase from the methods used in previous years.
Conclusions: Utilization of this survey mechanism resulted in a higher response rate than previous methods. With the assistance of a TA, the setup of the survey and reports of the results of the survey were easy to access. Staff reported satisfaction with the ease of transferring callers to the survey and the willingness of callers to participate. While the focus of these efforts was to determine whether this tool could be effectively utilized to track and record responses, the survey represented a convenience sample, which was at the discretion of the staff. Future efforts will be made to expand the participation rate through definitive staff guidelines for offering the survey to all home management cases.

KEYWORDS Patient satisfaction; phone survey; quality management

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223. Marine invasive species of concern to human health: recent envenomations due to *Rhopilema nomadica* in the Mediterranean Sea

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Background: The nomadic jellyfish, *Rhopilema (R) nomadica,* is native to the western Indian Ocean and has entered the Mediterranean Sea through the Suez Canal. Since the late 1980s, each summer it forms swarms as long as 100 km in the southeastern Levant. The objective of this study was to evaluate children seen in the emergency department after *R. nomadica* envenomations and to establish patterns of toxicity associated with this organism.
Methods: A retrospective chart review of all children presenting after *R. nomadica* envenomations to the pediatric emergency department during the jellyfish swarming seasons (June–August) between 2010 and 2015. Extracted data included age, location of envenomation, pain scores, local and systemic manifestations, treatment provided in the emergency department and hospital, and disposition.
Results: Forty-one patients met inclusion criteria; ages ranged from 1 to 16 years and median age was 9.4 years. Clinical manifestations were evident in all patients. Pain, present in 100% of patients, and an erythematous, whip-like, linear rash present in 87.8%, were the most common manifestations. The majority of 'burns' associated with jellyfish stings were first and second degree. The upper limb was affected in 34% and the lower in 61% of cases. One patient suffered a sting to the abdomen and three to the face. Treatment in the emergency department included pain control, with non-steroidal anti inflammatory drugs and opiates, and antihistamines and topical corticosteroids in some cases. Nearly 49% of patients were seen during the summer of 2015 alone and seven patients of this group needed hospitalization. Reasons for hospitalization included systemic symptoms such as fever, chills, tachycardia, and muscle spasms. Two patients developed severe cellulitis, one patient had an anaphylactoid reaction and one was admitted to the intensive care unit after suffering an anaphylactic reaction to a sting sustained while surfing.
Conclusions: The prevalence of the jellyfish *R. nomadica* swarms and the severity of clinical manifestations due to their envenomations suggest it should be considered as a health hazard in the Mediterranean Sea. We call for public health authorities in affected countries to initiate a health hazards database, familiarize medical and healthcare staff with the clinical syndromes, train medical, and healthcare staff in appropriate treatment, and initiate and continue public awareness campaigns.

KEYWORDS Rhopilema nomadica; alien species of human health concern; Mediterranean Sea

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224. Outcomes following accidental pediatric ingestions of $5HT_1$ agoinsts

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Background: The oral triptans are $5HT_1$ agonists used to treat migraine headaches via vasoconstriction. In adults serious cardiovascular events have occurred with therapeutic doses and overdose has caused HTN, other cardiovascular toxicity and rarely, death. This has led to concern that overdose in children might result in similar toxicity. The goal of this retrospective review was to attempt to determine the dose of each triptan that would require care beyond home observation in children <6 using National Poisons Data System (NPDS) data.
Methods: This is a preliminary review of accidental triptan ingestions in children <6years old submitted by US poison centers to (NPDS) from 1 January 2000 through 31 December 2016. All single entity accidental oral exposures to $5HT_1$ agonists in children <6-year-old followed to a known outcome with exact dose certainty, and an exact mg dose, or an exact mg dose calculated from number of tablets ingested and the Poisindex code, were included. Taste/lick level exposures were considered inexact and excluded.
Results: Over a 17-year span, the NPDS database contained of a total of 10,613 single entity triptan cases, of which 3971 occurred in children <6-year old. There were 844 cases with an exact dose, as defined, and 678 cases were followed to known outcome including: Almotriptan (10), Eletriptan (59) Frovatriptan (17), Naratriptan (7) Rizatriptan (80), Sumatriptan (260), Sumatriptan/Naproxen (6), and Zolmitriptan (239). Of the 678 cases meeting the inclusion criteria, 315 occurred in girls and 360 boys and three were coded unknown gender. No effect was coded in 585 cases (86%), Minor in 78 (11.5%), and Moderate in 16 (2.4%). In the single case coded with a major outcome, the only coded clinical effect was tachycardia prompting a call to the reporting PCC for clarification. After discussion, the case was determined to have been miscoded and reassigned as a moderate outcome. There were no deaths. About 157 cases were coded as not followed – no more than minor effect. The most commonly reported clinical effects coded as related were Drowsiness (21), Vomiting (20),Tachycardia (11), HTN (7), Nausea (6), and Erythema(4). Of the 678 cases, no effect was reported in 585. Of the remaining 85 cases where a clinical effect was reported, 47% cleared within 2 h, and 92% cleared by 8 h. No clinical effects persisted longer than 24 h. Case management was reported as conducted onsite (293), already en route to HCP (153), or referred to HCP by PCC (226) with an additional three cases coded as other.
Conclusions: This is the largest review to date of accidental overdose of triptans in the <6yo age group. It is not possible to determine what constitutes a significant dose from the data in its current form. However, regardless of dose, no patient in this suffered more than moderate outcome and no clinical effect persisted more than 24 h. Based on the available information poison centers may be referring more children to hospital for these ingestions than is necessary.

KEYWORDS Triptans; accidental overdose; children <6

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225. Empiric oseltamivir use associated with development of serotonin syndrome

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Background: Oseltamivir is a neuraminidase inhibitor prescribed for treatment of influenza, especially in high-risk patients. However, serious neuropsychiatric adverse reactions to oseltamivir, including death and abnormal behavior, have been reported after drug administration. The reported number needed to harm (NNTH) for abnormal behaviors was 25 (CI 95%: 19–35) on prospective cohort studies. We report a case of serotonin syndrome that developed after initiation of oseltamivir for treatment of suspected influenza.
Case report: A 54-year-old man with history of obsessive-compulsive disorder, depression and essential tremor presented to the emergency department with altered mental status, worsening tremors and bilateral lower extremity clonus. His home medications included lithium, clozapine, fluoxetine, propranolol, and primidone. Hours earlier, he received his first dose of oseltamivir for treatment of flu-like illness. Initially, he was febrile to 38.8 °C without tachycardia or hypotension. His exam showed profound tremors in all four extremities, worsening rigidity to the upper extremities, and inducible clonus with hyperreflexia in his bilateral lower extremities. He was actively cooled with IV saline and a cooling blanket, and given 4 mg of intravenous lorazepam and 20 mg of intravenous diazepam with significant improvement of his hyperreflexia and clonus. His lithium level was 0.7 mEq/L (normal range 0.6–1.5) and his phenobarbital level was undetectable. A clozapine level obtained later came back at 76 mcg/L (therapeutic range greater than 100mcg/L). His creatinine kinase, basic metabolic panel, thyroid-stimulating hormone, and complete blood count were within normal limits. He had an unremarkable electroencephalogram (EEG). Urine enzyme multiplied immunoassay technique (EMIT) screen was positive for barbiturates and benzodiazepines and qualitative urine gas chromatography/mass spectroscopic (GC/MS) evaluation was positive for primidone, phenobarbital, clozapine, and diazepam. His respiratory viral panel was positive for metapneumovirus. He was admitted to the intensive care unit and his mental state and clinical status rapidly improved to baseline within 24 h after discontinuing all prior agents.
Case discussion: Based on the patient's presentation, this constellation of symptoms and exposures is consistent with serotonin syndrome. In previous meta-analysis, oseltamivir has been associated with risk of gastrointestinal, neurologic, psychiatric, renal symptoms, and hyperglycemic events. *In vitro* studies have demonstrated competitive inhibition of human MAO-A by oseltamivir. Furthermore, *in vivo* studies have demonstrated a rise in CNS oseltamivir concentrations during infection. The association between his acute symptomatology and initiation of oseltamivir suggests a role in the development of serotonergic toxicity. Confounding this case was the number of other serotonergic medications, including lithium, clozapine, and fluoxetine, which could have contributed to this presentation. Sadly, given the lack of influenza virus on PCR testing, it appears this patient did not require oseltamivir treatment, which is not indicated for metapneumovirus.
Conclusions: Oseltamivir is an anti-viral agent that is commonly used for treatment of influenza. In combination with other serotonergic medications, the MAO inhibitor properties of oseltamivir may contribute to development of serotoninergic toxicity.

KEYWORDS Salma; Bashir; Osman

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226. Bullying and suicide attempts reported to a statewide poison system

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Background: Bullying is unsolicited, repeated, aggressive behavior among school-aged children that involves a real or perceived power imbalance favoring the perpetrator. it is reported to occur in about 28% of US students and is associated with self-harm attempts. Currently, bullying is not a required data field in reporting cases to the National Poison Data System and, therefore, may go under recognized. Our objective was to determine if bullying was reported in a conjunction with suicide attempts, and to describe the case frequency and patient demographics.
Methods: A statewide pison center system during 2013–2016 was searched for all patients aged 4–18 years using the term "bullying" in free text. A second search ws done for same-aged patients with suspected attempted suicide exposures. Variable searched included patient demographics, agents consumed, clinical effect, and medical outcome. Descriptive statistics were used.
Results: In this age group, 22 cases documented bullying, of which 16 (72.7%) were coded as suicide attempts. Twenty-one were female (95%). The mean age was 13.7 years. Analgesics were most commonly reported including acetaminophen products eight (36.3%) and ibuprofen four (18.2%). Escitalopram and fluoxetine appeared in three cases (13.6%) total. Eleven (50%) cases reported medical effects requiring intervention (four moderate effect, one major), while eight (36.3%) had no effects, three (13.6%) were unable to be followed and/or had unrelated effects, and no deaths. For a baseline comparison, suicide attempts were reported in 23,001 cases in 4–18 year olds. Of these, five (0.02%) died.
Discussion: Although bullying is not commonly mentioned in poison center data, it is likely under-reported. It is a well-known public health issue, and the low incidence in our data likely reflects a lack of asking about bullying or lack of recognition about bullying on health care evaluation. The need fro medical intervention was significant in many cases. It may be useful to capture these data and follow trends to assess for possible prevention. The peak age and female gender may be an intervention focal point.
Conclusions: Data from a statewide poison system documented bullying in 0.07% of suicide attempt cases over a 4-year period: however, potential for bad outcome was high. Bullying was more common in females, and in ages 13–17 years. This area may benefit from more investigation and attention.

KEYWORDS Bullying; depression; suicide

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227. Black box or pine box: methylene blue's inherited dilemma

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Background: The Food and Drug Administration (FDA) issues black box warnings when a medication is known to have a potentially serious or fatal risk. In 2011, the FDA issued such a warning concerning methylene blue, due to it being a potent monoamine oxidase inhibitor (MOAI) and potentially increasing patients' risk of developing serotonin syndrome. To date, the only indication for methylene blue is for methemoglobinemia, which in its own right can be life threatening if not treated. The goal of this study was to further examine the scope of knowledge of specialists in poison information (SPI) concerning the potentially fatal drug interaction when recommending methylene blue to health care providers for the treatment of methemoglobinemia.
Methods: A survey developed within Survey Monkey® was distributed to all members of the American Association of Poison Control Centers SPI email listserv. The survey addressed (a) knowledge of the black box warning, (b) analyzing the patient's current home drug usage, and (c) recommending precautions to prescribers.
Results: About 173 of the 850 SPI members responded to the survey (20% response rate). 60% identified themselves as nurses, 34% pharmacists, and 7% other educational backgrounds. 76% were certified SPIs and 55% had worked over 10 years in a poison center. Of the respondents, 15% were not familiar with the term black box warning, and 27% were aware of the black box warning concerning methylene blue. Of the 55% who in the past recommended methylene blue to a health care provider, only 19% had screened the patient for other home medications. When asked the question about advising the health care provider to avoid or discontinue the medications listed in the FDA's black box warning, only 53% of the respondents answered the question, of which 27% stated that they always or at least sometimes caution providers when using methylene blue as an antidote.
Discussion: Through the FDA Adverse Event Reporting System, it was noted that there were a significant number of cases of serotonin syndrome when patients received a recommended dose of methylene blue and while taking a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI).
Conclusions: SSRIs, SNRIs, and MAOIs are widely prescribed agents. In light of the FDA's black box warning concerning methylene blue with these classes of medications, it would be prudent to screen home medications and to alert prescribers of the potential of serotonin syndrome when recommending methylene blue. It is recommended that poison centers through their educational initiatives routinely monitor the FDA's safety alerts and inform their staffs of these alerts particularly when they involve a known antidote.

KEYWORDS FDA; black box; methylene blue

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228. Suicidal bupropion ingestions in adolescents: increased morbidity compared with tricyclic antidepressants

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Background: Bupropion is often categorized as a newer generation antidepressant, and assessed with serotonin reuptake inhibitors as a lower risk than older tricyclic antidepressants (TCA). Bupropion, in fact, does not inhibit serotonin reuptake in any appreciable amount, but rather is a cathinone derivative, not dissimilar to "bath salts". These share a similar mechanism of action, principally norepinephrine and dopamine reuptake inhibition, and has a risk of seizures especially in intentional self-harm scenarios.

Methods: An analysis of the National Poison Data System (NPDS) for exposures coded "suspected suicide" in adolescents (age 13–19) was undertaken for the years 2013–2016. Single ingestions of either bupropion or a TCA were included, or dual ingestions with alcohol. TCAs included amitriptyine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, and trimipramine. We compared clinical effects, therapies, and medical outcomes.
Results: Over the 4-year period, there were 2253 bupropion and 1496 TCA adolescent suspected suicide calls. There was a significant linear increase in bupropion ingestions over the 4 years. Across all years, there were on average 189.2 (95% CI: 58.1–320.4; $p=.014$) more ingestions of bupropion than TCA. When comparing bupropion to a TCA, ingestions of bupropion were significantly more likely to be in men (26.5% male versus 19.7% male; $p<0.001$), accompanied by seizure (30.7% versus 3.9%; $p<.001$), tachycardia (67.3% versus 56.6%; $p<.001$), and more likely to be admitted (74.8% versus 61.6%; $p<.001$). Medical outcomes were more likely to be coded as a major effect (19.3% versus 10.0%; $p<.001$) for bupropion. The number of cases with death or major clinical effect increased over the 4-year period ($p=.001$). Ingestions of bupropion were less likely to have hypotension (2.7% versus 8.0%; $p<.001$) and less likely to be intubated (5.6% versus 16.4%; $p<.01$) as compared with ingestions of TCA. There was no relationship between substance ingested (bupropion versus TCA) and co-ingestion of alcohol (1.7% versus 1.4%; $p=.500$) or the use of vasopressors (1.3% versus 1.2%; $p=.737$). Death occurred infrequently (0.3%) but at the same percent in each group. (TCA, 4/1496; Bupropion 6/2253).
Conclusions: Adolescents who overdose with bupropion in a suicide attempt have a statistically significant higher incidence of major outcomes and seizures. Over the 4 years studied, bupropion ingestions increased and severity increased. Bupropion should be considered a high-risk agent to treat depression in adolescents. Greater caution is warranted in prescribing to adolescents at risk for self-harm in addition to vigilance in emergency medicine providers caring for acute ingestions.

KEYWORDS Bupropion; antidepressants; suicide

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229. Angiography negative subarachnoid hemorrhage after single dose of phentermine

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Background: Phentermine is one of the most frequently prescribed medications to treat obesity in the Unites States. It is a sympathomimetic agent and CNS stimulant. Sympathomimetic drugs such as cocaine and methamfetamine can cause subarachnoid hemorrhage. However, it is unclear whether phentermine can do so.
Case report: A previously healthy 43-year-old female presented to the emergency department with headache, neck pain and stiffness, photophobia, and emesis that started a few hours prior to arrival. Two days prior, she had visited her primary care doctor for what she described as cold like symptoms (nasal congestion, dry cough) and was prescribed levofloxacin. She was also prescribed phentermine for weight loss, because she wanted to lose weight. She took the first dose of both medications in the morning and then developed symptoms within several hours. On examination, her blood pressure was 161/103 mmHg, Glasgow coma scale was 15, and neurologic exam was normal. CT scan revealed subarachnoid hemorrhage (Hunt and Hess grade II, Fisher grade II). CT angiogram of intracerebral vessels showed no evidence of aneurysm. She was given vasospasm prophylaxis (nimodipine) and IV fluids to maintain euvolemia and was admitted to the SICU under the neuroendovascular service. Cerebral angiography was negative for aneurysm, vascular malformation, and vasculopathy. She had no complications throughout her hospital stay, and a repeat CT scan 1 week after arrival showed resolution of the hemorrhage and hydrocephalus.
Case discussion: Phentermine induces the release of norepinephrine and, to a lesser extent, dopamine and serotonin. This effect in the hypothalamic nuclei reduces hunger perception and increases fat breakdown systemically. Several studies link other related sympathomimetic agents to cerebrovascular events. A case control study by Cantu et al. (2003) described 22 patients, 21 of whom had hemorrhagic stroke, related to over the counter cough suppressants phenylpropranolamine (PPA) and pseudoephedrine. Most of these involved vasculitis or hypertensive crisis. A case control study by Kernan et al. (2000) including 702 patients with hemorrhagic stroke showed that the use of PPA as an appetite suppressant was associated with an increased risk of hemorrhagic stroke in women aged 18–49. There is one previous case report of SAH in a 45-year-old woman taking phentermine intermittently for one year. Our patient was a 43-year-old female, hypertensive on arrival but with no previous history of hypertension. She had no known risk factors for SAH and did not smoke, drink alcohol regularly, or use recreational drugs (urine toxicology was negative for cocaine). The timing of her symptoms was directly related to her first time use of phentermine, and it is likely that phentermine-induced hypertension precipitated her presentation.
Conclusions: Sympathomimetics like phentermine are known to cause cerebrovascular events, but the effects of phentermine itself in this respect have not been well studied. We believe that phentermine use in this patient induced hypertensive or vasculitic events that resulted in spontaneous subarachnoid hemorrhage.

KEYWORDS Phentermine; subarachnoid; hemorrhage

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230. Button battery warning stickers do not prevent esophageal injury

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Background: Manufacturers have changed button battery packaging to limit child access based on recommendations from the Consumer Product Safety Commission; manufacturers have also attached a warning sticker to the negative pole of a button battery with language "harmful if swallowed." The button battery task force reports that injuries can still occur from ingestion of a button battery with an attached warning sticker; however consumers and healthcare providers may view these ingestions as less urgent because the warning sticker has to be removed before the battery can power an electronic device. The purpose of this study was to evaluate for the likelihood of esophageal burns from ingestion of a button battery with an attached warning sticker in a hotdog model.
Methods: Lithium ion button batteries (3V 2032) batteries from Manufacturer A and Manufacturer B were used for this study. Two batteries from each manufacturer – one with attached warning sticker (WS) and one without attached warning sticker (WOS) – were placed in a 1-in incision in a hotdog. Hotdogs were spritzed

with saline at 15-min time intervals to emulate physiologic conditions. After 2 h, hotdogs were cut open lengthwise and inspected for char. The extent of burning was evaluated by measuring the diameter of the char. This study did not involve human subjects and was, therefore, exempt from review by our Institutional Review Board.
Results: All hotdogs had significant charring after 2 h. Hotdogs with WS batteries had 2.6 cm (2.6–2.6 cm) char on the side of the hotdog facing the negative pole. Hotdogs with WOS batteries had 2.75 cm char (2.7–2.8 cm) on the side of the hotdog facing the negative pole. Amount of hotdog char did not differ between manufacturers.
Conclusions: Esophageal burns are likely after ingestion of a button battery with an attached warning sticker as demonstrated in our hotdog model. Manufacturers should consider adding language such as "sticker will not prevent injury if swallowed," to the button battery warning sticker and button battery packaging.

KEYWORDS Button battery; packaging; ingestion

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231. Cooking with cannabis: the rapid spread of (mis)information on YouTube

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Background: Among the variety of ways cannabis is consumed, forms of smoking or oral consumption are the most common. When eaten, the effects take substantially more time to come on, are described as being more intense, and last hours longer than when smoked. These factors, combined with a wide variation in potency, present a considerable risk of unpleasant, long-lasting, accidental overdoses. The purpose of this study was to characterize the content and popularity of dangerous trends involved in edible marijuana consumption by young adults on the video-sharing Web site YouTube.
Methods: This is a retrospective content analysis study. Using YouTube's search engine, data was collected by searching for videos on YouTube using twelve terms relating to marijuana (cannabis edibles). Videos were identified and viewed between November 2016 and December 2016. Key quantitative and qualitative descriptive variables included the number of views, participants, and the cooking technique used or described. Viewers' comments from the videos on YouTube were examined as an index of viewer response. The scientific claims made by the videos were classified as substantiated or unsubstantiated using opinions of two board-certified toxicologists.
Results: During the 2-month study period, 120 YouTube videos relating to edible marijuana consumption (cooking) were identified. The most common product described was cannabutter, a butter-based solution which has been infused with cannabinoids (39%). This was followed by cooking techniques for brownies/cake (10%), cookies (8%), cupcakes (8%), drinks (8%), and candy (7%). These videos were collectively viewed 15,559,614 times; the mean number of views per video was 129,663. A total of 25 videos (20.8%) had warnings associated with cooking using cannabis (e.g., potency of THC, danger to children, and risk of accidental overdose). Nine videos contained inaccurate or dangerous information; the majority of videos (97%) did not describe the amount or potency of the cannabis ingredient used in cooking.
Conclusions: Edibles have become more available in recent years as the marijuana market has matured. With key differences in dose, onset, duration and metabolism, oral cannabis presents a considerable risk of accidental overdoses, especially in inexperienced users. Video-sharing Web sites (e.g., YouTube) promoting cooking with cannabis are increasing in popularity. However, the majority of sites do not have warnings or precautions associated with using this drug in edibles. Knowledge about what people are viewing may help health care practitioners better understand their patients' own informational databank, stay informed about the latest trends in drug abuse, and position themselves as more credible resources to their patients.

KEYWORDS Edible marijuana; social media; drug abuse

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232. Mapping scorpion exposures reported to US poison control centers

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Background: Data from US poison control centers show that most scorpion exposures occur in southern states. Since the habitats for scorpion species are regionally limited, it would be useful to have more precise geographic data for public education and prevention efforts, especially for the most concerning species, *Centruroides sculpturatus* (Arizona bark scorpion).
Methods: Scorpion exposures from 1/2010 to 12/2015, obtained from the National Poison Data System, were mapped via a geographic information system (GIS) using US Census Bureau 5-digit ZIP code tabulation areas (ZCTAs) for the nine states reporting >100 calls per year. In addition, areas reporting clinical effects of nystagmus and fasciculations, which are unique to *C. sculpturatus* envenomations, were mapped using nationwide data.
Results: A total of 80,992 cases had complete data for mapping. Scorpion envenomations were broadly distributed at low levels throughout much of the nine states examined. Scattered areas of greater frequencies included several urban ZCTAs in Arizona, Nevada, New Mexico, Oklahoma, and Texas. Higher per capita exposure frequencies (Table 1) were found in Arizona, with the greatest being 677 per 100,000 population in a southern Phoenix ZCTA. Other areas of high per capita exposures included El Paso (TX), Oklahoma City and Tulsa (OK), and Las Vegas (NV). Nystagmus and fasciculations were reported in much of Arizona, Las Vegas, and at very low levels in southern California, southern Utah, and New Mexico.
Conclusions: Geographic analysis of NPDS data identified areas with greater scorpion exposures, especially those consistent with *C. sculpturatus* envenomation. By combining this information with GIS software, the resulting visual representations can be used to help guide public education and prevention efforts. The NPDS is a great source of geographic data that may be useful for public health studies.

KEYWORDS Scorpion; mapping; Poison Control Center

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State	Highest Per Capita Rates for 2015	
	ZCTA	Count Per 100,000 Population
Arizona	85045	677
	85718	584
	85085	548
Texas	79911	213
	78070	59
	78261	46
Nevada	89138	170
	89134	147
	89135	121
California	92277	33
	91302	28
	92262	22
	92101	22
Georgia	30016	23
	30263	11
Oklahoma	73102	209
	74120	178
New Mexico	87043	121
	88201	42
	88203	42
Florida	NONE	
Alabama	35244	18

233. Characterization of vaccine administration cases to a regional poison center

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Background: Vaccine use has exploded over the past 65 years. 1953 Centers For Disease Control (CDC) recommendations included 16 doses of four vaccines [primarily smallpox and diphtheria/pertussis/tetanus (DPT)] between 2 months of age and 6 years old (yo). The CDC now recommends 50 doses of 14 vaccines for this age group. Annual influenza vaccine is currently recommended after 6 months of age. Regional Poison Center (RPC) experience with vaccine-related cases have rarely been described.
Methods: All vaccination-related calls to an RPC with a National Poison Data System (NPDS) generic substance code of "miscellaneous serums, toxoids and vaccines" from 1 January 2012 through 21 December 2016 were retrospectively searched by a trained abstractor for vaccine type, dosing errors, and adverse events. All cases related to botulinum toxin type a were excluded.
Results: About 106 vaccine-related cases regarding 15 different vaccines were managed by this RPC. Ages ranged from 1 day old to 83 years old (37 cases <5 yo, 23 cases 5–20 yo, 52 cases >20 yo). One hundred and two cases originated from home and outcomes were coded as non-toxic or minimally toxic. Four cases were coded as potentially toxic (yellow fever vaccine given intramuscularly instead of subcutaneously; Infanrix® was administered instead of Adacel®; influenza vaccine associated with a bad taste in the mouth; Pneumovax® associated chest blisters) and all were lost to follow up. Therapeutic errors occurred in 87 cases: incorrect dose, $n = 16$; too frequent dosing, $n = 51$; incorrect route of administration, $n = 7$, 10 cases due to administration of wrong vaccine; and three cases were because the vaccine used was beyond its expiration date. 19 adverse events were reported for these vaccines: influenza $n = 6$; pneumococcal $n = 4$; human papilloma virus $n = 2$; measles/mumps/rubella $n = 1$; DPT $n = 2$; typhoid $n = 3$; rubella $n = 1$. All were systemic in nature and not reactions at the injection site. Although cases involving 15 different vaccines were reported, 26% of the RPC therapeutic errors were related to the influenza vaccine and 18% were related to the tetanus vaccine (either in combination or stand alone). About 32% of RPC adverse event cases resulted from influenza vaccine administration. No adverse event cases were associated with the tetanus vaccine.
Conclusions: Twenty-nine of 106 (27%) of cases in this study were secondary to administration of the influenza vaccine. RPCs need to be prepared to address vaccination related calls with special attention made to influenza vaccine, as this is the most frequently administered vaccine in the United States.

KEYWORDS Vaccination; therapeutic error; adverse event

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234. QT for cuties: ECG monitoring in pediatric exploratory ingestion of QT-prolonging drugs

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Background: Poison centers (PCs) are frequently called by health care facilities (HCFs) about pediatric exploratory ingestions (PEIs). These may involve drugs with the potential for QT prolongation and risk of dysrhythmias such as torsades de pointes (TdP). However, the incidence of conduction abnormalities and dysrhythmia following PEI appears to be low, and the optimal approach to ECG monitoring in the minimally symptomatic child remains unclear. A widely cited reference is the list of QT-prolonging drugs maintained by the University of Arizona's Center for Education and Research on Therapeutics at CredibleMeds.org (CM), which is stratified by TdP risk. The aims of this study were to (1) determine how frequently ECGs are recommended by the PC after PEI of QT-prolonging drugs, (2) estimate the incidence of QT prolongation, and (3) that of dysrhythmia in this setting.
Methods: The regional PC database was searched for suspected ingestions by children ≤6 years of age involving 28 QT-prolonging drugs listed in CM from 2005 through 2016. We reviewed all case narratives, recording age, substances involved, symptoms, whether the PC recommended one or serial ECGs, presence of conduction abnormalities, and medical outcome. Cases involving multiple substances and those that were not followed to a known medical outcome were excluded.
Results: The initial database search yielded 1087 cases. About 403 met exclusion criteria leaving 684 considered for analysis. Median age was 2.0 (IQR 1.7–3.0) years. About 53.6% were male. The most frequently involved drugs were diphenhydramine ($n = 346$) followed by neuroleptics (210), cyclic antidepressants (41), SSRIs (37), and antidysrhythmics (8). The most frequent medical outcome was no effect ($n = 360$, 52.6%) followed by minor (251, 36.7%), moderate (71, 10.4%), and major (2, 0.3%)) effects. There were no fatalities. The two patients with major effects had CNS depression due to risperidone and methadone (treated with naloxone infusion). Neither required endotracheal intubation, vasopressor support, or had QT prolongation.

The PC specialist in poison information recommended an ECG in 344 cases (50.3%), although in 30 cases this was recommended only if the child became symptomatic. Serial ECGs were recommended in 29 cases (4.2%). An ECG was performed in 399 cases; QTc prolongation was noted in 3 (470, 490, and 513 ms), all of whom were symptomatic with mental status changes. Agents involved in these three cases were olanzapine, risperidone, and clozapine, respectively. ECG findings subsequently improved. There were no dysrhythmias.
Conclusions: ECGs are unlikely to change management in minimally symptomatic children with suspected exploratory ingestion.

KEYWORDS ECG; QT prolongation; pediatric

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235. Tooth be told: homeopathic teething product exposures reported to US poison centers

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Background: Homeopathic teething products (HTPs) formulated as tablets or gels for relief of pain are purported to be non-toxic because they contain highly diluted ingredients. Proponents claim that trace amounts of substances which produce symptoms at higher doses exert a protective effect, though evidence is lacking. In January 2017, the US FDA reported that inconsistent amounts of belladonna had been found in HTPs and advised consumers against using them. The purpose of this study was to determine the medical outcome and clinical effects in children with HTP exposures reported to U.S. poison centers (PCs).
Methods: We requested data from the American Association of Poison Control Centers' (AAPCC) National Poison Data System on all HTP exposure calls for children $\leq$5 years old from 1/1/06 to 12/31/16. Aggregate data was reviewed for frequency of specific medical outcomes and clinical effects. De-identified case narratives, and fatality reports when applicable, were then requested for cases with medical outcomes of moderate or major effects or death. Narratives were independently reviewed by three investigators (C. F., J. M., and R. K.) for agreement with assessments by the original PC.
Results: During the study period 45,647 cases were reported to PCs. Of these, 17,237 (37.8%) were not followed because they were judged to be non-toxic, 17,078 (37.4%) were not followed because no more than minor effects were thought possible, 102 (0.2%) were unable to be followed, and 17 (0%) were confirmed non-exposures leaving 11,213 to be considered for analysis. Their median age was 2.0 years. Medical outcomes included 10,146 (90.5%) with no effect, 413 (3.7%) minor, 29 (0.3%) moderate, 4 (0.0%) major effects, two fatalities, and 619 (5.5%) with unrelated effects. Of 35 case narratives requested with moderate/major/fatal effects, 27 (22 moderate, three major, two death) were obtained as well as both fatality reports. In cases for which narratives were obtained, CNS effects deemed by the PC to be exposure related were drowsiness/lethargy ($n = 6$) and agitation (4). Seizure occurred in 6 but was assessed by the PC as unrelated in two and unknown if related in four cases. Regarding the two deaths, the three investigators agreed with PC assessments that the HTP was clearly not responsible. AAPCC fatality reviewers had judged one clearly not and the other probably not responsible. For the three narratives with outcomes coded as major effect, all three investigators would downgrade the assessment to no more than moderate effect. For 22 narratives that PCs had coded as moderate, in six cases (27.2%) at least one of the investigators would downgrade to mild or unrelated effect, and in 14 (63.6%) all three would do so. The investigators would not have upgraded any of the narratives to a more serious outcome.
Conclusions: Most HTP exposures reported to poison centers and followed to a known outcome result in no effect or minor effects. Although a small proportion are coded as moderate or major by PCs, two-thirds of these appear to have less serious or unrelated effects.

KEYWORDS Teething products; homeopathic; poison centers

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236. Characterization of poison center calls from critical access hospitals in rural Arizona

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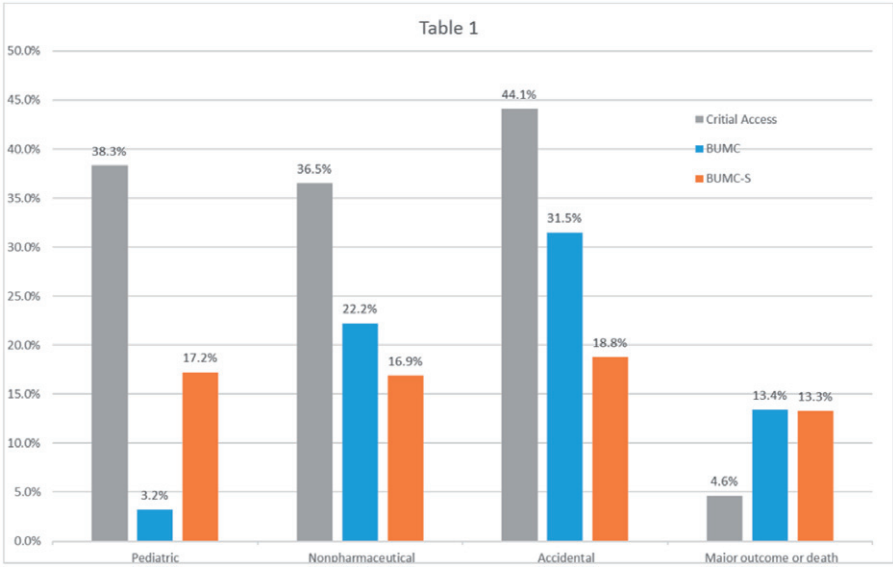
Background: Hospitals serving rural communities face challenges different from those serving urban and suburban populations. There are differences in demographics and available healthcare resources. There are also differences in the potential types of toxic exposures in rural areas. The designation of Critical Access Hospital (CAH) can be given to rural hospitals that meet certain criteria including having fewer than 25 acute care beds and location more than 35 miles from another hospital. The state of Arizona has 14 designated critical access hospitals. The Arizona Poison and Drug Information Center (AzPDIC) serves all 14 Critical Access Hospitals as well as numerous suburban and urban hospitals throughout in Arizona. In this study, we characterize the poisoning cases where the initial call to the AZDPIC is from a CAH. For comparison, we provide data pertaining to calls from two hospitals in Tucson Arizona; Banner University Medical Center, Tucson (BUMC) and Banner University Medical Center South (BUMC-S). BUMC is a large tertiary care academic center (with pediatric ED and ICU) and BUMC-S is a smaller academic affiliated hospital.
Methods: For this study, a database query was performed on the Toxical Database documenting calls to the AzDPIC from 1 January 2002 to 18 January 2017. Calls initiated from a CAH or one of the two reference hospitals were included. Data were organized according to the initial hospital where the patient was treated and demographic, outcome, and exposure type were tabulated for each hospital.
Results: A total of 10,710 exposures from CAH were analyzed. BUMC had 14,436 and BUMC-S had 9838 exposures. In CAHs, 3912 (36.5%) exposures were non-pharmaceuticals and 4724 (44.1%) were unintentional. In comparison to our reference hospitals, CAHs had higher percentage of non-pharmaceutical and accidental exposures. In CAHs, 1306 (4.6%) exposures had a major outcome or death, which was lower than in reference hospitals. In CAH, 4087 (38.3%) of cases involved patients less than 20 years old. This was slightly higher than BUMC, which has a designated pediatric ED and much higher than BUMC-S which does not have a designated pediatric ED. In CAH, there were a higher percentage of bites and stings as well as pesticide exposures and a lower percentage of street drugs.
Conclusions: Critical Access Hospitals face many unique challenges. In the domain of toxic exposures, CAH may have decreased burden of severe disease. Poison centers may have an



opportunity to reach out to rural communities to avoid unnecessary Emergency Department visits. Additionally, the higher burden of non-pharmacuetical exposures may reflect environmental and occupational exposures and bites and stings that are more prevalent in rural communities.

KEYWORDS Rural; critical access; poison center

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237. Improving detection of call clusters through surveillance of poison center data

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Introduction: The Centers for Disease Control and Prevention (CDC) and American Association of Poison Control Centers (AAPCC) uses the national poisoncenter (PC) reporting database known as the National Poison Data System (NPDS) to conduct surveillance for potential incidents of public health significance (IPHS). CDC uses automated algorithms to identify anomalies in calland adverse health effect (clinical effect) volume, and to identify calls reporting exposure to high priority agents. Call and clinical effect volume anomalies are identified when the number of calls exceeds a threshold based on historical data using the historical limits method (HLM). Clinical toxicologists and epidemiologists at AAPCC and CDC apply standardized criteria to determine if data anomalies represent a potential IPHS and which, if any, additional public health agencies should be notified (e.g., state health department). Past analyses of IPHS showed that this method yielded a high proportion of false positive anomalies resulting in a low positive predictive value (PPV). A low PPV can cause unnecessary waste of staff time and resources. As an alternative, we considered separating calls by toxicologically-relevant exposure categories prior toapplying the HLM. Our objective was to compare the effectiveness of applying HLM to PC total call volume both with and without stratifying by exposure category in order to detect data anomalies which may represent IPHS.
Methods: We derived our exposure categories based on the criteria that the categories must (1) relate to hazardous exposures of public health importance, (2) reflect categories based on clinical effects and treatment modalities, (3) avoid high-priority exposures that may be triggered by single calls, (4) be compatible with exposure substance identification codes currently used by PCs and NPDS, and (5) include enough calls for meaningful tracking. We queried all calls reporting exposures to the proposed categories between 1 January 2009 and 31 July 2015 for 10 PCs. We first applied the HLM method on the dataset without stratifying by exposure first to identify data anomalies that may represent IPHS (traditional, non-stratified approach). We then stratified the dataset by exposure category and applied the HLM method. We compared the combined anomaly burden generated by stratifying by exposure category with the anomaly burden for the non-stratified approach for varying time windows (1-, 2-, 4-, 8-, and 24-h). We conducted analysis in R.
Results: We derived a total of 20 exposure categories, including chemicals ($n = 4$), drugs of abuse ($n = 6$), pesticides ($n = 3$), gas/fume/vapors ($n = 2$), contaminated food/water ($n = 1$), and others ($n = 4$). Call counts during 2015 for these categories ranged from approximately 5000–90,000. There was a marked reduction of anomaly burden when we first stratified by exposure category for time windows shorter than 8 h compared with the anomaly burden for the non-stratified approach.
Conclusions: Initial stratification of call volume by exposure category and time window had a lower anomaly burden when compared with not stratifying for the 1-, 2-, and 4-h time windows. Further work should focus on refining the exposure categories and assessing other detection performance metrics such as sensitivity.

KEYWORDS Public health; surveillance; poison center

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238. Pembrolizumab induced autoimmune insulin resistance

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Background: Pembrolizumab is a monoclonal antibody reported to improve survival in patients with metastatic melanoma. In the tumor microenvironment, overexpression of cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), programmed death receptor protein (PD-1), and its ligand PD-L1 all contribute to tumor propagation. Pembrolizumab, a monoclonal antibody directed against PD-1, acts to activate the T-cell response against the tumor. However, pembrolizumab and other immunomodulators can precipitate the development of autoimmune manifestations termed immune-related adverse events (IRAE).
Case reports: An 84-year-old male with stage 4 melanoma and pre-diabetes (IA1c 5.7 1-month prior) was found unresponsive in his bathtub with a blood glucose "too high to read". Initial exam was significant for an ill appearing patient with Kussmaul breathing. Labs were significant for the following:VBG: pH 6.88, pCO2 37, pO2 37, Lactate 5.3CBC: WBC 15.2, Hgb 13.6, Plt 201Chem-7: Na 143, K 3.7, Cl 110, HCO3 5, BUN 68, Cr 2.12, Glucose 1,076 He was admitted to the intensive care unit (ICU) for treatment of diabetic ketoacidosis. Initial interventions included three liters of normal saline, sodium bicarbonate, intravenous regular insulin 10 units, followed by a regular insulin drip (10 units/h). He was also covered with broad-spectrum antibiotics for possible sepsis. In the ICU, he required escalating doses of insulin to control his blood glucose. With an insulin infusion of 800 units/h, his blood glucose remained in the 300 mg/dL range. Further history revealed that he was taking pembrolizumab. Endocrinology believed the likely precipitant of his DKA was an autoimmune reaction due to pembrolizumab resulting in severe type B insulin resistance. He was started on methylprednisolone 1000 mg, followed by dexamethasone with improvement in blood glucose control. Islet antigen-2 (IA-2) antibodies and zinc transport antibodies were negative. However, glutamic acid decarboxylase (GAD) antibody titers were positive suggesting an autoimmune response directed against pancreatic islet cells.
Case discussion: IRAEs are frequent and occur in up to 90% of patients treated with an anti-CTLA-4 antibody and 70% of patients treated with anti PD-1/PD-L1 antibody. Anti-PD1 antibiotics have been associated with a wide range of IRAEs including thyroiditis, pituitary dysfunction, adrenal insufficiency, rheumatoid arthritis, colitis, and diabetes. Most IRAEs occur within 3–6 months of initiation of the anti-CTLA4 or anti-PD1 medications, and risk appears to be dose-dependent for anti-CTLA-4 antibodies. In the majority of IRAEs, no circulating auto-antibodies are identified.Testing for IA-2, GAD, zinc transport antibodies, typically in combination with insulin antibodies, increases the sensitivity of detecting autoantibodies to 93–98%. However, the detection of GAD antibodies does not fully explain the patient's high insulin needs, and suggests that there may be additional antibodies directed against insulin receptors. Treatments include discontinuation of the drug and administration of steroids. The use of immunosuppressive agents such as rituximab and cyclophosphamide has also been suggested as well as plasmaphoresis and intravenous immunoglobulin therapy.
Conclusions: Given the increasing use of cancer immunotherapy, there should be increased vigilance for IRAEs related to anti-CTLA-4 antibody and anti PD-1/PD-L1 antibody use.

KEYWORDS Pembrolizumab; monoclonal antibody; immune-related adverse events

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239. Evaluating the Lo-Cal option in ethylene glycol poisoning

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Background: Ethylene glycol (EG) causes renal injury when its metabolite, oxalic acid, combines with calcium to form calcium oxalate crystals. Previously published case reports describe hypocalcemia in the setting of EG poisoning. These cases have led to contemporary medical textbooks recommending measurement of serum calcium concentrations and warning of hypocalcemic complications. However, this association has not been well studied. Our aim was to characterize the relationship between EG poisoning and calcium concentration.
Methods: Electronic regional poison center (RPC) records coded for EG 1/1/2002–12/31/2016 were retrospectively queried. Those cases where an EG concentration was detectable and a calcium concentration was recorded were included. Only the initial EG and calcium concentrations reported were collected during data abstraction. Hypocalcemia and severe hypocalcemia were defined as serum concentrations less than 8.5 mg/dL and 7.0 mg/dL, respectively. Secondary laboratory markers of EG poisoning severity (bicarbonate, pH, creatinine) were also abstracted in those cases that met inclusion criteria. Bicarbonate concentration $<$ 16 mmol/L, pH $<$ 7.3, and Cr $\geq$1.5 were defined as laboratory values consistent with significant EG toxicity.
Results: A total of 1647 cases of possible EG exposures were reported to our RPC over the 15-year study period. Ninety-seven cases met inclusion criteria. EG and calcium concentrations ranged from 3.67 to 889 mg/dL (mean 192.8 mg/dL) and 6.1 to 10.5 (mean 8.8 mg/dL) mg/dL, respectively (Figure). Pearson's Correlation was applied and no significant direct correlation was found between EG and calcium concentrations ($r = -0.16$, $p = .12$). Twenty-seven patients (28%) had calcium concentrations below 8.5 mg/dL, and in only two patients (2%) was it below 7 mg/dL. No clear difference was observed when comparing calcium concentrations between those with and without secondary markers of EG toxicity (Table).
Conclusions: Hypocalcemia was observed in a minority of patients, and was seen in patients with or without laboratory markers of significant toxicity. While measuring oxalate concentrations may best determine if a relationship between EG poisoning and hypocalcemia exists, this is not commonly recommended or recorded. Similarly, ionized calcium more accurately reflects hypocalcemic states, but was rarely measured. The timing of these various laboratory values was also difficult to ascertain in this retrospective study. Our data suggest that calcium concentrations have questionable utility in the routine evaluation of suspected EG poisoning. A prospective study is needed to further clarify this relationship.

KEYWORDS Ethylene glycol; hypocalcemia; calcium

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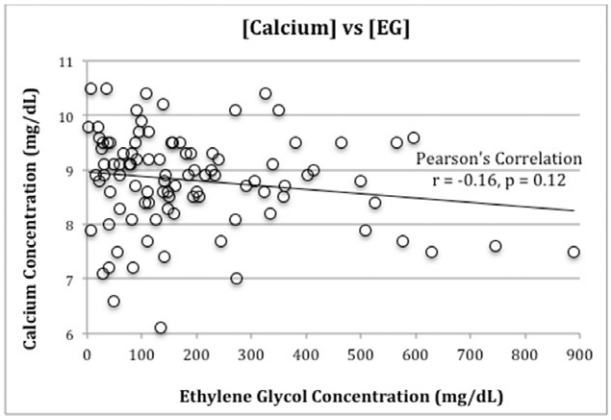

	Mean [Ca] in mg/dL (range)
[EG] < 50 mg/dL (n = 20)	8.9 (6.6-10.5)
[EG] > 50 mg/dL (n = 77)	8.8 (6.1-10.4)
[HCO3] ≥ 16 mmol/L (n = 48)	8.9 (7.2-9.8)
[HCO3] < 16 mmol/L (n = 49)	8.7 (6.1-10.5)
pH ≥ 7.3 (n = 32)	8.9 (7.1-10.5)
pH < 7.3 (n = 38)	8.7 (6.6-10.4)
Cr < 1.5 mg/dL (n = 80)	8.9 (7-10.5)
Cr ≥ 1.5 mg/dL (n= 16)	8.7 (6.1-10.5)

240. Cardiovascular and neurologic effects following overdose of citalopram versus escitalopram: an NPDS study

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Background: Citalopram is a selective serotonin reuptake inhibitor used to treat depression. Citalopram is a racemic mixture comprised of the *R*- and *S*-citalopram enantiomers. In overdose, citalopram has been associated with seizures, cardiac conduction abnormalities, and ventricular dysrhythmias. Escitalopram is the commercially available *S*-citalopram enantiomer. Originally thought to be less toxic, escitalopram has also been associated with similar effects. A previous review of six United States poison control centers found seizures to be more likely with citalopram but were unable to analyze difference in cardiac events. This study aims to analyze the comparative rates of moderate and major outcomes reported after ingestion of citalopram versus escitalopram in a large data set.

Methods: This retrospective review of human exposures reported to United States poison control centers included single substance ingestions of citalopram or escitalopram. Data was collected from the National Poison Data System (NPDS) from 1 January 2000 to 31 December 2015; cases were identified by product codes. The primary outcomes were the number of moderate or major outcomes (standard NPDS case outcome definitions) following citalopram versus escitalopram overdose. Secondary outcomes included difference in number of deaths, "all seizures", "all conduction disturbances", or "cardiac dysrhythmias", and correlation of dose with primary outcomes in citalopram versus escitalopram. Clinical effects were only considered present when coded as related or unknown if related. Definitions of the composite clinical effects were: "all seizures" included those coded as seizure (single), seizure (multiple/discrete), or seizure (status); "all conduction disturbances" included those coded as conduction disturbance or electrocardiograph change (other); "cardiac dysrhythmia" included those coded as dysrhythmia (v tach/v fib) or dysrhythmia (other). Statistical analysis included descriptive statistics with proportions to describe central tendencies. Chi-square and Chi-square 2 × k or Fisher's exact test was used for categorical data. Correlations were estimated with Kendall Rank Correlation (Kendall's Tau).

Results: A total of 100,754 cases were included with 54% including citalopram. Moderate and major outcomes were more likely to occur with citalopram versus escitalopram (2%, 95%CI 1.7–2.4% and 0.9%, 95%CI 0.8–1.1%; p <.0001). "All seizures" occurred in 2.7% of cases with citalopram and 0.25% with escitalopram (2.4%, 95%CI 2.3–2.6%; p<.0001). "All conduction disturbances" were more likely to occur in the citalopram group (2.6%) versus escitalopram (1.7%) (0.9%, 95%CI 0.7–1.1%; p<.0001). "Cardiac dysrhythmias occurred in (0.23%) of cases involving citalopram versus escitalopram (0.14%) (0.09%, 95%CI 0.04–0.14%; p=.001). Death occurred more in the citalopram versus escitalopram group (0.03%, 95%CI 0.01–0.05%; p=.0016). The cumulative dose was weakly concordant with the presence of moderate or severe effects in both citalopram and escitalopram, Kendall's tau $b = 0.24$ (95%CI 0.238–0.246; p<.0001) and 0.178 (95%CI 0.174–0.181; p<.0001).

Conclusions: Cardiovascular and neurologic events occurred following overdose with citalopram or escitalopram. Seizures occurred more frequently in the citalopram group. Additionally, cardiac events including conduction disturbances or dysrhythmia were more common in the citalopram group. Overdose with citalopram was also more likely to be associated with death versus escitalopram.

KEYWORDS Citalopram; seizure; dysrhythmia

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241. Comparison of moderate and major outcomes with venlafaxine versus desvenlafaxine exposures: an NPDS study

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Background: Venlafaxine belongs to the class of serotonin norepinephrine reuptake inhibitors and is used in the treatment of major depression and anxiety. Venlafaxine causes a dose dependent increase of central serotonin and norepinephrine levels. In overdose, venlafaxine causes seizures, dysrhythmias, and death. These effects may be due to the parent drug or a metabolite. Desvenlafaxine, a metabolite of venlafaxine, is also approved in the treatment of major depression. Although also associated with significant effects in overdose, these agents have not been comparatively evaluated for moderate and major outcomes after accidental or intentional overdose in a large data set.

Methods: This retrospective review of human exposure cases includes single substance exposures to venlafaxine or desvenlafaxine reported to the National Poison Data System (NPDS) by United States poison centers identified by product codes from 1 January 2000 to 31 December 2015. Primary outcome included

the difference in moderate or major outcomes (a standard NPDS case outcome definition) between venlafaxine and desvenlafaxine ingestions. Secondary outcomes included difference in death rates, number of "all seizures", "all conduction disturbances", "cardiac dysrhythmia", and evaluation of potential dose correlation with primary outcomes. Definitions of the composite clinical effects were: "all seizures" included those coded with seizure (single), seizure (multiple/discrete), or seizure (status); "all conduction disturbances" included those coded as having conduction disturbance or ECG change (other); "cardiac dysrhythmia" included those coded as dysrhythmia (v tach/v fib) or dysrhythmia (other). Clinical effects were only considered present when coded as related or unknown if related. Statistical analysis included descriptive statistics with proportions to describe central tendencies. Chi-square and Chi-square 2 × k or Fisher's exact test was used for categorical data. Correlations were estimated with Kendall Rank Correlation (Kendall's Tau).

Results: A total of 46,793 cases were included which predominantly included venlafaxine (94%). Males comprised 35.2% and females 64.2% of cases. Moderate and major outcomes were reported more commonly with venlafaxine versus desvenlafaxine (2.7%, 95% CI 1.54–3.48% and 0.73%, 95% CI 0.35–0.96%, respectively; $p < .0001$). Deaths did not occur more frequently in venlafaxine (0.08%) versus desvenlafaxine (0.04%) (0.0479%, 95%CI −0.12 to 0.094%; $p=.726$). "All seizures" occurred in 2.1% and 0.4% of venlafaxine and desvenlafaxine cases, respectively (1.63%, 95%CI 1.28–1.89%; $p<.0001$). "All conduction disturbances" occurred in 1.1% and 1% of venlafaxine and desvenlafaxine cases (0.1%, 95%CI −0.35 to 0.43%; $p=.61$). "Cardiac dysrhythmias" did not occur more frequently in the venlafaxine (0.2%) versus desvenlafaxine (0.07%) (0.14%, 95%CI −0.051 to 0.217%; $p=.1293$). The cumulative dose was weakly concordant with the presence of moderate or severe effects in both venlafaxine and desvenlafaxine, Kendall's tau $b=0.196$ (95%CI 0.192–0.1999; $p<.0001$) and 0.145 (95%CI 0.132–0.159; $p<.0001$).

Conclusions: In overdose, venlafaxine and desvenlafaxine were associated with significant neurologic and cardiovascular events. Overdose with venlafaxine was more likely to cause moderate and major outcomes and seizures. Conduction disturbances, dysrhythmias, and death was not more likely to occur in either medications.

KEYWORDS Venlafaxine; seizure; dysrhythmia

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242. Desvenlafaxine versus venlafaxine: comparative toxicity utilizing data reported to the National Poison Data System

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Background: Desvenlafaxine (DVF) and venlafaxine (VLF) are antidepressants that inhibit the neuronal reuptake of serotonin and to a lesser extent norepinephrine in the CNS. DVF is the major active metabolite of VLF. Retrospective reviews have characterized the toxicity of each medication separately. A single state review compared a small number of DVF and VLF cases and found no significant differences between the two. The objective of this study was to compare the clinical effects and medical outcomes between DVF and VLF exposures reported to the National Poison Data System (NPDS).

Methods: A retrospective cohort study was conducted analyzing NPDS data for single agent DVF or VLF exposures reported to the American Association of Poison Control Centers (AAPCC) from April 2008 through December 2015. Excluded cases included multiple medication ingestions, non-ingestion route, outcomes that were unrelated, confirmed non-exposures, and patients not

Table 1. DFN vs VLN symptom comparisons (>1% incidence).

	DFN (%) n = 1548	VLN (%) n = 9884	P values	RR (95% CI)
Clinical Effects				
Agitated/irritable	67 (4.3)	732 (7.4)	0.000004033	0.58 (0.46-0.75)
Conduction disturbance	19 (1.2)	237 (2.4)	0.002794	0.51 (0.32-0.81)
Confusion	4 (0.3)	291 (2.9)	<0.0000001	0.09 (0.03-0.23)
Dizziness/vertigo	39 (2.5)	411 (4.2)	0.001542	0.61 (0.44-0.84)
Drowsiness/lethargy	171 (11.1)	1612 (16.3)	<0.0000001	0.68 (0.58-0.79)
Hallucinations/delusions	8 (0.5)	111 (1.1)	0.02873	0.46 (0.23-0.94)
Hypertension	70 (4.5)	706 (7.1)	0.00008298	0.63 (0.50-0.80)
Hypotension	10 (0.7)	146 (1.5)	0.006926	0.44 (0.23-0.83)
Mydriasis	26 (1.7)	386 (3.9)	0.000002804	0.43(0.29-0.64)
Seizure (single)	8 (0.5)	309 (3.1)	<0.0000001	0.17 (0.08-0.33)
Seizures (multi/discrete)	3 (0.2)	147 (1.5)	0.000001434	0.13 (0.04-0.41)
Tachycardia	179 (11.6)	2169 (21.9)	<0.0000001	0.53 (0.46-0.61)
Tremor	31 (2.0)	474 (4.8)	<0.0000001	0.42 (0.29-0.60)

followed to a known outcome. Case outcomes as defined by AAPCC criteria and the presence of specific symptoms were analyzed. Fisher's exact test was used to compare DVF and VLF outcomes and clinical effects.
Results: There were 1548 DVF and 9884 VLF cases that met inclusion criteria. Most patients were female, 58.9% for DVF and 64.4% for VLF. Median age was 9.5 years old (5 months–90 years) for DVF and 21 years old(24 d–93 years) for VLF. The risk of all adverse outcomes was less for DVF exposures; except death (no difference between the two groups). VLF patients were at significantly greater risk for the following neurological symptoms, agitation, confusion, hallucinations, vertigo, sedation, tremors, seizure (single),seizure (multiple discrete) and the following cardiovascular effects, hypertension, hypotension, tachycardia, conduction abnormalities (Table 1). In a subset analysis of patients >19 years old, there were 637 DVF and 5395 VLF cases (median age of 36.5 and 39 years old respectively). VLF exposures had a significantly greater risk for agitation, confusion, drowsiness, hallucinations, seizure (single),seizure (multiple discrete), elevated CPK, and tachycardia.
Conclusions: In this review of national data comparing DVF and VLF, the risk for adverse outcomes was significantly less for DVF. There was a greater incidence of neurologic and cardiovascular clinical effects associated with VLF. The same trend was observed in a subset analysis of adult patients.

KEYWORDS Venlafaxine; desvenlafaxine; comparative toxicity

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243. Exposures in pregnant women recorded in the National Poison Data System (NPDS), 2011–2015

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Objectives: Toxicological exposures in pregnant women represent a unique challenge to medical professionals. Toxicants and their antidotes pose potential acute and long-term risks to both the fetus and the mother. The objective of this study was to characterize toxicological exposures in pregnant females as reported to regional poison centers.
Methods: The American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS) was queried for all encounters involving pregnant patients aged 12–44-years-old from 2011 to 2015. Frequency statistics were used to report distributions of age, trimester, reason and category of exposure, interventions performed, and clinical outcome of mother and fetus.
Results: In the 5-year study period, there were 32,578 calls to poison centers regarding pregnant patients representing 0.3% of total calls. The average age of study subjects was 27.4 years. More calls involved women in their second trimester of pregnancy (35.8%), than women in their first (29.5%) and third (29.5%) trimesters. Calls involved exposure to a range of 1–13 substances per patient, with most cases involving exposure to one (86.3%) or two (9.4%) substances. The majority of exposures were acute (85.2%) or acute-on-chronic (8.5%) in nature, occurred at home (89%) or at the workplace (4.5%), and resulted from ingestion (60.5%) or inhalation/intranasal (21.4%) exposure. The primary reason for exposure was unintentional in 72.1% of cases and intentional in 21.7%. Suspected suicide attempts were responsible for most (69.3%) intentional exposures. Suicide attempts were less likely in the third trimester (18.2%), compared with attempts made in the first (37.2%) or second (35.1%) trimesters. The most common substances include isolated acetaminophen exposures (3.6%), bleaches (3%), scorpion stings (2.9%), pyrethroids (2.7%), and carbon monoxide (2.5%). Gastrointestinal decontamination and enhanced elimination interventions were performed in a minority of cases. The vast majority of exposures did not result in any clinically significant effect (70.7%) or had only a minor effect (21.4%). There were 11 deaths reported in pregnant mothers over the study period. Substances most commonly involved in maternal deaths were methadone (14.3%), acetaminophen-containing products (14.3%), and tramadol (14.3%). In addition to maternal deaths, there were 21 fetal deaths reported during the study period that were related or potentially related to the maternal toxic exposure. Acetaminophen was the most common substance of exposure associated with fetal death.
Conclusions: Clinically significant toxicological exposures in pregnant women are primarily the result of intentional, single-substance ingestions that occur at home in early pregnancy. Further research into the best treatment and preventative interventions is needed for this unique population.

KEYWORDS Pregnancy; toxic exposures in pregnancy; NPDS

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244. Use of topical capsaicin cream for the treatment of cannabinoid hyperemesis syndrome

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Objectives: Cannabis is the most widely used illicit drug in the United States. Recently, clinicians have identified a syndrome of cyclic episodes of nausea, vomiting and abdominal pain in patients who have heavy, long-term cannabinoid use called Cannabinoid Hyperemesis Syndrome (CHS). These patients tend to be refractory to traditional anti-emetic and analgesic therapies, and alternative treatment regimens are needed. Patients with CHS have reported relief of symptoms by taking hot baths, which has led to the theory that TRV1 receptor agonists, such as capsaicin, could potentially alleviate the symptoms of CHS. Capsaicin has been reported to treat CHS in case reports published in the peer-reviewed medical literature. The goal of this study was to determine the efficacy of topical capsaicin cream in relieving the symptoms of CHS relative to traditional therapies for patients with multiple emergency department (ED) visits for CHS.
Methods: A single-center retrospective chart review was conducted at an urban tertiary care hospital for patients who received topical capsaicin cream in the ED from October 2015 to July 2016. Adult patients aged 18 years and older were included if they had physician documentation of marijuana use and received topical capsaicin cream for two or more symptoms of CHS (nausea, vomiting, abdominal pain, relief of symptoms with shower, symptoms worse in the morning). Patients with additional visits to the ED during the study period for CHS symptoms wherein capsaicin was not used as an antiemetic were used as a control group. Primary outcome measures included time to discharge after initial anti-emetic therapy administration and the need for admission.
Results: Capsaicin was administered for suspected CHS in 24 individual cases corresponding to 22 patients over the 22-month study period. The majority of patients were female (81.8%) and African-American 17 (77.5%). The mean age was 30.2 years. Ten of the study patients had an additional 21 visits to the ED for CHS symptoms wherein capsaicin was not administered as a part

of the treatment regimen. An independent *t*-test was performed to evaluate significant differences in time to discharge after initial anti-emetic administration in the capsaicin treatment group and the non-capsaicin group. Mean time to discharge was 51.1 min longer in the capsaicin group (95% CI, −17.6 to 119.9), but the result was not statistically significant (p=.137). In addition, eight (33.3%) patients required admission in the capsaicin group, whereas 13 (61.9%) patients were admitted in the non-capsaicin group (p=.055).

Conclusions: Topical capsaicin cream is an inexpensive, over-the-counter, safe adjunctive therapy to traditional therapies for the treatment of CHS. While the results of our study did not show a significant decrease in ED length of stay or need for admission when using topical capsaicin cream. A prospective study evaluating capsaicin against traditional anti-emetics would be useful to further delineate the appropriate use of capsaicin in CHS.

KEYWORDS Capsaicin; cannabinoid hyperemesis syndrome; marijuana

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245. Ethanol measurement and wait times of adult emergency department patients awaiting psychiatric assessment: could a breathalyzer help?

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Introduction: Psychiatric complaints represent up to 10% of all emergency department (ED) visits. On an average, this population also experiences longer wait times. A contributing factor to the length of stay (LOS) for psychiatric patients is the time spent waiting for an ethanol (ETOH) level. ETOH is a common intoxicant in this group, and determination of serum levels are often required prior to medical clearance for psychiatric assessment.The current process is time consuming and resource intensive. Phlebotomy and laboratory analysis is required of blood samples causing discomfort to patients, utilizing resources, and potentially exposing staff to harm. Breathalysers are used in some American and European EDs as a non-invasive means of measuring alcohol levels, but there is no evidence to date that this reduces ED LOS. The objective of this pilot study was to calculate the median times from triage to reported ETOH level for three different concentrations. Secondary objectives included the median times from serum ETOH reporting to psychiatric consultation and to disposition. Further studies will look at implementing a breathalyser at triage, which may lead to shorter average ED LOS, especially for patients with undetectable ETOH levels.

Methods: The study design was a descriptive, retrospective chart review with data accessed electronically through Sunrise Clinical Manager®. Patients were included if they were ≥18 years of age, seen in an ED in Calgary in 2015 with a primary psychiatric complaint, and had ETOH measured. Patients were excluded if they had a medical/surgical consult or admission, and ETOH levels >26mmol/L. The primary outcome was median times from triage to serum ETOH report for three different ETOH concentrations: group 1 (<2mmol/L), group 2 (3–17mmol/L), and group 3 (18–25 mmol/L). Secondary outcomes were median time from ETOH reporting to psychiatric consult; ETOH reporting to disposition.

Results: A total of 1660 patients were included. The average age was 35.8. Males accounted for 57%. The most common psychiatric complaint was depression/suicidality (table 1).

Primary outcome: The median times from triage time to ETOH report for groups 1, 2, and 3, respectively, were 2.90 h (IQR 2.00–4.19), 2.31 h (IQR 1.62–3.50), and 2.24 h (IQR 1.73–3.47) (Table 2). See Figure 1. *Secondary outcomes*: The median times from ETOH report to time of disposition (admission or discharge) for groups 1, 2, and 3, respectively, were 4.62 h (IQR 2.36–8.50), 6.08 h (IQR 3.18–9.86), and 5.83 h (IQR 2.87–9.37). Using the Kruskal–Wallis test, there was a significant difference detected between the groups (p = .012). The median times from ETOH report to psychiatric consult for groups 1, 2, and 3, respectively, were 0.19 h (IQR 1.14–1.60), 0.86 h (IQR 0.40–3.22), and 0.63 h (IQR 0.40–1.37). There were no significant differences detected between the groups.

Conclusions: Patients with undetectable ETOH levels had longer median times to ETOH report. However, a subsequent disposition decision was made faster for patients with an undetectable ETOH level. This result could be used to support a trial looking at the utility of breathalysers in the ED to reduce LOS, especially in sober patients.

KEYWORDS Breathalyser; ethanol level; psychiatric patients

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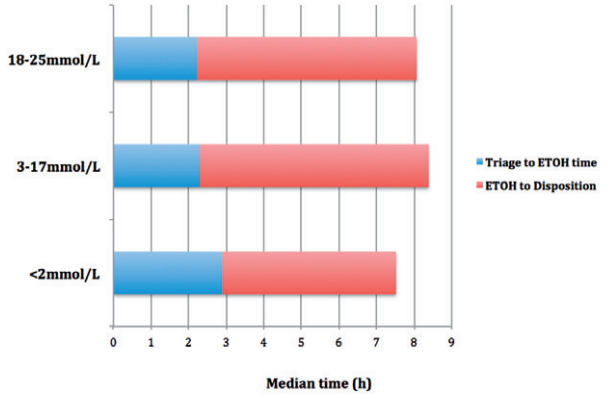

Figure 1: Median times from triage to ETOH reporting, and ETOH reporting to disposition for each ethanol concentration

Table 1 – Patient characteristics by groups

	ETOH <2mmol/L	3-17mmol/L	18-25mmol/L	Total
N	1439	130	91	1660
Male	820.2 (57%)	71.5 (55%)	61.9 (68%)	946.2 (57%)
Age (mean)	35.8	35.5	36.2	35.8
% FMC	26.6%	28.5%	23.1%	26.5%
% PLC	36.5%	35.4%	28.6%	36.0%
% RGH	27.3%	26.2%	36.3%	27.7%
% SHC	9.6%	10.0%	12.1%	9.8%
Psychiatric Complaint				
Depression/suicidal	573	73	55	701
Bizarre behavior	225	7	6	238
Hallucinations/delusions	200	8	3	211
Ingestion	107	16	7	130
Substance misuse	87	8	5	100
Concern for welfare	48	2	2	52
Deliberate self harm	36	5	6	47
Anxiety	43	1	1	45
Situational Crisis	36	1	2	39
Altered LOC#	25	2	1	28
Violent behaviour	24	2	2	20
Homicidal behavior	20	1	0	21
Substance withdrawal	16	4	1	21
Social problem	7	0	0	7

Foothills Medical Centre (FMC), Peter Lougheed Centre (PLC), Rockyview General Hospital (RGH), South Health Campus (SHC), level of consciousness (LOC).

246. Toxicity of double-dose medication ingestions

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Background: People frequently either intentionally or unintentionally take a double or extra dose of their medication. When the poison control center is contacted regarding these ingestions, it is specifically documented, and frequently patients are referred to healthcare facilities for evaluation. We evaluated the outcomes after double-dose drug ingestions across all drug categories. We sought to determine if there are certain classes of medications that are more problematic and necessitate more intensive monitoring and potential treatment in this scenario.
Methods: We conducted a retrospective review of all documented double-dose medication ingestion cases reported to a statewide poison system between 2006 and 2015. *Inclusion criteria*: all ages, single substance cases only, cases coded as "double-dose" that were evaluated at a healthcare facility. Cases involving more than one substance were excluded. We evaluated generalized outcomes per AAPCC criteria (major, moderate, mild, or no effect) as well as specific symptoms and interventions.
Results: Between 2006 and 2015, we reviewed 1384 cases of double-dose ingestions involving single agents that were referred to a health care facility. The medications classes that were most frequently reported included calcium channel blockers (145, 10%), anticonvulsants (102, 7%), alpha-2 agonists (98, 7%), and atypical antipsychotics (98, 7%). The medication classes associated with the most serious symptoms were calcium channel blockers, alpha-2 agonists, and beta-blockers. There were only 12 documented cases with severe effects and no deaths were noted. Of those cases coded as severe, there was one propafenone case (syncope, ventricular tachycardia), one risperidone case (unresponsive), two beta-blocker cases (hypotension, bradycardia), four calcium-channel blocker cases (syncope, hypotension, bradycardia, and conduction abnormalities), one bupropion case (seizure), one mood stabilizer (altered mental status), and two opioid cases. Both opioid cases involved tramadol, and seizures was the coded effect.
Discussion: The majority of cases had outcomes listed as no effect and minor effect. We found regarding calcium channel blockers, alpha-2 agonists, beta-blockers, calcium channel blockers and sulfonylureas, moderate to severe effects were more likely than other drug classes, and referral to a healthcare facility for further monitoring should be considered. However, for some medication classes such as vitamins, SSRIs, insulin, NSAIDS, antipyretics, and most opioid analgesics, close home observation is likely sufficient in unintentional double-dose ingestions.
Conclusions: We found that overall, most classes of medications do not pose serious health risks in the setting of a double-dose; however, some classes of medications, particularly cardiac medications, do carry enough risk for serious adverse effects that evaluation in a healthcare facility may be warranted.

KEYWORDS Double-dose; overdose; management

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247. Sentinel carfentanil deaths in a midwestern state: findings and interagency response

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Background: Heroin adulteration with ultra-potent opioids has changed the face of the American opioid epidemic. Carfentanil, a μ-receptor agonist approximately 10,000 times the potency of morphine, heightens overdose risk. We describe the first epidemic of carfentanil-related deaths in three Midwestern counties, and the multiagency task force convened to present a unified message to media and health professionals.
Case series: An urban medical examiner's office evaluated five decedents with suspected opioid toxicity. All underwent autopsies revealing no life-threatening natural diseases or traumatic injuries; one patient had non-contributory arteriosclerotic heart disease. Initial testing revealed no toxic concentrations of commonly encountered medications or illicit substances. Clinical suspicion for opioid toxicity as the cause of death led to additional testing at NMS Labs for novel psychoactive substances and designer opioids. Decedents were found over an 18-d period in three non-contiguous counties. All had measurable blood carfentanil levels (median 0.27 ng/mL, range 0.13–0.64 ng/mL, Table 1). Four of the five had measurable blood ethanol concentrations; three had evidence of co-ingested substances including alprazolam, clonazepam, methamfetamine, benzoylecgonine, and 6-monoacetyl morphine. Three deaths were attributed in whole or part to carfentanil toxicity; the remainder were attributed to mixed drug toxicity. At the time of writing, two more decedents have tested positive for novel opioids, with quantitative testing in process.
Case 1: A 31-year old male with reported history of heroin abuse found deceased near drug paraphernalia. Blood testing revealed evidence of both carfentanil and ethanol. Cause of death was attributed to mixed carfentanil and ethanol toxicity.
Case 2: A 33-year old male with reported history of substance abuse, including heroin and fentanyl, found deceased near drug paraphernalia. Blood testing revealed evidence of carfentanil and ethanol. Cause of death was attributed to acute carfentanil and ethanol toxicity.
Case 3: A 42-year-old female with history of recent overdose reversed with naloxone found deceased near drug paraphernalia. Blood testing revealed carfentanil, methamfetamine, morphine, and alprazolam. Cause of death was attributed to mixed drug toxicity.
Case 4: A 34-year-old female with history of substance abuse including heroin found deceased near drug paraphernalia. Blood carfentanil, methamfetamine, benzoylecgonine, morphine, clonazepam, and 7-amino-clonazepam were detected. Cause of death was attributed to mixed drug toxicity.
Case 5: A 23-year-old male with history of heroin abuse found deceased near drug paraphernalia. Blood carfentanil, ethanol, and urine 6-monoacetyl morphine were detectable. Cause of death was attributed to acute carfentanil toxicity.
Case discussion: Human carfentanil toxicity is minimally described. Two previously published cases of confirmed carfentanil toxicity not resulting in death are reported; blood carfentanil concentrations were an order of magnitude lower than the present series (0.0133 and 0.0435 ng/mL). This microepidemic of carfentanil-related deaths lacked tight geographic clustering, suggesting the possibility of additional deaths not identified as carfentanil-related.
Conclusions: Carfentanil's arrival to the Midwest has been heralded by multiple deaths. Local collaboration by the county

Table 1: Carfentanil Deaths – Case Details

Case	History	Geographic location	Temporal spacing	Blood carfentanil concentration	Other quantitated substances (blood)
31yo male	Heroin abuse	Metro county A	Index case	0.13 ng/mL	Ethanol 0.226 g/dL
33yo male	Heroin, fentanyl abuse	Metro county A	Index + 5 days	0.64 ng/mL	Ethanol 0.177 g/dL
42yo female	Recent overdose with naloxone reversal	County outside of metro area	Index + 15 days	0.27 ng/mL	Ethanol 0.02 g/dL
					Methamphetamine 0.02 mg/L
					Morphine 0.03 mg/L
					Alprazolam 15 ng/mL
34yo female	Heroin abuse	Metro county A	Index + 17 days	0.44 ng/mL	Methamphetamine 0.18 mg/L
					Benzolecgonine 0.15 mg/L
					Morphine 0.06 mg/L
					Clonazepam 2.7 ng/mL
					7-amino-clonazepam 160 ng/mL
23yo female	Heroin abuse	Metro county B	Index + 18 days	0.14 ng/mL	Ethanol 0.023 g/dL
					Urine 6-monoacetyl morphine 0.006 mg/L

medical examiners and sheriffs, forensic toxicologists, medical toxicologists, state health department, and regional Poison Center established a clinical diagnosis and identified the culprit agent and presented a unified message to the public.

KEYWORDS Carfentanil; adulterant; opioid

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248. Heroin overdoses? No such thing

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Background: As the opioid epidemic continues to burn, novel adulterants continue to appear. Over the course of time, the notion of a binary distinction between "heroin overdose" and "prescription opioid overdose" has blurred, with adulteration and clandestine manufacture of heroin and illicit pills emerging as the new normal across the United States.
Report: In early November 2016, the Violent Offender Task Force of a midwestern county sheriff's office seized three containers with a combined total of approximately 3L (100 ounces) of a clear liquid suspected to contain an unknown concentration of fentanyl (image provided at time of poster presentation). Also seized were handguns, shotguns, tactical rifles, large amounts of US currency, prescription pills, and 25.15 g of powdered fentanyl (image provided at time of poster presentation). Neither the Sheriff's Office nor local Bureau of Criminal Apprehension offices possessed the capability to evaluate the fentanyl concentration of the confiscated liquid, and thus the regional Poison Control System (Poison Control) was contacted. Poison Control, in collaboration with the the chemistry and toxicology laboratory of a local county hospital, facilitated transfer of the three containers to the hospital's toxicology laboratory. The three vessels were found to contain between 136 and 150mcg/mL of fentanyl, or roughly 424,000 μg of fentanyl in solution without other significant constituents on mass spectrometry.
Discussion: Local seizure of clandestinely manufactured liquid fentanyl is a new wrinkle to the opioid epidemic. Microepidemics of morbidity and mortality attributed to heroin adulteration points to the new reality in which we now practice medical toxicology and emergency medicine: we no longer treat "heroin overdoses"; we treat opioid overdoses. The persistence of high-potency opioids adulterating the nation's heroin supplies (as well as reports of fentanyl and its analogs masquerading as other illicit psychoactive chemicals) highlights this point and signals that it may be our "new normal". New and emerging psychoactive substances have changed our understanding of "pot," "molly," and "LSD." Fentanyl, fentanyl analogs, and novel opioids such as U-47700 now contort the new reality of heroin. We are now in an era where our patients are "undifferentiated opioid overdoses" regardless of the clinical history. The composition of "heroin" can no longer be presumed, and we must acknowledge this in our emergent cares of the heroin overdose patient.
Conclusions: This seizure highlights the new face of the opioid epidemic, which includes innumerable emerging substances with toxicokinetics that remain unclear to us. The recent suggestion that observation periods following the administration of naloxone may be safely foreshortened fails to account for the emerging threat of widespread heroin adulteration with ultra-potent and minimally characterized opioids. These images underscore our new reality: now is the time for a conservative approach to patients presenting after a "heroin overdose."

KEYWORDS Fentanyl; Clandestine manufacture; adulterant

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249. When the story runs: short-term impact of a single, sensational news broadcast about PEG 3350 toxicity on constipation concerns at a pediatric emergency department

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Background: On 14 February 2017, the Philadelphia ABC television news affiliate aired a single "investigative" story renewing concerns about alleged neuropsychiatric side effects from PEG 3350 (polyethylene glycol) laxative use by children. It pointed out that its prescription was "off-label" for children, it stated that it may contain the "same toxic chemicals as antifreeze," and it interviewed parents from a social media site purporting neuropsychiatric toxicity of the laxative. This project aimed to evaluate the short-term impact that story had within an academic pediatric emergency department (Peds ED) within the same city.
Methods: On February 28, 2 weeks after the news story, an electronic survey was sent to the attending physicians, pediatric emergency medicine fellows, and nurse practitioners regularly staffing a single, tertiary-care Peds ED (annual patient volume ~90,000) within the city in which the news story broadcast. Only a single email solicitation was sent, responses were gathered anonymously, and clinicians had one week to respond so that results would reflect their experiences only in the first 2–3 weeks of the news broadcast. Survey results were summarized. The study was deemed exempt from IRB committee review.
Results: Survey responses were received from 49/64 (77%) attending physicians, 19/37 (51%) nurse practitioners, and 3/12 (25%) fellows (overall response rate 63%). Among respondents, 65% of ED clinicians reported hearing medical colleagues question the safety of PEG 3350 use in children in response to the news broadcast, and 45% reported having cared for a family expressing new concerns about the relationship between PEG 3350 and autism, psychosis, or other neuropsychiatric toxicity. About 27% of ED clinicians reported caring for children with exacerbations of constipation after stopping their laxative use in response to the news story. About 17% of the ED clinicians admitted that the news story gave them new doubts about the appropriateness of PEG 3350 as a daily use laxative among children with constipation. Methodological limitations of these results include potential differences between those who responded to the survey and those who did not, and recall bias.
Conclusions: A single television news event can create considerable short-term medical concern within a community. That concern can create real impact on health care providers, parents and their children; it can lead to an increased use of emergency medical care services. Public news agencies bear responsibility in providing accurate medical information; care should be taken when making such news sensational. Clinical toxicologists may have a role in providing expert information or analysis for news reporters concerning medication-related adverse effects and toxicities. In this case, the regional poison control center responded to the news story through creation of an informational bulletin for health care providers related to PEG 3350 safety.

KEYWORDS PEG 3350; laxative; news broadcast

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250. Pseudohematochezia among infants associated with cefdinir use – a case series

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Background: The development of brick-red or "currant jelly" stools during infancy may elicit concerns of gastrointestinal bleeding among clinicians and parents. The differential diagnosis for hematochezia among infants taking antibiotics is broad and may include infectious enteritis, antibiotic-associated pseudomembranous colitis or intussusception. However, reddish discoloration of stool may not be the result of blood. We report a large case series of factitiously "bloody" stools associated with oral cefdinir administration.
Case reports: In the 3-month period from 1 January 2017, through 31 March 2017, the five authors encountered eight infants within the same tertiary-care children's hospital pediatric emergency department (ED) with dramatic-appearing red stools that were found to be guaiac-negative – each had been recently prescribed oral cefdinir. Photographs of soiled diapers from these infants demonstrate that the pseudohematochezia could easily be misidentified as bloody stool. The age range was 5–11 months. Five of the eight infants were referred to the ED, based on a provided history or visual inspection of "bloody stools", by a healthcare provider for acute evaluation of presumed lower gastrointestinal bleeding. Three had had stool studies sent to evaluate for potential infectious causes of hemorrhagic enteritis. Only one of the infants was noted to be taking a vitamin supplement with iron, but each of the infants was at least partially fed with iron-containing infant formula. None of the infants was further evaluated at the children's hospital for persistent red or bloody stools after cessation of the cefdinir.
Case discussion: Cefdinir is an oral cephalosporin with broad-spectrum antimicrobial activity that is frequently prescribed to children for bacterial infections such as acute otitis media. Cefdinir can combine with dietary iron to form a precipitate that may produce a red or maroon color to stool. This drug interaction is mentioned, but not highlighted, in at least one manufacturer's FDA prescribing information. An Ovid Medline search of the medical literature using ["cefdinir" AND "red OR stool OR stools"], and a Google internet search, did not find any case series larger than this reported collection. These cases are remarkable in that they were identified by a small group of physicians in a small amount of time; we are unable to estimate incidence rates.
Conclusions: Oral administration of cefdinir to infants fed iron-fortified infant formulas may develop red stools. Despite the popularity of cefdinir as an antibiotic for common pediatric infections, this stool discoloration phenomenon may be underappreciated by healthcare providers and parents. Teaching this benign side-effect to parents may alleviate fears and prevent unnecessary utilization of medical services. Health care providers are encouraged to test red stools for the presence of blood and to inquire about recent use of cefdinir.

KEYWORDS Cefdinir; stool discoloration; factitious GI bleeding

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251. National trends in the use of naloxone, 2011–2016

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Background: As the number of deaths from opioid overdose have grown over the last two decades, several states have passed laws expanding public distribution of naloxone. The objective of this study is to evaluate the trends and characteristics of the cases reported to US poison centers (PCs) where naloxone was being recommended or utilized as therapy with focus on the role of the PCs in making the initial decision on naloxone administration.
Methods: The National Poison Data System (NPDS) was queried for all closed, human records where naloxone as therapy was recommended or performed from 01/01/11 through 12/31/16. We identified and descriptively assessed the relevant demographic and clinical characteristics. Proportion of annual "not recommended but performed" (NRP) naloxone therapy reports among overall naloxone reports was evaluated. Yearly trends in overall and NRP naloxone therapy reports were analyzed using simple linear regression methods. The patterns in the rates of NRP naloxone calls per 1000 human exposure calls and 1000 intentional human exposure calls were also descriptively evaluated.
Results: There were a total of 137,076 calls where naloxone was recommended or performed as therapy from 2011 to 2016, with the number of calls increasing from 21,894 in 2011 to 26,816 in 2016, despite an overall drop in poison center calls. The proportion of NRP naloxone reports among overall naloxone calls demonstrated a significant increase from 2011 (72%) to 2016 (81.4%). Of calls where naloxone was recommended or performed as therapy, 82.7% were intentional exposures, 20.5% exhibited major effects, and 95.4% of cases were enroute to the hospital when the PC was called. In terms of the demographic characteristics of the patients, 52.8% were female, and the most frequent age groups were 30–39 years (18%) and 40–49 years (18%). The most frequent substances associated with the cases where naloxone was administered included benzodiazepines (27.4%), acetaminophen with hydrocodone (13.7%), heroin (9.8%), and oxycodone (8.6%). The rate of NRP naloxone reports per 1000 human exposures increased from 2011 (6.7) to 2016 (10.1). Similarly, the annual trends in the NRP calls per 1000 intentional exposure calls also increased during the same time period (42.8–55.8). Regression analysis demonstrated the number of overall and NRP naloxone calls to the US PCs increased at a rate of 879 (95% CI: 334.3, 1124.2; $p < .001$) and 1,109 (95% CI: 708.7, 1509.8; $p < .001$) more calls per year, respectively.
Conclusions: Analysis of calls to US PCs from 2011 to 2016 indicated an increasing trend of naloxone use as therapy without recommendations from the PCs. More efforts should be devoted to analyze NRP naloxone therapy outcomes to help determine the overall safety and efficacy of this intervention and the role of poison centers in recommending naloxone as therapy.

KEYWORDS Epidemiology; naloxone; poison centers

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252. National trends and characteristics of buprenorphine exposures reported to US poison centers, 2011–2016

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Background: The use of buprenorphine has increased dramatically in the last 10 years with the ambulatory treatment visits for the drug increasing from 0.2 million visits in 2003 to 2.1 million visits in 2013. The extent of misuse and abuse of buprenorphine has not been clearly delineated. In the present study, we investigated the trends and characteristics of buprenorphine exposures reported to the U.S Poison Centers (PCs).
Methods: We retrospectively queried the National Poison Data System (NPDS) for all closed, human exposures to buprenorphine from 1/1/2011 to 12/31/2016, as specified by the AAPCC generic code 0200625. Buprenorphine exposure reports were categorized by year to evaluate the annual trends. We also assessed the distributions of several key characteristics of the exposures, including demographic characteristics, reason of exposure, clinical effects, medical outcomes, and therapies. We generated descriptive statistics after having segmented the relevant characteristics of exposures into appropriate categories. Rates of buprenorphine calls per 1000 human exposure calls (HE) nationally were calculated and compared with the rates observed at the regional level, which were identified using the Toxicall™ database for the same criteria.
Results: Nationally, the number of buprenorphine exposure calls reported to the PCs, increased from 3651 calls in 2011 to 3785 calls in 2016, at an annual percentage change (APC) of 0.7%. The number of calls demonstrated a decline from 2011 to 2013 with a significant increase thereafter. Intentional and unintentional exposures accounted for 47.1% and 43.4% of calls, respectively. The proportion of unintentional exposure calls was higher than intentional exposures calls from 2011 to 2013, but this trend reversed from 2014 to 2016. Single exposures accounted for 62.1% of the calls with benzodiazepines, ethanol, and acetaminophen (alone and in combination) being the highly prevalent co-occurring substances. The most frequent age groups included children $<= 5$ years (29.3%), followed by ages 20–29 years (22.6%) and 30–39 years (16.4%). Males comprised 53.4% of the cases. The exposure site was predominantly residence (87.9%) while the route of exposure was majorly ingestion (86.5%). Among the cases, 20.7% were admitted to the critical care unit. Major clinical effects were demonstrated in 19.2% of exposures and minor in 40.4%. Deaths (0.3%) associated with buprenorphine were rare. The most frequent clinical effects reported included drowsiness/lethargy (40.8%), vomiting (16.0%), and tachycardia (11.0%). Naloxone was reported in 19.4% of cases, while intubation and ventilation were reported in 3.9% and 3.6% of the cases, respectively. Nationally, the rates of buprenorphine per 1000 HE increased from 1.6 to 1.8, and were significantly lower than the rates at the regional level (2.2–3.6)
Conclusions: This study reflected an increase in the reported calls for buprenorphine exposures affecting small children. This increase parallels the increase in the number of buprenorphine prescription. Several key characteristics were identified that were associated with buprenorphine exposures as reported to the PCs that are important to evaluate to develop proper and safe buprenorphine prescription guidelines.

KEYWORDS Buprenorphine; epidemiology; national trends

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253. Poison center utilization: trends in reported National Poison Data System (NPDS) exposures (2009–2015)

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Background: Decreases have been observed in reported exposures to poison centers, with overall call volume decreasing 13.6% for pharmaceuticals and 16.1% for non-pharmaceuticals from 2009 to 2015. The purpose of this analysis is to explore trends in poison center utilization.
Methods: Data for single exposures in children (≤5 years) and adults (≥20 years) were extracted from the 2009 to 2015 Annual Reports of the American Association of Poison Control Centers' National Poison Data System (NPDS). Poisson regression was used to estimate and compare the percent decreases over the given year period for all products for pharmaceuticals and non-pharmaceuticals within age groups. Changes in the most frequently reported substances are described.
Results: Pharmaceutical exposures decreased 24.8% in children ($p<.001$) and only 1.01% in adults ($p=.720$; Figure). Non-pharmaceutical exposures decreased 18.8% in children ($p<.001$), and 10.2% in adults ($p<.001$; Figure). Given that exposures in children were decreasing at a higher magnitude, trends in this population were further explored. Among the generic codes with the highest frequency of exposures, the largest increase was observed in melatonin (394.2%). The largest decreases were in diaper care and rash products (43.6%), pediatric acetaminophen alone (33.2%), and calcium salts (32.6%), all of which decreased at a much higher rate than the decrease in utilization for pediatric products.
Conclusions: Poison center utilization is an important consideration in interpreting exposure trends. Adult pharmaceutical exposures have not changed significantly hence poison center utilization is not likely associated with observations made with these products. Despite a decrease in pediatric poison center utilization, significant increases in specific products may indicate potential safety concerns worth further study.

KEYWORDS Poison center utilization; NPDS data trends; poison center data

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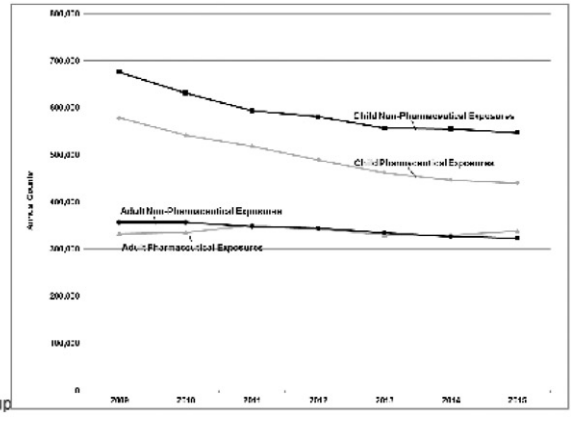

Figure. Annual Pharmaceutical and Non-Pharmaceutical Exposures by Age

254. Trends in pralidoxime chloride availability: preparedness, efficiency, complacency, and obsolescence

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Background: Our poison center has monitored antidote stocks maintained in acute health care facilities (HCFs) since 1990. Pralidoxime Chloride (2-PAM) stocking increased between 1990 and 1999, arguably related to terrorist events in Japan, as well as local organophosphate insecticide (OP) exposures. "Expert Consensus Guidelines for Stocking of Antidotes in Hospitals That Provide Emergency Care" published in 2009 recommended stocking of 2-PAM as one of 24 antidotes. Given the competing influences of marked decrease in OP use, the introduction of the CHEMPACK program, drug and delivery mechanism out-dates, we reviewed 2-PAM stocking over the past 17 years to determine state-wide inventories. Are we prepared to treat local or larger terrorist events related to OP or nerve-agent exposures?
Methods: Antidote surveys were emailed, faxed, and/or mailed to 31 acute health care facility pharmacy directors every 1–2 years from 1990 through 2016. A 17 year retrospective analysis was performed to examine the trend in pharmacy stocking of 2-PAM.
Results: Between 2000 and 2016, insufficient stocking to treat one patient for 24 h, ranged from 70% of responding HCFs in 2000 to 89% in 2016. Overall, 75% of acute HCFs decreased inventories of 2-PAM during the past 17 years, especially in the last 4 years. Three hospitals had 1–2 year spikes in stocking. This followed an acute OP poisoning in two of these hospitals. Nineteen of 31 acute HCFs in this state store CHEMPACK containers. Of five major healthcare networks in the state, one network has two HCFs with sufficient 2-PAM to treat one patient for 24 h. A second network has one HCF with adequate stock.
Conclusions: We documented decreasing and insufficient stocking of 2-PAM in our state over the past 17 years. Multiple factors may be responsible including general drug shortages, lack of utilization, and resulting complacency. Temporary spikes in stocking occurred immediately following local OP events; however, these were followed by sustained decreases. CHEMPACKS are inappropriate for use following small-scale OP exposures. More than half of the HCFs in state store CHEMPACK 2-PAM with FDA-extended expiration dates. A formal sharing plan between HCF networks to maintain sufficient stocking of 2-PAM is advisable, given the continuance of global and domestic terrorist events, some using nerve-agents and organophosphates.

KEYWORDS Pralidoxime chloride; antidote stocking; preparedness

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255. Validation of decision rule for sending pediatric clonidine exposures to a health care facility

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Background: Previous studies evaluating pediatric clonidine exposures have been sited in Micromedex to support recommendations for direct medical evaluation of children. The main study cited (Spiller et al., J Pediatr. 2005;146:263–266) described

exposure of 113 patients up to 12 years old with the dose ingested reported for 80%. The current study was undertaken with a larger population to validate these recommendations, e.g, referral of children < 4 y/o with >0.1 mg ingestion, or children >4–8 y/o with >0.2 mg ingestion.
Methods: All clonidine ingestions (without co-ingestion) reported to a statewide poison center between 2000 and 2016 in patients < 8 years of age were evaluated. Medical outcomes, clinical effects, age, and reported dose was extracted.
Results: Of the 2567 cases evaluated, 1114 had an estimated dose reported. In the age category 0–4 years old with ≤0.1 mg ingestion reported ($n = 44$), none developed respiratory depression, hypotension, or coma. In the 4–8 y/o with dose ≤0.2 mg category ($N = 67$), one patient developed respiratory depression. In the category 0–4 y/o with >0.1 mg ingestion, 43/772 developed respiratory depression, hypotension, or coma. For the category 4–8 y/o with >0.2 mg reported exposure 6/231 developed respiratory depression, hypotension, or coma.
Discussion: Although estimates of pediatric exposure amounts may be misleading they may provide a starting point regarding need for referral to a health care facility.
Conclusions: The current study supports current recommendations for direct medical evaluation for children with clonidine exposure based on reported exposure amounts.

KEYWORDS Clonidine; pediatrics; triage

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256. Pharmacy-based prescription naloxone: the final step for a system-wide implementation

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Background: Prescription naloxone programs have become an important method of harm reduction for patients at risk for death from opioid-related overdose. Illinois state law requires that patients receive training on how and when to administer naloxone prior to receiving a prescription. In September 2015, Illinois passed PA99-0480, allowing trained pharmacists to counsel and prescribe naloxone for patients and/or their loved ones. This abstract describes the third phase of an initially emergency department (ED) based prescription naloxone program, to a pharmacy-based training structure.
Methods: A naloxone-working group began a prescribing program that included an Opioid Overdose Education and Naloxone Distribution (OEND) training as an outgrowth of a community-based program. Phase one of the program initiated prescribing from the ED, with physicians providing patient training. Phase two expanded the program to the inpatient unit with Screening, Brief Intervention, and Referral to Treatment (SBIRT) counselors providing training. The current and third phase involved training all pharmacists in the outpatient pharmacy to either train patients that presented with a naloxone prescription, or to both train and prescribe from the pharmacy.
Results: As a result of the three-step evolution of our prescription naloxone program, patients can receive a prescription initiated at any point in our health system. This includes prescriptions written from the ED, clinics and inpatient units. Further, patients and/or loved ones can present directly to the pharmacy to obtain both naloxone training and a prescription. Data collection regarding the impact of prescribing at the various sites in our system is ongoing.
Conclusions: We describe the progression of a prescription naloxone program from ED-only prescribing with a heavy workload for physicians, to a system-wide approach with an interdisciplinary team. We found that the time required to provide patient training was a barrier to physicians prescribing naloxone. We learned that dedicated SBIRT counselors were more effective at providing training, and physicians were more likely to prescribe if they were not responsible for providing training. In the final phase, with pharmacists able to both provide training and prescribe naloxone, we anticipate improved rates of prescribing from a larger number of clinical areas within our healthcare system. We will follow the trend of naloxone prescribing in an effort to improve availability of naloxone for appropriate patients and their loved ones.

KEYWORDS Naloxone; overdose prevention; harm reduction

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257. Snakebites: a 10 year review of Louisiana Poison Center data

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Background: While snakebite is uncommon they generate a disproportionate amount of anxiety, interest, and confusion from the person bitten to the physician managing what may well be the first snakebite they have ever treated. We sought to characterize cases of snakebite reported to the Louisiana Poison Center (LPC) during the years 2006–2015.
Methods: We conducted a retrospective review of LPC calls using National Poison Data System (NPDS) generic codes related to snakebites. Institutional Review Board approval was obtained. Individual case records were collected with the study authors then comparing the individual case notes with the data entered into our records database. After review, the data were entered into Excel and further analysis conducted.
Results: About 1902 snakebite cases were identified. There were 1311 males (68.9%) and 591 females (31.1%). The mean age was 34 years, with age extremes < 1 year and >90 years. Bite sites were located on feet, legs, hands, arms, torso and the head. Males were bitten more on the hands and arms, with females bitten more on the foot or leg. 87.3% of patients were managed in a healthcare facility. LPC specialists in poison information are trained to refer all snakebite patients to an emergency department (ED) for evaluation. About 43.4% of patients received antivenom. When analyzed over the time frame of the study the percent of patients treated with antivenom has increased. About 5.3% of patients had no effect, 56.9% had minor effect, 28.8% had moderate effect and 0.76 had a major effect. There were no deaths reported during the study period. LPC specialists in poison information are trained to refer all snakebite patients to an emergency department (ED) for evaluation. Where case notes indicated a positive identification was likely copperheads made up the greatest percentage of bites, followed by water moccasins (cotton mouth) and rattlesnakes. There were 24 coral snake bites reported during the study period. Snakebites reported to the LPC exhibit a bi-modal distribution with peaks in May and September of each year. Most bites occurred on Saturday and Sunday with the fewest bites occurring on Wednesday. For every day of the week, the majority of bites occurred between 1800 and 2200. While no

longer recommended and often found to be detrimental cases of cut and suck and electric shock therapy were noted in this study.
Conclusions: While the number of deaths caused by snakebite is very small considerable effort and dollars are expended in response to being bitten by a snake. The number of snakebites reported to the LPC remains fairly constant from year to year. The copperhead snake is responsible for the majority of snakebites reported in Louisiana. This study is limited by its retrospective design and reliance on poison center charts, which may have incomplete reporting of data.

KEYWORDS Snakebite; antivenom; Louisiana

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258. Evaluation of pharmacists' knowledge in role of naloxone dispensing

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Introduction: The opioid epidemic presents a rising public health crisis in the United States. Many states, including New Jersey have implemented Good Samaritan Laws allowing naloxone to be available via standing order in an effort to respond to the crisis. Pharmacists have been called by the National Association of Boards of Pharmacy to promote and expand access to the opioid overdose reversal medication naloxone. Under the Overdose Prevention Act, signed into law in May 2013, pharmacists in New Jersey are able to provide naloxone without a prescription through a standing order. This allows friends, family, and concerned citizens to legally obtain naloxone without a prescription from their provider. However, it is unclear if pharmacists are aware of this new legislation and are being proactive in this new role.
Objectives: The objective of this study was to determine the baseline knowledge of pharmacists in their role of dispensing Naloxone. Secondary outcomes were to determine if naloxone was stocked in the pharmacies, and how often it was being dispensed.
Methods: This was a cross-sectional, IRB approved study of pharmacies in Camden County. An anonymous survey was conducted to pharmacists in either chain or independent pharmacies to assess pharmacists' knowledge of the standing order. Data included pharmacists' knowledge of the standing order, formulations carried by pharmacies, and how often naloxone in any formulation were dispensed. Of the 118 pharmacies in Camden County, 114 pharmacies were surveyed and 98 were included in the study. One pharmacist from each pharmacy completed the survey.
Results: Of the 98 included, 64(65%) pharmacists reported awareness and understanding of the legislation. Thirty-four (36%) were unaware of said legislation. Only 50 (51%) of those included had naloxone in stock and seven (8%) of pharmacies had dispensed it within the previous month. The formulations of naloxone carried are reported in Table 1. Some pharmacies reported carrying more than one formulation of naloxone.
Discussion: Despite proactive legislation allowing for open dispensing of a potentially life-saving antidote, only two-thirds of pharmacists in Camden County were aware of its existence. Additionally, only one-half carried the antidote on site. Based on these findings, more education is necessary to increase naloxone dispensing and availability.

KEYWORDS Naloxone; pharmacy; legislation

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Naloxone Formulations in Stock	
Pre-filled syringe	12
Narcan Nasal Spray	27
Naloxone Solution for Injection	15
Evzio Autoinjector	18
Do not Carry	48

259. Epidemiology of opioid-related visits to US emergency departments between 1999 and 2013: a retrospective study from the National Hospital Ambulatory Medical Care Survey

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Introduction: Prescription and non-prescription abuse has reached epidemic proportions in the the United States. The Emergency Department (ED) plays a key role in the treatment of patients with opioid-use disorders and related complications. While the worsening opioid epidemic has been widely recognized, its direct impact on the ED has not been well described.
Objectives: To characterize the epidemiology of opioid-related visits to United States Emergency Departments and describe trends in opioid-related visits over time.
Design: A retrospective cohort study using the National Hospital Ambulatory Care Survey (NHAMCS) database. We utilized ICD-9 codes to identify ED visits related to opioid use and abuse. We then applied visit weights calculated by NHAMCS to generate nationwide estimates regarding the overall prevalence of opioid-related visits, along with demographic characteristics of these patients. We also report trends with respect to opioid-related visits and associated ED resource utilization between 1999 and 2013.
Results: About 1072 visits met inclusion criteria, representing 2,731,000 nation-wide opioid-related ED encounters between 1999 and 2013. During this time, opioid-related ED visits steadily increased, with over 300,000 visits in 2013. As compared with 1999–2001, by 2011–2013 opioid-related visits had increased by 170%. Substantial increases occurred across nearly all demographic groups, and throughout all regions of the US (Table 1). Over the same period opioid-related ED visits resulting in hospital admission increased by over 240%. Men account for the majority of opioid-related ED visits. However, visits among women increased by 250% over the study period. Additionally, visits by those aged 18–34 years increased by over 250% over the study period. Additionally, the use of pre-hospital and ED resources for opioid-related visits increased over the course of the study period. (Figure 2) By 2011–2013, approximately one-third of opioid-related ED visits arrived via EMS services. Imaging studies were

Table 1: Comparison of patient and hospital characteristics for opioid-related visits from 1999-2001 and 2011-2013.

Patient/hospital characteristics	1999-2001 Weighted N, (%)	95% CI	2011-2013 Weighted N, (%)	95% CI	Change
Total	358,000 (100%)	273,000-443,000	966,000 (100%)	783,000-1,150,000	+170%
Sex					
Male	237,000 (66%)	157,000-318,000	552,000 (57%)	422,000-682,000	+133%
Female	121,000 (34%)	79,000-163,000	424,000 (43%)	292,000-537,000	+250%
Age					
<18	15,000[a] (4%)	0-34,000	14,000[a] (1%)	10,000-76,000	-6%
18-34	145,000 (40%)	83,00-206,000	516,000 (53%)	382,000-651,000	+256%
35-64	196,000 (55%)	134,000-257,000	393,000 (41%)	290,000-496,000	+101%
≥64	3,000[a] (1%)	0-8000	43,000[a] (4%)	10,000-76,000	+1333%
Race					
White	302,000 (84%)	214,000 391,000	873,000 (90%)	688,000 1,057,000	+189%
Other	56,000 (16%)	30,000-81,000	94,000 (10%)	46,000-141,000	+68%
Payment source					
Medicare	28,000[a] (9%)	6,000-50,000	88,000[a] (11%)	39,000-136,000	+214%
Medicaid	91,000 (29%)	53,000 129,000	275,000 (33%)	168,000 383,000	+202%
Private Insurance	61,000[a] (20%)	18,000-104,000	273,000 (33%)	182,000-363,000	+348%
Self	130,000 (42%)	66,000-194,000	187,000 (23%)	120,000-255,000	+44%
Region					
Northeast	104,000 (29%)	62,000-146,000	294,000 (30%)	162,000-425,000	+183%
South	69,000[a] (19%)	28,000-110,000	227,000 (24%)	150,000-298,000	+234%
Midwest	74,000[a] (21%)	43,000-104,000	211,000 (22%)	151,000-272,000	+185%
West	112,000 (31%)	60,000-165,000	234,000 (24%)	144,000-324,0000	+109%

[a] Estimates are based on fewer than 30 cases, and may not be reliable

Table 2: Pre-hospital and ED resource utilization during opioid-related ED visits.

Visit characteristics	1999-2001 Weighted N, (%)	95% CI	2011-2013 Weighted N, (%)	95% CI	Change
Arrived by EMS	56,000[a] (16%)	21,000-91,000	326,000 (34%)	228,000-424,000	+482%
EKG	56,000[a] (16%)	26,000-86,000	309,000 (32%)	217,000-402,000	+452%
CT Scan	4000[a] (2%)	0-12,000	130,000[a] (14%)	70,000-206,000	+3150%
Toxicology screen			357,000 (37%)	250,000-464,000	
Hospital Admission	65,000 (18%)	39,000-90,000	222,000 (23%)	138,000-305,000	+242%

[a] Estimates are based on fewer than 30 cases, and therefore may not be reliable

obtained in approximately 29% (95%, CI 22–36%) of patients included in the 2011–2013 period, including 14% (95%, CI 8–21) who had computed tomography (CT) imaging. The mean ED length of stay for opioid-related visits between 2011 and 2013 was 257 min (95%, CI 228–287), with a median of 193 min (IQR 163 min). From 2011 to 2013, not including medications administered prior to ED arrival, naloxone was administered in 13% (95% CI 8–19%) of included visits. Hospital admissions increased by nearly 250% over the study period, from approximately 65,000 admissions between 1999 and 2001 to approximately 222,000 between 2011 and 2013.

Conclusions: Opioid-related ED encounters rose dramatically between 1999 and 2013, with consistent increases across a broad spectrum of demographic groups. Resource utilization due to opioid-related ED visits also increased consistently throughout the study period.

KEYWORDS Opioid; epidemic; national

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260. A toddler, methadone and mom's naloxone

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Background: The opioid epidemic is a medical and public health crisis. Naloxone prescriptions are an important tool in reducing harm and saving lives in the event of an opioid overdose. Naloxone is often delivered by non-medical personnel. We present a case of a toddler receiving intranasal naloxone, administered by her mother, after an unintentional overdose of methadone.

Case report: A healthy 22-month-old female presented to the emergency department (ED) after an unintentional ingestion of liquid methadone. While getting ready for the day, the patient's mother left out her methadone. The patient drank an unknown volume of it. When the patient became drowsy, the regional Poison Control Center (PCC) was called. The PCC recommended calling 911. Prior to calling 911, the patient became somnolent with respiratory depression and cyanosis. Her mother delivered 4mg of intranasal naloxone (a prescription that she had at home) to her daughter. When paramedics arrived, the patient was alert, awake, well appearing and with a normal physical exam. On presentation to the ED, the patient's exam was stable. She was placed on end-tidal CO2 monitoring. Electrocardiogram was within normal limits. Urine toxicology tested positive for methadone. During a period of observation in the emergency department, she had recurrence of respiratory depression and required additional boluses of naloxone followed by a naloxone infusion. She was transferred to a pediatric ICU. The remainder of her hospital course was uneventful.

Case discussion: The opioid epidemic is well discussed in medical literature and the media. Given the prevalence of opioid and prescription methadone use, children are at risk of unintentional overdose. Prescriptions of naloxone and training of how to deliver the medication to others has the potential to reduce harm and

save the lives of those using opioids and others who may unintentionally overdose.
Conclusions: Naloxone prescription and training should be provided to those who use opioids. This can save lives, such as this case where a toddler survived an unintentional overdose. As standard practice, it has the potential to have a significant impact on public health.

KEYWORDS Naloxone; methadone; public health

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261. Prevalence of acute liver injury associated with exposure to acetaminophen-opioid combination products reported to the National Poison Data System pre- and post-reformulation

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Background: Acetaminophen overdose is the most common cause of acute liver failure in the United States. In January 2011, the US Food and Drug Administration (FDA) issued a safety announcement requesting that manufacturers limit the amount of acetaminophen in prescription combination drug products to 325 mg per tablet or capsule. This action was intended to reduce the risk of acute liver injury (ALI) and allergic reactions associated with acetaminophen. It is currently unknown whether the dose reduction of acetaminophen to 325 mg in these prescription combination products resulted in the intended decrease in the risk of ALI. Therefore, the purpose of this study was to determine the prevalence of ALI among patients exposed to acetaminophen-opioid combination products reported to the National Poison Data System (NPDS) before and after 2011.
Methods: All reported exposures to a single acetaminophen-opioid combination product from 2006 to 2016 were extracted from NPDS. Patient demographic information, outcome, and exposures with elevated serum creatinine, prolonged prothrombin time (PT), and aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >1000 were collected. ALI was defined as AST or ALT >1000. Descriptive statistics were performed.
Results: From 2006 to 2016 the median age of patients exposed to a single acetaminophen-opioid combination product was 25 years (interquartile range, 12–44 years) and 55% were female. The total number of reported exposures to these combination products rose from 775 in 2006 to a maximum of 1000 in 2009 and then fell to a minimum of 538 in 2016 (Figure 1). The rate of ALI per 1000 exposures rose from 6.45 in 2006 to a maximum of 26.4 in 2013 (Figure 2). Similarly, the rates of serum creatinine elevation, PT prolongation, and death per 1000 exposures rose from 5.16, 2.58, and 0, respectively, to maximums in 2013 of 10.87, 13.98, and 4.66, respectively (Figure 3). In 2016, while the total number of exposures fell, the rates of ALI, serum creatinine elevation, PT prolongation, and death per 1000 exposures remained relatively stable in 2016 at 20.45, 7.43, 7.43, and 3.72, respectively (Figures 2 and 3).
Conclusions: Our data suggest that although the total number of exposures to acetaminophen-opioid combination products seems to have decreased following the issuance of the FDA safety announcement in 2011, the rates of ALI, serum creatinine elevation, PT prolongation, and death per 1000 exposures appear to have increased. Therefore, clinicians should be aware that despite a reduction in the amount of acetaminophen in prescription acetaminophen–opioid combination products, the rate of ALI appears to not have decreased as intended.

KEYWORDS Acetaminophen; acute liver injury; combination product

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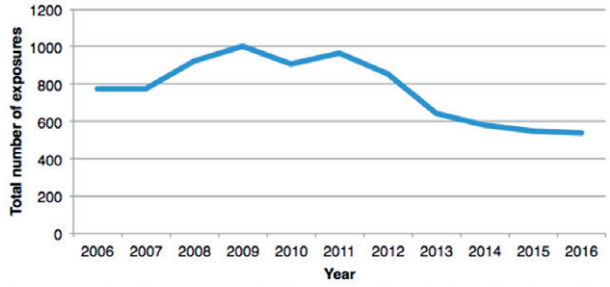

Figure 1. Number of exposures to a single acetaminophen-opioid combination product reported to the National Poison Data System from 2006-2016

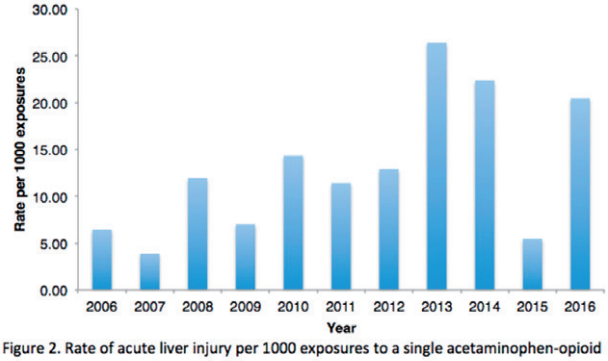

Figure 2. Rate of acute liver injury per 1000 exposures to a single acetaminophen-opioid combination product from 2006-2016

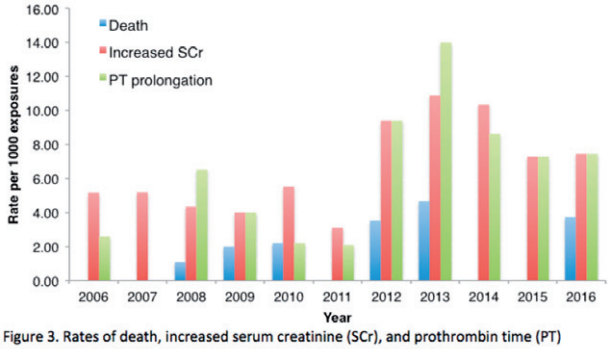

Figure 3. Rates of death, increased serum creatinine (SCr), and prothrombin time (PT) prolongation per 1000 exposures to a single acetaminophen-opioid combination product from 2006-2016

262. Citation status and frequency in a toxicology journal

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Objective: To determine factors associated with an item's citation status and citation frequency in a medical toxicology journal.
Design: We reviewed the Web of Science (WoS) index of manuscripts (items) published in a single journal. Included items were between 3 and 10 years post-publication and were analyzed by item type, number of authors, keywords, and pages, and whether funded. Item citation status and citation frequency were determined counting accumulative citations since publication. Included item types were Articles (original and poison center research, short communications), AAPCC Annual Reports, Biographies, Case Reports, Case Series, Editorials, Letters to the Editor, and Systematic Reviews.
Results: There were 1261 included, referenceable items published during the study period, 2006–2013. Biographies were least likely to be cited and had the lowest average number of citations, followed by letters to the editor (LTE), case reports in LTE format, editorials, single case reports, articles, case series, systematic reviews and American Association of Poison Control Centers annual reports (AAPCC; Table). Items without a reported funding source ($N = 1072$) were less likely to be cited (82% versus 96%; OR 5.0622; 95%CI 2.4521–10.4506; $p < .001$) and to have fewer citations than those with funding (8.2 versus 11.6; $p = .0156$). The number of author keywords and manuscript pages (excluding the AAPCC Annual Report) were not associated with likelihood of citation. As an incidental finding, a highly cited item was discovered to have been omitted from indexing in the Web of Science database.
Conclusions: In our journal, uncited manuscripts are more likely to be biographies, letters, case reports in LTE format, and editorials, with the most cited items being the AAPCC annual report, followed by systematic reviews, case series, and original research articles. In addition to the type of manuscript, certain demographic features are associated with the likelihood and number of citations, which have implications for the journal's article mix and Impact Factor. Periodic surveillance of the Web of Science may reveal errors in item indexing.

KEYWORDS Toxicology journal; citations; article type

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	All Items (N = 1261)	AAPCC (N = 7)	Reviews (N = 86)	Case Series (N = 56)	Articles (N = 562)	Full Case Report (N = 210)	Editorials (N = 90)	LTE Case Report (N = 171)	LTE (N = 66)	Biographies (N = 3)
Cited %	82	100	98	94	93	93	72	58	52	0
Uncited %	18	0	2	6	7	7	28	42	48	100
Ave. No. of Citations	9	172	24	11	9	7	3	2	2	0

Citation status and citations per item type, 2006 – 2013; AAPCC = Annual report of the American Association of Poison Control Centers; LTE = Letter to the Editor

263. Exposures to liquid laundry detergent pods among young children in Italy following the introduction of new EU safety rules

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Objectives: In Italy, liquid laundry detergents pods (LLDPs) were launched in August 2010. Immediately after, the National Poison Control Centre in Milan (PCCMi) documented an increased number of incidents involving young children [1]. On that basis, different preventive actions had been voluntary undertaken by industry in three subsequent steps: precautionary statements on outer packaging (from January 2011); child-resistant closures (from February 2012); obscure boxes (from August 2012). Four months after the last measure implementation (December 2012), a 50% reduction of frequency of cases aged <5 years was observed, strongly suggesting that reducing LLDPs visibility was the most effective action. In June 2015, the safety measures on boxes, i.e., labeling, closure, and opacity, adopted in Italy in previous years became compulsory in Europe (Regulation (EC) No 1297/2014). In addition, soluble packaging was required to contain an aversive agent, improve its ability to retain liquid content in water and resistance to mechanical compressive strength. The present study is aimed to evaluate effectiveness of these new rules in Italy.
Methods: Series of cases aged <5 years exposed to laundry detergents (LDs) between 1 January 2013 and 31 December 2016 and referred to PCCMi. Frequency of exposure was estimated as mean daily number of cases/month for both LLDPs and taditional laundry detergents (TLDs) exposures. The quantity of LLDP sold by month, as provided by industry, was used to calculate number of cases exposed to LLDPs/millions units sold/month by year. Changes in exposure rates were identified using Taylor change-point analysis. A change was considered significant when the level of confidence (CL) was 95% or higher. Logistic regression models were used to estimate the strength of the association between exposure to LDs and poisoning, adjusting by age and exposure period.
Results: Among the identified cases (*n* 1853), 819 (44%) were exposed to LLDPs and 872 (47%) to TLDs. The detergent form was unknown for 162 (9%) cases. The odds of suffering at least one sign/symptom following exposure to LDs was 10 times higher for exposures to LLDPs in comparison to TLDs. During the observation period, no changes of frequency of TLDs exposure were observed (estimated average: 0.71 cases/d), while the mean daily number of cases exposed to LLDPs/month underwent a change in October 2013, from 0.78 to 0.61 cases/d (98% CL: August 2013–June 2014), and August 2015, from 0.61 cases/d to 0.42 cases day (100% CL: April–November 2015). Adjusting the frequency of LLDP exposures by quantity sold, confirmed that a change occurred between April and November 2015 (100% CL),

but the change point was postponed to September 2015. The exposure rates lowered from 0.88 cases/million units sold (pre-change point period), to 0.56 cases/million units sold (post-change point period).
Conclusions: The observations here presented suggest that safety improvements of the LLDCs water soluble membrane are associated with a further 35% reduction of exposure rates. However, exposure to LLDPs remains more hazardous than TLDs, indicating that further efforts are needed to reduce LLDPs intrinsic toxicity and their attractiveness to children.

KEYWORDS Liquid laundry detergent pods; poisoning; prevention

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Reference

[1] Settimi L, Giordano F, Lauria L, et al. Surveillance of paediatric exposures to liquid laundry detergent pods in Italy. Inj Prev. 2017[Feb 10];[17]. [Epub ahead of print]. doi: 10.1136/injuryprev-2016-042263.

264. Phenytoin-induced DRESS syndrome leading to flecainide toxicity

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Background: Phenytoin has been associated with Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, which involves a rash, eosinophilia, lymphadenopathy and solid organ injury. Accumulation of the arene oxide metabolite is thought to be involved. Flecainide is a class 1c antiarrhythmic with sodium channel blockade properties that can accumulate in patients with renal dysfunction. We present a patient who developed DRESS syndrome associated with phenytoin, whose course was complicated by flecainide toxicity, likely secondary to decreased renal clearance.
Case report: A 59-year-old female with a history of atrial fibrillation on flecainide, and a seizure disorder secondary to a prior stroke, presented as a transfer from an outside hospital for a diffuse body rash and renal injury. She had been on phenytoin, levitiracetam, and lacosamide for antiepileptic maintenance, but 2 weeks prior to presentation, she had developed a diffuse rash. The phenytoin was discontinued and she was placed on steroids. Despite cessation, the rash continued to worsen. Her erythematous rash had spread to her torso, face, and extremities with perioral ulceration. She was bradycardic with a bizarre irregular wide complex rhythm (QRS duration 240 ms, QTc interval 585 ms) and hypotensive. She was started on an epinephrine drip and given empiric cefepime due to pyuria on urinalysis. Her initial WBC was 17.9×10^9/L with an eosinophilia of 19%, creatinine was 3.420, ALT 916, AST 954, and INR 7.90. 100 mEq of sodium bicarbonate was given, narrowing of her QRS to 200 ms and improving her heart rate. The patient was placed on a bicarbonate drip at 150 mL/h and her QRS narrowed to 148 ms after 24 h. Skin biopsy suggested an exuberant drug eruption or SJS/TEN. She was treated with etanercept and a high dose steroid taper. Her flecainide level was 0.79 mcg/mL. She had improvement in her rash and renal function, and was discharged after eight hospital days.
Discussion: The patient exhibited DRESS syndrome based on cutaneous findings, multi-organ involvement, eosinophila, and latent exposure to phenytoin. While biopsy results could also suggest SJS/TEN, neither would account for the patient's transaminitis or bradydysrhythmia in the absence of myocardial involvement. Decreased renal clearance likely led to sodium channel blockade from flecainide and the patient's significant bradyarrhythmia. She had improvement with sodium bicarbonate therapy and no signs of myocardial injury from her multi-organ system failure.
Conclusions: While both DRESS and flecainide toxicity have been observed, this is a unique case where both co-exist and with her organ failure leading to significant flecainide toxicity.

KEYWORDS DRESS; flecainide toxicity; arrhythmia

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265. Opioid epidemic – heroin versus other opioid exposures reported to the National Poison Center Network; an NPDS Analysis: the heroin disaster – far surpassing the opioid epidemic

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Background: The rapid increase in the use and abuse of prescription and illicit opioids in the US over the past 15 years has been termed the opioid epidemic. The DEA reports, "overdose deaths, particularly from prescription drugs and heroin, have reached epidemic levels." The latest data from The Centers for Disease Control and Prevention report heroin use in the United States increased 63% from 2002 through 2013. To objectively characterize this premise using US poison center data, we examined heroin and opioid analgesic exposures reported to the National Poison Data System (NPDS).
Methods: NPDS classifies drugs using a hierarchical, structured categorical system of generic codes. We examined human exposures reported to NPDS by generic code (GC) category for all analgesics (64 GCs), opioids (23/64 GCs), opioid combination products (10/64 GCs) and heroin (1 GC) nationally, by year and by day for 1 January 2000–31 March 2017. Descriptive statistics, graphical displays, smoothing spline fits, linear and non-linear regression, were performed using SAS JMP version 12.0.1 (SAS Inc., Cary, NC). To compare recent increases, we examined linear regressions of annual exposures by GC for 2011–2016. We described morbidity using the Morbidity Index (MI) where MI = more serious (medical outcome = death, major, or moderate) × 1000/total exposures for 2011–2016 for each GC of interest.
Results: Figure 1 shows heroin exposures reported to NPDS between 1 January 2010 and 31 March 2017. Through 2015 exposures/month increased at a rate of ~53/month, but from 2016 through March 2017 the rate increased to ~450 exposures/month. The table shows the slope of 2011–2016 heroin exposures and 95% confidence interval (870 [503, 1237] exposures/year). The top 20 GCs shown in the table included 99.7% of the exposures reported for all 34 GCs (opioids and heroin) examined. Only three of the other GCs showed increases (20–41 exposures/year) while exposures to the other 16 GCs have actually decreased over the last 6 years. Figure 2 displays the MI [95% CI] rankings for the largest 12 GCs (93.8% of all 33 GCs) with heroin at 504 [497, 513]. The next highest MI is 392 [378, 406] for fentanyl. As summarized in Figure 2, all other MIs are considerably lower, with the lowest, codeine MI of 24.5 [21.3, 28.1].
Conclusions: The increase (and increasing rate of increase) in heroin exposures reported to NPDS, especially in relation to the

distinct lack of similar increase in any of the other opioids, is remarkable and alarming. The morbidity associated with heroin exposures (last 6 years) is distinctly higher than any of the 33 other opioids generic code opioids or 10 opioid combination product generic codes collected in NPDS. The number of opioid cases reported to poison centers is relatively small compared with other data sources owing to the enhanced exposure treatment knowledge developed over time and the fact that poison center exposure reporting of is not mandatory. Nevertheless, NPDS data provide a distinct advantage for outbreak monitoring, morbidity assessment, and situational awareness by the system's near real-time ability to detect trends and changes over time.

KEYWORDS Heroin; opioid epidemic; Morbidity Index

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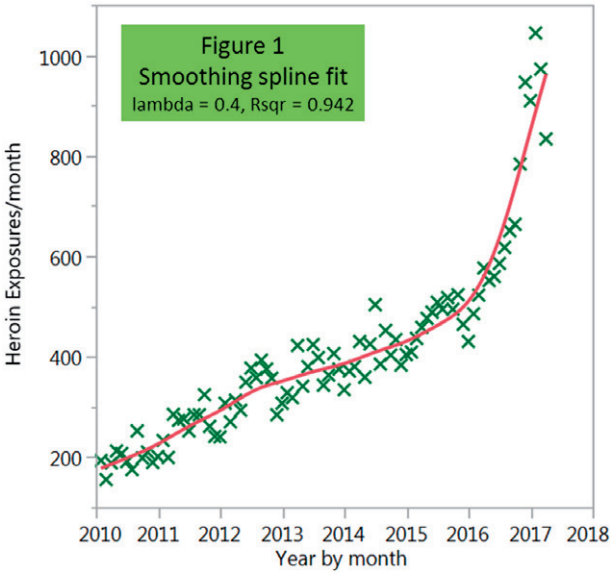

266. Benefits of a poison center's partnership with local health departments

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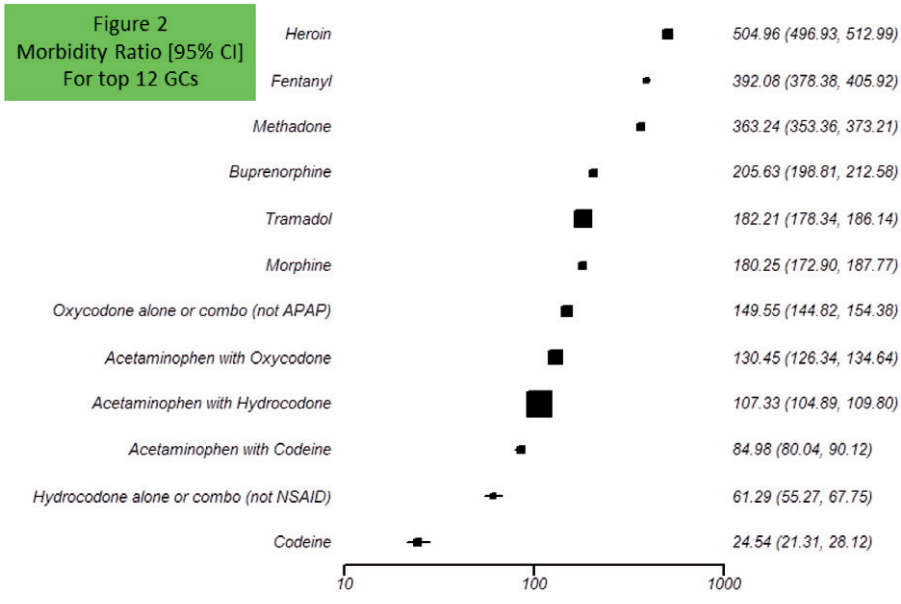
Background: Poison control centers (PCCs) have worked with local health departments, serving as resources and assisting with improved community health care. A description of a PCC's partnership the local County Department of Public Health (DPH) is described.

Method: Our PCC has two phone lines dedicated to the DPH activities: (1) the Disease Reporting Line (DRL), and (2) the public health information line (PHIL). The DRL is used by County health care providers (and facilities) to report (24/7) and discuss (in real-time) a variety of public health concerns. These include: animal bites, rabies inquiries, communicable disease reporting and micro-biological test results. Other layperson (and veterinarian) inquiries (e.g., mosquitos, irritant smells, and Animal Care & Control) are reported via the PHIL. All PCC staff receive training on how to manage these lines with new-hire orientation and annual staff in-services. The DPH provides a review manual (annually updated with PCC input) that is down-loaded to PCC computers for quick reference. The DPH also provides an on-call physician and non-urgent contacts for community health nurse and epidemiologist. All PCC calls received on both lines have a chart documented within the PCC electronic medical record system, which is immediately copied and faxed to DPH via secure transmission. Weekly case logs are prepared by the PCC and provided to DPH leaders. These lines are also used to immediately identify (potentially) emerging public health concerns (e.g., influenza or contaminated water) as well as surge capacity for large public events.



	Generic Code Name	Slope (Exposures/yr)	95% CI	Mean (Exposures/yr)	Slope (%/yr)	p-value
1	Heroin	870	[503, 1237]	4901	17.7%	0.0028
2	Other or Unknown Narcotics	40.7	[-160, 241]	1758	2.32%	0.6033
3	Buprenorphine	28.2	[-74.9, 131]	3595	0.785%	0.4900
4	Hydromorphone	20.5	[-142, 183]	1507	1.36%	0.7445
5	Meperidine	-28.1	[-37.3, -18.9]	159	-17.7%	0.0011
6	Hydrocodone Alone or Combo	-29.7	[-41.6, -17.8]	1916	-1.55%	0.0023
7	Tapentadol	-31.4	[-62.8, 0.006]	374	-8.39%	0.0500
8	Ibuprofen with Hydrocodone	-37.8	[-47.1, -28.6]	212	-17.8%	0.0003
9	Acetaminophen with Codeine	-44.7	[-356, 266]	3925	-1.14%	0.7106
10	Codeine	-48.3	[-97.4, -0.870]	1847	-2.61%	0.0526
11	Fentanyl	-56.2	[-89.8, -22.7]	1475	-3.81%	0.0096
12	APAP with Other Narcotics	-68.7	[-97.4, -40.0]	608	-11.3%	0.0026
13	Tramadol	-69.3	[-366, 228]	12758	-0.543%	0.5525
14	Oxymorphone	-92.9	[-178, -7.64]	651	-14.3%	0.0390
15	Oxycodone Alone or Combo	-110	[-389, 169]	8288	-1.33%	0.3351
16	APAP with Propoxyphene	-134	[-243, -25.1]	292	-45.9%	0.0269
17	Morphine	-157	[-206, -109]	3720	-4.23%	0.0008
18	APAP with Oxycodone	-344	[-553, -135]	9443	-3.64%	0.0102
19	Methadone	-350	[-437, -263]	3653	-9.59%	0.0004
20	APAP with Hydrocodone	-2361	[-2774, -1948]	23482	-10.1%	0.0001

Results: Tables 1–2; May and June highest months of calls received; overall highest use of DRL and PHIL by the public and healthcare providers.

Conclusions: Partnerships between PCC and local departments of public health offer resources for both parties. These advantages include enhance community health resources, disease monitoring and increased PCC call volume.

KEYWORDS Poison center; partnership; local health departments

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Table 1. Monthly Number (Percent) of DRL/PHIL Calls Received: 01/01/2016-12/19/2016

Month Call Received	Number of Calls	Percent of Total
January	55	6.5
February	76	9.0
March	60	7.1
April	59	7.0
May	120	14.3
June	118	14.0
July	66	7.8
August	95	11.3
September	59	7.0
October	48	5.7
November	52	6.3
December	34	4.0
Total	842	100.0

Table 2. Source of Calls Received through DRL/PHIL Data: 01/01/2016-12/19/2016

Source of Report:	Number of Calls	Percent of Total
Member of the Public	405	48.2
HC Provider/Facility	334	39.7
Veterinary/Animal Facility	48	5.7
Government Agency	19	2.3
School/Child Care	14	1.7
First Responder	11	1.3
Hospital – Lab	4	0.5
Alternative Care Facility	3	0.4
Organization/Business	2	0.2
Other/Unidentified	1	0.1
Total	841	100.0

Table 1: The patient's active medications.

Medication	Dose
phenytoin	75/100 mg PO every morning/evening
levothyroxine	0.100 mg PO daily
buspirone	10 mg PO twice daily
hydroxyzine	50 mg PO every night
topiramate	50/25/50 mg PO every morning/noon/evening
lorazepam	1 mg PO daily as needed
ciclopirox	1% cream topical twice daily

267. Qualitatively assessing barriers to poison control center utilization

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Background: Nationwide, poison center call volume has been declining since 2008. Informal observations and formal qualitative data show that few people know the number to reach their poison control center or the degree to which centers can triage poisoned patients. A needs assessment was conducted to identify commonly-held barriers that prevent people from contacting a poison control center. Under the lens of the Stages of Change model, research also attempted to measure participants' readiness level to contact a poison control center.
Methods: Thirty-nine people participated in two online focus groups segmented by age. The first group included 20 participants aged 19–34; the second group included 19 participants aged 35–74. Participants were recruited throughout the statewide regional territory of the poison control center and screened to identify the healthcare decision makers of the household (77% female). Participants also reflected the urban/rural population of the state (77% urban). Ethnically, they were 64% white, 21% black, 13% Hispanic, and 2% Asian/Pacific Islander.
Results: Findings revealed participants' natural instinct to call 911 in the event of a suspected or actual poisoning. Half (49%) reported they would call 911, one-third (33%) were not sure whether they would call 911 or the poison center, and only 15% said they would call the poison center. Thus, roughly half of participants indicated they were in the Precontemplation stage of choosing a poison center for care. Participants expressed distrust that the value of calling a poison center would exceed that of calling 911. Being helped fast was most important to participants (84%), above being helped by an expert (16%). Secondarily, 77% thought that "poison center" and "poison control center" represented different concepts. In many cases, "poison center" implied more informational help or a physical location, whereas "poison control" implied assertiveness and authority in dealing with poisonings. Sixty-two percent preferred the phrase "poison control." Participants were also unfamiliar with the Poison Help logo. About three-fourths (74%) reported never seeing the Poison Help logo before, and 80% reported never hearing of the regional poison control center.
Conclusions: Participants described three primary barriers that threaten the utilization of poison centers: the inclination to call 911 in a perceived or real poison emergency, a lack of information about how a poison control center helps poisoned individuals, and a lack of awareness that poison centers exist. Post-intervention, one-quarter (25%) of participants indicated movement from Precontemplation to either Contemplation or Action in regard to their readiness to contact a poison control center. Stated behavior change included talking to a family member about the poison center, bookmarking the poison center website, or downloading a poison control app. Awareness efforts that assume a precontemplative audience and clarify the distinction between poison control centers and 911 might be beneficial in helping poison centers emerge as the first and best choice for poisoning care.

KEYWORDS Poison center; public outreach; needs assessment

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268. Poison control centers (PCCs) and alternative forms of communication: what's all the chatter about?

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Background: Short messaging service (SMS), also known as text messaging, allows for the exchange of short electronic messages via mobile devices. Online chat refers to Internet-based transmission of short messages between senders and receivers for real-time conversation. Currently, telephone calls are the primary form of communication used by Poison Control Centers (PCCs) in the United States. However, a growing number of people prefer the convenience of SMS and online chatting. The SMS function on mobile devices is used by 81% of Americans, and 29% of smartphone users have messaging applications that function like a traditional chat or SMS. Incorporation of SMS and chatting services allow PCCs to reach a broader population base.
Objective: To assess the current use of texting and chatting by PCCs.
Methods: Survey questionnaires were distributed to all 56 PCCs in the United States and Puerto Rico. The survey obtained data on PCC experiences with SMS and chatting services and were administered via Internet-based Google Form, paper-based written form, or telephone. Responses were analyzed for established protocols for responding to SMS and chats, privacy protocols, volume of inquiries, efficacy, and staff satisfaction.
Results: The survey response rate was 95% (53 of 56 PCCs). Six of the 56 PCCs reported current or previous use of SMS and chatting as an alternative method of capturing toxic exposures. Three PCCs currently offer both SMS and chatting. Two PCCs offer only chatting. One center previously offered only SMS but discontinued their program. Startup dates for SMS and chatting services ranged from 2010 to 2015. The six PCCs that either currently offer or formerly offered SMS and chatting interfaces reported startup costs ranging from $0 to $25,000. The case volume for both systems typically ranged from 0 to 20 inquires per day among all the PCCs. In terms of efficacy, two PCCs rated these services as "Very Effective", two as "Effective", and two as "Neutral". None rated them negatively. The majority of the PCCs offering SMS

completed text messaging interactions within 10 min, whereas the majority of the PCCs offering chatting completed chatting interactions within 30 min. In comparison, all six PCCs completed telephone interactions within 10 min. The most beneficial aspect of these services was providing an alternative form of contact for the general public (cited by 66.6% of the six PCCs). The most disadvantageous aspects were staff apprehension and interaction length (cited by 33.3% of the PCCs each). Finally, the greatest barriers to implementation were logistical concerns and technological barriers (cited by 60.0% and 55.0% of the PCCs, respectively) (see Tables).

Conclusions: A minority of PCCs in the United States currently use SMS and online chatting. Of the PCCs that utilize these services, most felt positively about their use. SMS interaction length was comparable with the length of telephone calls, whereas chatting was more time-intensive. Further research is necessary to determine if these modalities effectively expand public access and result in greater comfort in contacting PCCs.

KEYWORDS Texting; chatting; poison control centers

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Advantages of SMS or online chatting services *(n=6)*	% of responses
Alternate form of contact	66.6%
Greater population reach	50.0%
User appreciation and effectiveness	33.3%
Multiple case management	33.3%
SPI satisfaction	16.6%
Less documentation	16.6%

Disadvantages of SMS or online chatting services *(n=6)*	% of responses
Staff apprehension	33.3%
Longer interaction time	33.3%
Lack of automated system	16.6%
Inappropriate interactions	16.6%
Abbreviated information	16.6%
Lack of auditory context	16.6%
Patient inclination to disconnect	16.6%

Barriers to Implementation *(n=20)*	% of responses
Technological Barriers	60.0%
Logistical Issues	55.0%
Cost	30.0%
Quality of Care	10.0%
Staff Apprehension	10.0%
Lack of Interest	5.0%

Advantages and disadvantages were collected from PCCs that either currently or formerly offered SMS or online chatting services. Barriers to implementation were collected from PCCs that do not offer SMS or online chatting services. Responses among all PCCs in each category were pooled together, and reasons cited were tallied.

269. Impact of carisoprodol scheduling on abuse and misuse: a retrospective review of California poison control calls from 2008 to 2015

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Background: In January 2012, carisoprodol was classified as a Schedule IV substance under the controlled substances act from a previously non-controlled, non-scheduled classification. Carisoprodol is marketed as a skeletal muscle relaxant and is commonly cited for its abuse potential, particularly since its active metabolite, meprobamate, is already classified as a Schedule IV substance. The aim of this study is to examine whether there were any significant changes in reporting trends to a statewide poison control system following the scheduling of carisoprodol. We hypothesized that the number of carisoprodol calls would decrease after scheduling.

Methods: The study is a retrospective review of California Poison Control calls involving carisoprodol from 2008 to 2015. Data were manually extracted from poison control calls coded as "misuse/abuse" involving carisoprodol, as either a single or multi ingestion, from 4 years before (2008–2011) and 4 years after (2012–2015) the scheduling change. Information extracted included general patient demographics (age and gender) as well as year of the call. Data were then analyzed using STATA14.2 (College Station, TX). Yearly California census data was used to adjust carisoprodol related poison center calls for the state of California for each of the years included in the study. The number of calls from pre and post schedule time periods were compared using Wilcoxon rank sum test, after assessing the normality of data distributions.

Results: A total of 1646 patients were included in this study, 802 (49%) of which were female and 841 (51%) were male. Population adjusted rates of carisoprodol related calls to California Poison Center generally decreased from 2008 to 2016 (Table 1). There were significantly greater rates of carisoprodol related calls in the 4 years prior to scheduling than in the 4 years following the change ($z = -2.37$; $p = .02$). Further analyses also revealed the median age of patients before scheduling was 34 years (Interquartile range (IQR), 24), which was significantly younger than the median age of 36 years (IQR, 22) after scheduling ($z = -4.595$; $p < .0001$).

Conclusions: Calls related to the misuse and abuse of carisoprodol appeared to decrease over time from 2008 to 2015. Furthermore, scheduling of carisoprodol appeared to be temporally related to decreased exposures as reported to California Poison Control Centers.

KEYWORDS Carisoprodol; scheduling; drug trends

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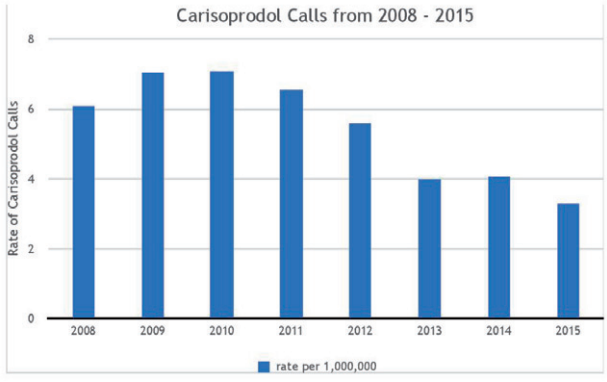

270. Therapeutic opioid prescription use and hearing loss among US adults

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Background: Opioid-induced sensorineural hearing loss is a recognized complication of opioid abuse. Most cases describe rapidly progressing auditory dysfunction following heroin use or prescription opioid abuse. The effect of therapeutic prescription opioid use on hearing ability among the US population is currently unknown. Our objective was to examine the National Health Assessment and Nutrition Examination Survey (NHANES) 2011–2012 to determine if therapeutic prescription opioid use is associated with hearing loss among US residents.
Methods: We analyzed the NHANES 2011–2012 as it was the most recent dataset available to include audiometry testing. We examined 3708 participants ages 20–69 years old with an audiometry examination reported. Hearing loss was defined as per the World Health Organization standard as a hearing threshold above 25 decibels (dB). Audiometry data included hearing loss thresholds for frequencies between 500 and 8000 Hz. Participant's reported home prescription medications were reviewed for opioid and opioid combination products. Chi square analysis, Mann–Whitney *U* test, and multiple regression analysis were performed to determine if an association between hearing loss and therapeutic prescription opioid use exists.
Results: Chi-square analysis showed no association between hearing loss and therapeutic prescription opioid use. Age was controlled for using a hierarchical multiple regression analysis. There was no association between hearing loss, at any single or combination frequency, and therapeutic prescription opioid use ($p>.05$). Mann–Whitney *U* test demonstrated the pure-tone average threshold (the mean hearing threshold at 500, 1000, and 2000 Hz) was higher in prescription opioid users compared with non-users; however, this was significant only for patient ages 40–49 years old ($p<.05$).
Conclusions: This is the first epidemiologic study, to our knowledge, to investigate a relationship between hearing loss and therapeutic prescription opioid use. No association was found save for the finding that therapeutic prescription opioid use may alter auditory function in certain subsets of the population as evidenced by a higher hearing threshold among 40–49 year old users. A limitation of the data is that it cannot be determined if patients were abusing their opioid prescriptions.

KEYWORDS Opioid; hearing loss; audiometry

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271. Phenibut: High school vital sign lows, patient woes, and poison center kudos

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Background: Phenibut (β-phenyl-γ-aminobutyric acid) is a powder marketed as a supplement, previously available at a large national supercenter, and still readily available on the Internet. Legally unregulated, it is not without dangers, as this GABA-derivative has properties similar to the prescription muscle relaxant baclofen. Phenibut use/abuse appears to be increasing, with our state poison center network recording 33 exposures since 2007, with 25 of these between January 2015 and April 2017. As new substances of abuse arise, the regional poison center is uniquely placed to serve as a "hub" of information assimilation and dissemination. We report on three teenage females who together ingested Phenibut powder for recreational use while at school, and the role of the poison center.
Case reports: Patient #1, a 15-year-old, arrived at a health care facility (HCF) about 6 h post-exposure unresponsive, with hypotension and respiratory depression. A few minutes later Patient #2, her 15-year-old friend, presented to another HCF with progressive somnolence leading to intubation. Her pulse decreased from 115 to 68 beats per minute (bpm), and her core temperature fell to 94 °F. Several hours later Patient #3, the 18-year-old sister of Patient #1, began vomiting and became difficult to arouse. Her pulse was 42 bpm, and temperature 94.3 °F. All three patients were admitted to intensive care units at different hospitals. Neither the 3 treating physicians nor the poison Specialist was familiar with Phenibut, and the drug was not yet in Poisindex. Nevertheless, the Specialist found historical and structural information online, which provided a starting point for understanding and treating the drug effects. The Specialist pieced together information from each of the three patients' exposures and shared with the treating physicians. Symptomatic treatment included IV fluids, ventilatory support, and external rewarming blankets. All regained a normal mental status and vital signs within 24 h of ingestion, and all were discharged within 48 h.
Case discussion: These three cases not only demonstrate some of the expected effects of a newer GABA-agonist drug of abuse but also highlight a benefit of the regional poison center concept. The same Specialist received calls from the three treating physicians, as well as from the father of two of the patients. The Specialist assimilated the accruing information and shared it with each of the physicians and the other specialists at the poison center. The Specialist rapidly increased knowledge about this unfamiliar substance to multiple healthcare providers.
Conclusions: Poison Center Specialists may play a key role in toxicosurveillance, knowledge assimilation, and education dissemination to other healthcare providers.

KEYWORDS Phenibut; GABA-derivative; role of poison centers

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272. The poison patch: adult transdermal drug delivery system exposures reported to NPDS

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Background: Transdermal drug delivery systems (TDDS) offer a unique method of administration for medications. While there are a limited number of these products available, they can be associated with significant toxicity due to the large amount of drug they may contain and their extended release properties. We sought to characterize adult exposures to TDDS reported to the National Poison Data System (NPDS).
Methods: This was a cross-sectional study consisting of NPDS data collection utilizing both qualitative and quantitative data for the time period of 1/1/2006–1/1/2016. A qualitative analysis of NPDS fatality abstracts was conducted to characterize adult (>19

year of age) human exposures to TDDS (recorded as "patch"). A quantitative search in NPDS was conducted for all closed, adult human exposure cases to TDDS. All data entered into NPDS was collected and analyzed using Microsoft Excel (*Microsoft Corp., Redmond, Washington*, 2010).

Results: A total of 8136 cases were identified. The average age was 46.8 years (range 19–101, SD 18.9) and 60% of cases were female ($n = 4910$). Sixty-nine percent ($n = 5595$) of cases involved exposure to only one substance. The highest number of cases were reported in 2011 ($n = 941$) with a subsequent yearly decline to 551 cases in 2015. In all, intentional exposure, including misuse, abuse, and suspected suicide accounted for 42% ($n = 3436$) of exposures. Ingestion of the TDDS was reported in 2197 (39%) of the single substance exposure. Fentanyl ($n = 4794$) was the most common substance involved, accounting for 59% ($n = 4794$) of exposures. Table 1 lists the five most common substances reported. Eighty-nine percent ($N = 7268$) of exposures occurred at the caller's residence but 42% ($n = 3450$) of calls originated from a health care facility (HCF). Sixty percent ($n = 4907$) of cases were either referred to or managed in a HCF. The most common disposition for those referred/treated at a HCF was admission to a critical care unit ($n = 1504$). Of the 4872 cases that were followed to a known medical outcome there were 63 deaths, 698 major outcomes and 1917 moderate outcomes. There were an additional 10 deaths deemed to be indirect. Fentanyl was involved in 90% ($n = 66$) of all deaths.

Conclusions: Adult TDDS exposures reported to the NPDS decreased over the duration of this study. These exposures frequently involved fentanyl and resulted in high rates of major or moderate medical outcomes.

KEYWORDS Transdermal; fentanyl; poison control

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Agent	Number of cases
Fentanyl	4794
Lidocaine	834
Rivastigmine	477
Nicotine	427
Scopolamine	248

273. Patch of death? Transdermal fentanyl delivery system exposures reported to the NPDS

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Background: Transdermal fentanyl delivery systems (TFDS) are used to deliver continuous, parental amounts of fentanyl. While initially used to treat severe cancer pain, their use for non-cancer, chronic pain has increased dramatically in the last 10 years. TFDS have the potential to cause significant toxicity due to the large amount of drug they may contain and their extended release properties. We sought to characterize TFDS exposures reported to the National Poison Data System (NPDS).

Methods: This was a cross-sectional study consisting of NPDS data collection utilizing both qualitative and quantitative data for the time period of 1/1/2006–1/1/2016. A qualitative analysis of

Characteristic	Adult	Pediatric
Mean age in years [SD]	43.1 [18.1]	11.3 [6.1]
%Female (n)	53% (2525)	(153)
% Single Substance Exposures (n)	62% (3050)	60% (201)
% Of Single Substance Exposure Reporting Ingestion of Patch [n]	54% [1634]	56% [112]
Most Common Reason for Exposure (%) [n]	Intentional (61%) [2927]	Unintentional (59%) [185]
Most Common Exposure Site (%)[n]	Own Residence (88%) [4233]	Own Residence (87%) [272]
Most Common Caller Site(%)[n]	Health Care Facility (58%) [2804]	Own Residence (45%) [141]
% Referred to or Managed in HCF [n]	75% [3590]	65% [205]
% Naloxone Administered [n]	37% [1775]	38% [121]
% Those Referred/Managed in HCF Admitted to Critical Care or Non-Critical Care Unit [n]	49% [1744]	36% [74]
% Moderate or Major Medical Outcomes [n]	43% [2046]	23% [71]
Death- All	66	2

NPDS fatality abstracts was conducted to characterize all human exposures to TFDS. A quantitative search in NPDS was conducted for all closed human exposure cases to TFDS. All data entered into NPDS were collected and analyzed using Microsoft Excel (*Microsoft Corp., Redmond, Washington*, 2010).
Results: A total of 5105 cases were identified. There were 4794 adult (age ≥19 years) and 311 pediatric cases. Table 1 shows the characteristics of the adult and pediatric cases. For both the adult and pediatric group the highest numbers of cases were reported in 2011 with 656 and 51, respectively. Both groups have seen a downward trend over the subsequent 4 years with totals of 236 and 13 cases, respectively, reported in 2015. For both adult and pediatric TFDS only exposure cases, there was no difference in reported medical outcome regardless of whether route of exposure was dermal or ingestion. However, all pediatric deaths were associated with dermal exposures. In total, 57 adult deaths were attributed to TFDS with an additional nine indirect deaths for a total of 66 deaths. Two pediatric deaths were reported and none since 2008.
Conclusions: Both adult and pediatric TFDS exposures reported to the NPDS have trended downward. Adult exposures are more likely to be intentional in nature and associated with higher admission rates, moderate/major medical outcomes and deaths. Pediatric exposures are more likely to be unintentional resulting in less moderate/major outcomes and only rarely deaths. Naloxone was used equally in both groups. Further studies are warranted to determine if the downward trend in TFDS exposures continues.

KEYWORDS Fentanyl; transdermal; poison control

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274. A new Day (trana) for methylphenidate? Transdermal methylphenidate delivery system exposures reported to the NPDS

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Background: A transdermal methylphenidate delivery system (TMDS), marketed as Daytrana, was FDA approved in 2006 for the treatment of attention deficit hyperactivity disorder for children 6 years and older. TMDS has the potential to cause significant toxicity due to the large amount of drug it may contain and its extended release properties. We sought to characterize TMDS exposures reported to the National Poison Data System (NPDS).
Methods: This was a cross-sectional study consisting of NPDS data collection utilizing both qualitative and quantitative data for the time period of 1/1/2006–1/1/2016. A qualitative analysis of NPDS fatality abstracts was conducted to characterize all human exposures to TMDS. A quantitative search in NPDS was conducted for all closed, human exposure cases to TMDS. All data entered into NPDS was collected and analyzed using Microsoft Excel (*Microsoft Corp., Redmond, Washington*, 2010).
Results: A total of 688 cases were identified. There were 71 adult (age ≥19 years) and 617 pediatric cases. Table 1 shows the characteristics of the adult and pediatric cases. There was a peak of 97 pediatric exposures in 2007. Over the last 4 years the number of pediatric cases had declined to 31 cases in 2015. The highest number of adult cases was reported in 2012 with 11. There was no difference in reported medical outcomes regardless of whether the TMDS exposure was dermal or ingested. There were no deaths reported during the study period.

Characteristic	Adult	Pediatric
Mean age in years [SD]	32.5 [18.1]	8.3 [6.1]
% Female (n)	58% (41)	30% (183)
% Single Substance Exposures (n) [CL]	86% (61) [+/- 9%]	81% (502) [+/-3%]
% Of Single Substance Exposure Reporting Ingestion of Patch (n)[CL]	28% (17) [+/- 12%]	34% (172) [+/- 4%]
Most Common Reason for Exposure (%) [CL]	Intentional (44%) [+/-11%]	Unintentional (71%)[+/- 4%]
Most Common Exposure Site (%)	Own Residence (96%) [+/-8%]	Own Residence (87%) [+/-3%]
Most Common Caller Site(%)[CL]	Health Care Facility (51%) [+/- 12%]	Own Residence (59%) [+/- 4%]
% Referred to or Managed in HCF (n)[CL]	59% (42) [+/-11%]	42% (257)[+/- 4%]
% Benzodiazepines Administered [CL]	3% [+/- 7%]	3% [+/- 2%]
% Those Referred/Managed In HCF Admitted to Critical Care or Non-Critical Care Unit [CL]	31% [+/- 13%]	21% [+/- 5%]
% Moderate or Major Medical Outcomes	27% [+/- 10%]	17% [+/- 3%]

Conclusions: While adult TMDS exposures are rarely reported to the NPDS, pediatric exposures appear to be decreasing. Exposures to TMDS alone are common in both groups, but pediatric patients were more likely to be exposed unintentionally. In both groups, moderate or major medical outcomes were rare and no mortality was seen.

KEYWORDS Methylphenidate; transdermal; poison control

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275. Use of a prescription drug monitoring program among emergency department providers

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Background: Several solutions are being pursued to address the continued rise in opioid related mortality, one of them being use of prescription drug monitoring programs (PDMPs). PDMPs are statewide databases intended to monitor controlled substance dispensing and enable informed prescribing practices. In spite of the high prevalence of opioid use and mortality, it is hypothesized that PDMPs are underutilized. The objective of this project was to establish baseline provider attitudes and PDMP use in clinical practice.
Methods: An online survey was disseminated to emergency medicine groups. The population included midlevel providers, attending physicians and resident physicians prescribing controlled substances in the emergency department (ED). Descriptive statistics were performed.
Results: Eighty-nine complete surveys were returned by emergency providers. 78% of respondents report working 11 or more shifts per month in the ED with an average of 12 shifts per month. Of the 96% of respondents that had previously heard of the PDMP, 98% perceived it as moderately to extremely useful and 78% were already registered. Lack of understanding on how to register for the PDMP was cited as the main reason for not being registered. Lack of time and was cited as the main reason for not using the program. Provider usage frequency averaged at 2.75 times per week. Of those registered, 100% used the PDMP to help identify prescription drug abuse. About 30% of providers voluntarily accessed the PDMP for all patients before writing a controlled substance prescription. About 26% of providers surveyed voluntarily consulted the PDMP for all patients currently on a controlled substance.
Conclusions: Despite high registration and perceived usefulness, PDMP use varied but was low compared with provider presence in the ED (averaging <1 consultation of the PDMP per ED shift). This suggests barriers to use in practice which can be addressed through educational intervention. Intervention should focus on efficient use of the PDMP and how to integrate this tool into practice. PDMP education is of increased relevance with increasing legislative mandates that providers check the PDMP prior to controlled substance prescribing. Further efforts should be made to address the use of PDMP data in starting conversations with patients on substance abuse and treatment options.

KEYWORDS Prescription drug monitoring; opioid; emergency department

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276. US poison center's experience with hearing loss associated with opioids 2012–2016

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Background: Therapeutic use of prescription opioids have been associated with several adverse effects, including, constipation, nausea, vomiting, and itching. Non-prescription opioids use has been associated with similar effects, however, due to the impurities in the formulation, unexpected and unusual effects have been reported. Over-dose of prescription and non-prescription opioids may result in respiratory depression and coma. Our Poison Control Center (PCC) has experienced an anecdotal increase in a unique adverse effect, hearing loss, which is an adverse effect that has been previously documented with both prescription and non-prescription opioids, but with limited reports. We sought out to review the experience of all of the US PCCs in regard to hearing loss associated with opioid use/abuse.
Methods: We performed a retrospective observational study using the National Poison Data System (NPDS) from January 2012 to December 2016. Cases with substance coded were either acetaminophen with opioid, opioid, or heroin and were exported into an Excel® database. Cases involving salicylates were excluded. We, then further filtered the data by extracting cases in which "deafness" was coded as a "related, not related, and unknown if related" clinical effect. The "deafness" cases were further analyzed with descriptive statistics.
Results: A total of 105 reported deafness cases were analyzed. Just over half (58%) were male. Mean age was 31 years with a range of 14–64 years. Only cases involving single substances ($n = 60$) were further analyzed. The majority (61%) involved heroin and 49% were prescription opioids. All cases were already in health care facility at time of call to the PCC. The most common exposure reason was intentional abuse (58%) and suspected suicide (17%). Naloxone was administered in 60% of cases.
Discussion: Our data report a number of cases involving deafness related to opioid use. Although opioid induced deafness is rare, it is concerning to see a number of cases reported throughout the years. We decided to include all deafness cases regardless of coded relational status, do to this rare and sometimes unrecognized adverse drug event. Our data did show an increase in "related" deafness cases over "unrelated and not related" in the years after 2012. Previous studies of opioid induced hearing loss suggest vascular dysfunction secondary to opioid use/abuse may have synergistic affect when an individual is exposed to loud noises. However, the pathophysiology of opioid induced hearing loss merits additional studies. Better understanding the pathophysiology, duration, and substance association may aid in preventing hearing loss.
Conclusions: Deafness associated with opioid use is rare. Despite an increased trend in opioid use over the last 5 years, the reports of hearing loss to PCCs did not appear to be proportionally follow the increased opioid use. However, there may be under recognition and under reporting of hearing impairment among opioid users.

KEYWORDS Hearing loss; opioid; adverse effect

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277. A close collaboration between a regional poison control center and a clinical chemistry laboratory: a descriptive study

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Background/objective: The management of acutely intoxicated patients is often complicated by an unclear history of ingestion due to patients' unwillingness or inability to disclose information. In many cases, supportive care is the primary treatment modality irrespective of the particular toxin involved. However, some instances do necessitate laboratory analysis of biologic samples to confirm an exposure. Laboratory confirmation frequently requires "send out" testing, which may take days to weeks to result. Our regional poison control center (PCC) maintains a unique relationship with a clinical chemistry laboratory at an academic center with close proximity and turnaround time. The laboratory fellows and corresponding mentors have the ability to analyze samples on request to potentially affect patient care. When the laboratory is consulted, a database is maintained with analysis results and patient clinical data. This study describes the outcomes of this collaboration.
Methods: This was a retrospective, descriptive study of all patients in which the clinical chemistry laboratory was consulted by its regional PCC between 1 January 2015 and 31 December 2016. The study sample was compiled from a manual search of data from the laboratory consultation database, and then the corresponding PCC text-based notes of the case. Two authors (K. V. and D. R.) reviewed charts in tandem based on a standardized abstraction form created prior to data collection. Cases were excluded if no laboratory analyses were performed. The sample size was described in terms of dates of consultation, patient demographics, whether the consultation originated from the academic center, if a substance/unknown was qualified and/or quantified, the laboratory method used in analysis of samples, whether the laboratory result changed clinical management of the patient, if the laboratory result confirmed a suspected diagnosis, and if the case/results lead to a peer-reviewed publication. Descriptive statistics were used for analysis.
Results: A total of 76 cases were identified in which the clinical chemistry laboratory was consulted and an analysis was performed. In this cohort, patients' mean age was 38.4 years (range: 8 month–87 years) and 47 (62%) were male. Only 41% of consult cases originated from the academic center, and all consults to the laboratory occurred within 0–9 d of initial PCC involvement. In 64 cases (84%), a substance was identified. Of these, 37 (49%) involved the quantification of a suspected ingestion. In 37 cases (49%), a positive qualitative analysis of an unknown and unexpected ingestion resulted and of these, nine (24%) had quantitative analyses to confirm concentrations. The laboratory results yielded an expected finding in 48 cases (63%). While no results were deemed to alter acute patient management, the laboratory findings confirmed diagnoses in 44 cases (58%). Additionally, this collaboration resulted in peer-reviewed publications in 19 (25%) of cases.
Conclusions: A close collaboration between a regional poison control center and a clinical chemistry laboratory may be valuable in cases of acute poisoning, particularly in offering a confirmatory diagnosis and promoting academic proliferation.

KEYWORDS Poison control center; laboratory; collaboration

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278. Use of data from AHRQ Healthcare Cost and Utilization Project (HCUP) and NPDS to benchmark poison center utilization

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Background: Benchmarking regional poison center (RPC) utilization against national data sources can measure achievement of some of the essential functions of a poison center. Previous methods of benchmarking utilized NDPS data versus population (i.e.,

Table 1: Rate of poisoning cases per population presenting to ED National vs. Region

	# CCS poisoning cases in ED	Population in 2014	Rate per 100,000 population	Difference from Benchmark
National Data	1,315414	318.9 million	412	
RPC region	43,609	12.9 million	339	-18%

Table 2: Rate of ED Consults to PCC National vs. Region

	# CCS poisoning cases in ED	Number of HCF consults in NPDS Table 10	% CCS poisoning cases consulted	Difference from Benchmark
National Data	1,315414	613,412	47%	
RPCC Data	43,609	25,094	58%	+23%

Table 2: Rate of ED Consults to PCC National vs. Region

	# CCS poisoning cases in ED	Number of HCF consults in NPDS Table 10	% CCS poisoning cases consulted	Difference from Benchmark
National Data	1,315414	613,412	47%	
RPCC Data	43,609	25,094	58%	+23%

Penetrance); however, this method does not take into account regional variances in rate of poisoning events or differences in utilization rate of the RPC by healthcare providers (HCP).
Methods: The RPC used HCUP, NPDS and regional and national population data to compare rate of poisoning cases presenting to emergency departments (ED), percent of ED and admitted cases PCC are consulted on. HCUP data were extracted from hcupnet.ahrq.gov for state and national ED visits and hospitals admissions using Clinical Classifications Software (CCS) for all diagnoses of poisoning by psychotropic drugs, other medications and drugs, and non-medicinal substances for 2014. NPDS data downloaded from NPDS utilizing the enterprise report Table 10: management site of human exposures for RPC region and nationally. Population data for the region and nationally was extracted from Census.gov.
Results: For population rate presenting to ER, the national and RPC rate was 412/100,000 population and 339/100,000 population (Table 1); the RPC rate was −18%. For percent of ED admissions, the national and regional percent of cases consulted was 47% and 58% (Table 2); the RPC rate was +23%. For admitted patients, % consulted for national and RPC was 42 and 52% (Table 3); the RPC rate was +25%.
Discussion: There are regional variation for poisoning and deaths due to poisoning. Utilizing an external benchmark of patients that present to an ED can be a proxy of poisoning in a population; RPCs should strive to have a low rate of poisoning cases presenting to EDs in their region (e.g., through essential functions of poison prevention education and raising awareness of RPC services). The percent of consults on poisoning cases in the ED or admitted to HCF is a measure of utilization of RPC services by healthcare providers. Poison Centers should strive to have a high utilization by healthcare providers so that more critically ill patients can benefit from RPC expertise. This RPC had a lower population rate of presentation for poisoning and a higher percentage of HCF consults for ED and admitted patients compared with national benchmark.
Conclusions: Benchmarking of RPC essential functions can be accomplished by using HCUP data and comparing national averages with regional state results.

KEYWORDS Poison center; utilization; data

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279. Phenytoin-induced polyendocrinopathy in an autistic patient

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Background: Phenytoin is a highly protein-bound anticonvulsant that blocks voltage-gated sodium-channels. Toxicity may occur as a result of direct drug effect, medication interactions, or both. We report on an autistic patient who developed multiple endocrine abnormalities in association with chronic phenytoin toxicity.
Case report: A 39-year-old man from a foster home was brought to the emergency department (ED) for three months of progressive stupor and ataxia. The patient was known for non-verbal autism and was taking phenytoin for secondary epilepsy following a recent traumatic brain injury. He was diagnosed with hypothyroidism 6 months after starting phenytoin and was prescribed levothyroxine. His caregiver provided a medication list (Table 1) and noted that the phenytoin dose had been reduced twice in the past two months for supratherapeutic concentrations (Figure 1). On arrival, his vital signs revealed: blood pressure, 104/70 mmHg; heart rate, 54; rectal temperature, 33.0 Co; respiratory rate, 20; oxygen saturation, 94% on room air; glucose, 5.4 mmol/L. Physical exam demonstrated generalized weakness and confusion. In the ED, the patient received intravenous fluids, piperacillin–tazobactam, stress–dose hydrocortisone, and active external rewarming. The patient's serum potassium was 6 mmol/L, for which intravenous insulin was given. Plasma phenytoin concentration on presentation was elevated (117 μmol/L) and the drug was immediately stopped. Over the subsequent days, phenytoin elimination followed zero-order kinetics with an extremely prolonged half-life despite normal renal function (126 h, Figure 1). His caregiver did not consent for extracorporeal toxin removal (ECTR). Further testing (Table 2) showed hypogonadotropic hypogonadism, elevated thyroid stimulating hormone, and decreased triiodothyronine, despite ongoing levothyroxine supplementation. The patient's hypotension, bradycardia, hypothermia, and hyperkalemia were highly suggestive of adrenal insufficiency despite a normal cosyntropin stimulation test. Magnetic resonance of the brain and sella and computed tomography of the abdomen did not identify a structural cause for his illness.The patient received seven days of antibiotics after a urine culture grew enterococcus. Phenytoin was stopped permanently, exogenous steroids were tapered to discontinuation, and the patient's gait recovered. He was discharged home after eighteen days in hospital with endocrinology follow-up.
Case discussion: Hypothyroidism, hypogonadism, and hypoadrenalism have been independently reported in phenytoin-poisoned patients but never simultaneously in the same patient. In this case, the patient's autism likely contributed to delayed recognition and insidious progression of phenytoin-associated endocrine dysfunction. Phenytoin induces both cytochrome oxidase metabolism and sex hormone binding globulin synthesis, thereby decreasing the biologic activity of corticosteroids, thyroid hormones, and sex hormones. Although the patient had a normal response to cosyntropin stimulation, this test cannot reliably rule out secondary adrenal insufficiency. The patient's plasma half-life of phenytoin was 128 h, while the therapeutic range is 6–60 h. Though ECTR was not used in this patient, it may accelerate symptom resolution in cases with severe toxicity and prolonged plasma elimination.
Conclusions: Patients with intellectual impairment may be at increased risk of chronic phenytoin toxicity with unrecognized endocrine manifestations. ECTR may be considered in severely symptomatic patients and those with prolonged plasma elimination.

KEYWORDS Phenytoin; endocrine; toxicity

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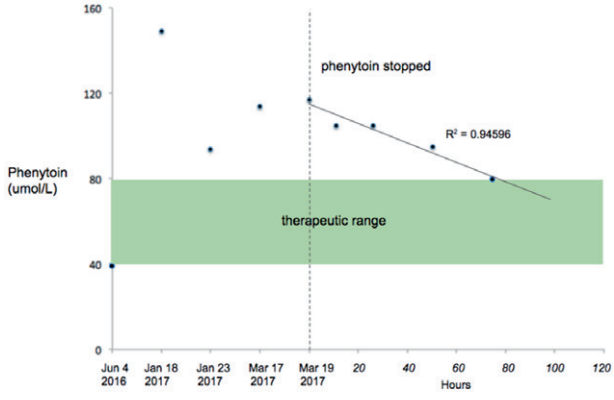

Figure 1: Corrected plasma phenytoin concentration was supratherapeutic for at least two months prior to ED presentation. After stoppage, it decreased in a linear fashion and reached a therapeutic concentration of 80 umol/L after 74 hours. Square of Pearson's correlation coefficient is indicated as R^2.

Table 1: The patient's active medications.

Medication	Dose
phenytoin	75/100 mg PO every morning/evening
levothyroxine	0.100 mg PO daily
buspirone	10 mg PO twice daily
hydroxyzine	50 mg PO every night
topiramate	50/25/50 mg PO every morning/noon/evening
lorazepam	1 mg PO daily as needed
ciclopirox	1% cream topical twice daily

280. Significant gaps in knowledge in individuals 65 years of age and older observed by a poison center's Older Adult Medication Safety Program

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Background: Americans 65 years of age and older only account for 14.5% of our population in the United States, but are responsible for a third of prescription medications dispensed. Of this age group, 39% take five or more prescriptions. With the older population expected to grow to 21.7% by 2040, medication safety is a priority. The poison center conducted a study in 2014 using local data from 2010 to 2013, which revealed an increase exposure call volume of 14% in the 65 and older population regarding therapeutic errors. This study precipitated our goal to educate the older population regarding therapeutic errors and medication safety. Preliminary data from the teaching sessions will be evaluated here.

Table 2: Laboratory endocrinologic investigations. Investigations were drawn during hospitalization unless otherwise specified. Abnormal values are indicated by an asterisk. Abbreviations: thyroid stimulating hormone, TSH; levothyroxine, T4; triiodothyronine, T3; anti-thyroid peroxidase antibody, Anti- TPO; sex hormone binding globulin, SHBG; luteinizing hormone, LH; follicle stimulating hormone, FSH; insulin-like growth factor 1, IGF-1.

Lab	Result	Normal Range	Units
TSH (mU/L;)	4.1 before phenytoin >50.60* before T4 6.55*	0.4-4.50	mU/L
Free T4 (pmol/L; 9.0-26.0)	6.2* before T4 10.6	9.0-26.0	pmol/L
Free T3 (pmol/L; 2.8-7.1)	1.8*	2.8-7.1	pmol/L
Anti-TPO	5.3	0.0-9.0	UI/ml
Free testosterone	6*	200-620	pmol/L
SHBG	98.2*	20-60	nmol/L
LH	3.7	0.8-6.1	U/L
FSH	3.7	1.6-11.0	U/L
Prolactin	10.3	2.7-16.9	U/L
IGF-1	17.7	14.2-42.1	nmol/L
Aldosterone	338	37-640	pmol/L
Cortisol, random (nmol/L)	327	--	nmol/L
ACTH (AM, 60 minutes)	338, 1000 on hospital day two 337, 924 on hospital day twelve	AM: 172-497 60 minutes: >560	nmol/L

Objective: To evaluate a medication safety program for the 65 and older population.
Methods: Our target audience was located by contacting local senior centers (seniordirectory.com). Doctor of Pharmacy candidates were trained to present a medication safety lecture using a 30-min program modified from http://www.scholastic.com/otc-med-safety/. Our program also included prescription medication information, auxiliary labels, storage information, importance of child resistant closures, and the importance of having a medication list with you at all times. Then a 15-min question and answer session followed. A pre-and post-test were administered and analyzed by a *Z* test of proportions stratified by survey site and for all sites combined. Each participant received a Poison Help brochure, magnet and sticker, pill planner with the national 1-800 number, large and wallet size medication sheets. Pre/post-test

1. Do you know the number for the poison center? Yes/No
2. It is okay to measure medicine using a silverware spoon? True/False
3. Are inactive ingredients in medicine ever a concern? Yes/No
4. The direction section of a label tells you how to take the medication properly. True/False

Results: See Table 1. Results from the preliminary trial programs revealed statistically significant increases in knowledge for all but one question. Interestingly, the largest gap in knowledge was related to the single easiest source for answers on poisonings, the 1-800-222-1222 phone number. During the discussion (question/answer session), it was routinely mentioned by the attendees that they were not aware that poison centers took calls about adults. Question 1: 0% correctpretest versus 87.7% correctposttest, $z = 10.4$, $p < .005$ Question 2: 80.6% correct pretest versus 82.5% correct posttest, $z = 0.3$, $p = .76$ Question 3: 34.3% correct pretest versus 100% correct posttest, $z = 8.4$, $p < .005$ Question 4: 86.6% correct pretestversus 100% correct posttest, $z = 3.3$, $p = .005$.
Conclusions: This was a successful program, which the poison center will continue with modifications. Our plans are to modify the survey and education to address the misconceptions and gaps in knowledge regarding poison centers, with an emphasis on how to contact a poison center and the populations we serve.

KEYWORDS Medication safety; geriatrics; public education

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Table 1. Survey Results of All Sites Combined

	Pre-Test		Post-Test	
	Yes/True	No/False	Yes/True	No/False
Q1	0	68	64	9
Q2	13	54	14	66
Q3	22	42	76	0
Q4	71	11	77	0

281. Use, misuse and overdose of quetiapine; keeping up to date with current trends in Australia

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Background: Quetiapine is an atypical antipsychotic used as treatment for schizophrenia, bipolar disorder, general anxiety disorder and refractory major depressive disorder in Australia. It is commonly used in overdoses as part of deliberate self-harm, and due to its anxiolytic and hedonic effects, it is becoming a popular drug for misuse and abuse in the wider community. The culture of off-label prescribing of low-dose quetiapine could be contributing to the problem and is a source of concern. This study aims to investigate quetiapine-related calls to a large Australian poisons centre, coronial data looking at fatal cases, as well as prescribing rates to understand the current trends.
Methods: Calls regarding quetiapine to a poisons centre between 2006 and 2016 were extracted from the centre's database. Data collected includes demographic data, strength and dose of tablets, intent, co-ingested drugs, route of ingestion, symptoms experienced and final advice given. Data on prescriptions were obtained from the Pharmaceutical Benefits Scheme, Australian Statistics on Medicines website for absolute numbers and daily dose. Coronial data were obtained through the Victorian Institute of Forensic Medicine where all quetiapine-related cases between 2006 and 2016 were reviewed.
Results: Results showed a 5.5-fold increase in the number of calls regarding quetiapine from year 2006 (126 calls) to 2016 (751 calls) per annum. Many were overdose-related (77%), followed by therapeutic error (11.7%), accidental (5.6%), misuse (5.0%), and miscellaneous (<1%). Females were more likely to be overdose victims (68%) and misusers (54.8%). Twenty-five milligrams and 100mg immediate release tablets were the most common strengths seen in overdose and misuse. Median dose was 1.5g and maximum dose recorded 56g ingested in overdose. Antidepressants and benzodiazepines were the most common co-ingestants in overdose. Call numbers regarding misuse increased by 6.6-fold between 9 in year 2006 and 60 in 2016. The most common reasons for misuse were for sleep and recreational abuse. Coronial data showed 359 quetiapine-related deaths on an increasing trend where most were males (56.5%). Average age was 42 with age range of victims between 15 and 79 years old. Suicide accounted for 25.1% of cases and accidental death accounted for 17.8% of cases. Intent for remaining cases were either undetermined or undisclosed. Prescriptions in Australia increased from 3468 in year 2000 to 988,541 in 2015 and defined daily dose per 1000 of the population per day increased by 225-fold.
Conclusions: This study revealed an increasing trend of both non-fatal and fatal overdoses in Victoria, misuse, as well as dramatically increasing prescription rates over the last decade. Further research is required to understand the causality of this worsening phenomenon and if there are any prevention measures that can be implemented.

KEYWORDS Antipsychotics; antidepressants; mood stabilisers

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282. Myocardial injury and coma were associated with both persistent and delayed neurological sequelae of acute carbon monoxide poisoning in Taiwan

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Background: Carbon monoxide (CO) poisoning has become a serious health problem in some Asian countries, including Taiwan. The aims of this study are to evaluate the changing trend of CO poisoning and to identify the predictors of neurological sequelae of CO poisoning in Taiwan between 1990 and 2011.
Methods: This retrospective cohort study included all eligible patients with acute CO poisoning reported to the Taiwan National Poison Control Center (NPCC) during the study period. Patients with CO poisoning were classified into intentional or unintentional exposure. The changing trend of CO poisoning and its impacts on the primary outcomes, i.e., persistent neurological sequelae (PNS) and delayed neurological sequelae (DNS), were assessed. Multiple logistic regression analysis was performed to identify the predictors of both PNS and DNS.
Results: There were 786 CO poisoned cases reported to the Taiwan NPCC during 1990–2011. Among them, 467 were intentional. Notably, intentional CO exposure started to become the major cause of CO poisoning in Taiwan in 2002. Increase in the number of intentional CO poisoning significantly correlated with the increase in the overall number of CO poisoning ($r = 0.972$, $p < .001$). In multivariate logistic regression analyses, patients who took tranquilizer (OR 3.89; 95% CI 1.94–7.77), had myocardial injury (OR 1.70; 95% CI 1.03–2.82), had been stayed in intensive care unit (ICU) (OR 2.03; 95% CI 1.13–3.62), and presented with GCS less than 9 (OR 4.05; 95% CI 2.32–7.08) and abnormal brain image in emergency department (OR 14.46; 95% CI 5.83–35.83) had a higher risk of PNS. Moreover, patients who were older age (OR 1.04; 95% CI 1.02–1.07), had psychiatric disorder history (OR 2.82; 95% CI 1.35–5.89), had myocardial injury (OR 1.33; 95% CI 1.16–1.53), and presented with GCS less than 9 after arrival at hospital (OR 3.23; 95% CI 1.65–6.34) were at a higher risk for developing DNS.
Conclusions: The pattern of CO poisoning had changed markedly during the study period, with a significant increase in both the numbers of intentional and overall CO poisoning. Although intentional CO poisoning was not associated with a higher risk of both PNS and DNS directly, it may influence the neurological outcome through other factors associated with poisoning severity such as myocardial injury and coma. More aggressive treatments are needed for patients with intentional CO poisoning.

KEYWORDS Acute CO poisoning; charcoal-burning; neurological sequelae

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283. Electrocardiographic changes associated with hyperkalemia in patients with chronic digoxin toxicity

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Background: The classic electrocardiographic (ECG) changes of hyperkalemia are well-known and are often the first clue to an elevated potassium concentration. However, the major mechanism of digoxin-induced hyperkalemia is potassium shifting from the intracellular to extracellular space. We hypothesized that the ECG manifestations will differ in hyperkalemic patients with elevated serum digoxin concentration (SDC) and hyperkalemic patients not taking digoxin.
Methods: This was a multicentre retrospective cohort study of hyperkalemic patients with chronic digoxin toxicity. Following institutional review board approval, patients were identified through search of electronic medical records between 2008 and 2016. Inclusion criteria were: patients $\geq$18 years of age; a concurrent serum potassium greater than 5.0 mmol/L; SDC $>$2.0 ng/mL, and an available ECG. Patients with acute digoxin toxicity, ventricular pacing, hemolysis, chronic hemodialysis, and administration of anti-digoxin Fab prior to their ECG were excluded. Clinical data were independently abstracted by three investigators on a standardized data collection tool. The primary outcome was the presence of hyperkalemic ECG changes in patients with elevated SDC. The presence of ECG changes consistent with hyperkalemia and/or digoxin effect were independently evaluated by two blinded experts in toxicology and emergency medicine. A 3:1 ratio of hyperkalemic patients not taking digoxin were included for evaluation. A third expert adjudicated disputed ECG's. Cohen's kappa were calculated for agreement between experts on hyperkalemic and digoxin-associated ECG changes. Descriptive non-parametric statistics were used.
Results: Eleven patients met all inclusion criteria (Figure 1). The median SDC was 2.4 ng/mL with an interquartile range (IQR) of 2.1–2.6 ng/mL. Median potassium concentration was 5.5 nmol/L (IQR, 5.3–6.1). Only six ECGs were interpreted as having digoxin-associated changes while none had hyperkalemic changes. The 35 hyperkalemic patients not taking digoxin had a median potassium concentration of 5.7 nmol/L (IQR, 5.6–6.1). Only nine of these ECGs were interpreted as having hyperkalemic changes. Two of these ECGs had digoxin-associated changes in isolation, and another one had both hyperkalemic and digoxin-associated changes. The kappa values for digoxin-associated and hyperkalemic ECG changes were 0.79 and 0.87, respectively.
Conclusions: These results suggest that the ECG may be an insensitive tool for diagnosing hyperkalemia in patients with chronically elevated SDCs. In this small cohort, no classic hyperkalemic ECG changes were identified. This finding was consistent with our hypothesis that digoxin-mediated potassium shifts are less likely to generate classic ECG changes but could also be explained by the mild hyperkalemia values observed in our study population. While ECG interpretation can be subjective, the high interobserver agreement indicates good internal validity among blinded toxicology/emergency medicine experts. Future investigations would benefit from a prospective design, larger sample size, systematic analysis of ECG findings, and an additional control set of patients with therapeutic SDC and higher serum potassium values.

KEYWORDS Hyperkalemia; digoxin; electrocardiogram

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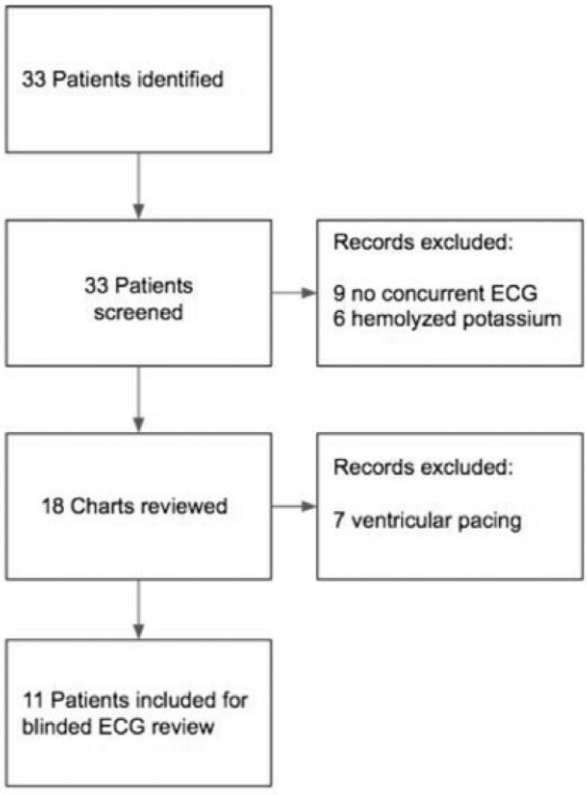

Figure 1: Flow diagram for the identification, screening, and inclusion of hyperkalemic patients with chronic digoxin toxicity

284. Pediatric poisoning deaths in a large urban setting: a review for prevention and education strategies

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Background: The epidemiology of pediatric poisoning fatalities is not well-characterized in our large urban setting. The regional medical examiner (ME) office investigates all suspicious deaths as well as deaths involving persons who were in apparent good health, prior to their death. The purpose of this study was to utilize ME records in order to describe the epidemiology of pediatric poisoning deaths and to find themes and scenarios that may be useful for developing a future poison prevention program.

Methods: The initial data were obtained from the Office of Vital Statistics (OVS) for a previous study by the regional poison control center and contained all documented poison-related deaths in 0–18 year olds occurring in the region from 2000 to 2012. Cases involving the region's residents with poisoning-related diagnosis codes (ICD 10 T36-T65.94XS) were extracted while excluding all fire/smoke-related codes (ICD 10 X00-X08, X88, X97). Medical examiner records for these cases were manually reviewed and the following variables were collected: decedent demographics, place of death, substance(s) mentioned as a cause of death, qualitative circumstances/reasons for death. The cases were grouped by ages (0–9 years-old, 10–18-years-old) for analysis.

Results: There were 539 pediatric poisoning deaths identified in our initial OVS dataset, and 125 cases fit our selection criteria. The average age was 13.8 years-old (± 5.8) with 26 cases in the 0–9 year-old group and 99 in the 10–18 year-old group. The other 414 cases were excluded due to being fire/smoke/burn related, non-poison related cause of death, or decedent was from another region. Decedent demographic data, intent, and location of death were summarized by age group (Table 1). Most deaths were unintentional (70%, $n = 88$). The most common substances mentioned in autopsy report for the 0–9 year-old age group were opioids 42% ($n = 11$), antihistamines 12% ($n = 3$), carbon monoxide 12% ($n = 3$), and cocaine 12% ($n = 3$). A common reason for deaths in this group involving 31% (8/26) of deaths, was improper storage of a family member's prescription medication or storage of toxic chemicals without labeling or in a child accessible location. At least 35% (9/26) of the cases involved families with known prior involvement with child protective services. In the 10–18-year-old group, the most common substances were opioids 65% ($n = 64$), benzodiazepines 32% ($n = 32$), cocaine 18% ($n = 18$), antidepressants 12% ($n = 12$). With respect to benzodiazepine-related fatalities, 31 out of 32 had opioid co-ingestion. Male sex was more common. At least half of the decedents (all intents) in this older group had known psychiatric or drug abuse history.

Conclusions: In our large urban setting, poison prevention programs for parents of young children should stress the importance of properly storing medications and chemicals. Caretakers should also be made aware disposal methods for unwanted medications and chemicals. Adolescents and parents should be warned about the harm and abuse potential of prescription opioids and benzodiazepines especially for those with known psychiatric disease.

KEYWORDS Pediatric fatalities; medical examiner; overdose

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Table 1. Poisoning deaths among 0 to 18 year-olds in Large urban setting 2000-2012 by age group, sex, race/ethnicity, and place of death.

	0 to 9 years		10 to 18 years		Total	
Variable	**N**	**%**	**N**	**%**	**N**	**%**
Intent						
Unintentional	11	42%	80	81%	88	70%
Intentional	8[1]	31%	19[2]	19%	30	24%
Undetermined	7	27%	0	0%	7	6%
Gender						
Male	12	46%	64	65%	76	61%
Female	14	54%	35	35%	46	39%
Race/ethnicity						
Non-Hispanic black	11	42%	16	16%	27	22%
Non-Hispanic white	6	23%	48	48%	54	43%
Hispanic	7	27%	31	31%	38	30%
Asian	1	4%	3	3%	4	3%
Other	1	4%	1	1%	2	2%
Place of death						
Home	3	12%	32	32%	35	28%
Dead on arrival	4	15%	6	6%	10	8%
Emergency room	10	38%	23	23%	33	26%
Inpatient	7	27%	18	18%	25	20%
Other	2	8%	20[3]	20%	22	18%
Total	**26**		**99**		**125**	

[1]All 8 were classified as homicide.
[2]All 19 were classified as suicide.
[3]Majority (14/20) occurred in a friend or family member's residence. The rest were public streets (2), hotel room (2), parking lot, and homeless shelter.

285. Toll-like receptor 9 mediates paraquat-induced acute lung injury: an *in vitro* and *in vivo* study

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Objective: This study aimed to investigate the role of Toll-like receptor 9 in paraquat-induced acute lung injury (ALI).
Methods: For this *in vivo* study, C57BL mice were randomly assigned to the vehicle control group, paraquat group, paraquat + antagonist (ODN2088) group, and antagonist (ODN2088) group ($n = 24$ per group). After paraquat 30mg/kg IP for 2, 24, and 48 h, serum samples and lung tissues were collected to evaluate ALI and TLR9 signaling. As for *in vitro* research A549 cells were randomly divided into the control group, paraquat group, paraquat + TLR9 siRNA group, and TLR9 siRNA group. After paraquat treatment for 24 h, the cells and supernatant were collected to evaluate apotosis and TLR9 signaling.
Results: *In vivo*, the lung injury score, the TLR9, MyD88, p-IRAK4, and p-p65 protein levels, and cytokines TNF-α and IL-1β levels in paraquat group were significantly higher than that in the control group;TLR9 blocker odn2088 pretreatment attenuated lung injury, inhibited MyD88 and NF-κB activation, and reduced TNF-α and IL-1β in serum. *In vitro* results show that the gene silencing of TLR9 reduced the mRNA expression of TLR9, TNF-α and IL-1,inhibited NF-κB activation, attenuated cell apoptosis.
Conclusions: TLR9 mediates paraquat-induced ALI, antagonizing TLR9 or silencing TLR9.

KEYWORDS Paraquat; toll-like receptor 9; acute lung injury

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