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1. Montelukast and risk of neuropsychiatric events in children with asthma: a population-based, nested case-control study

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Background: Asthma is the most common chronic condition in children, affecting 13% of children in the general population, and up to 300 million people worldwide. Montelukast, a leukotriene receptor antagonist, is primarily indicated for long-term asthma maintenance. In the United States, 2.6 million children under age 16 were dispensed prescriptions for montelukast in 2013. In 2009, the FDA announced a label change for montelukast to include neuropsychiatric events, following post-marketing case reports of sleep disturbance, depression, anxiety, suicidal ideation and attempts. Given the serious safety signals and the high prevalence of childhood asthma, we sought to investigate the association between montelukast prescription and neuropsychiatric events in children with asthma.
Methods: A matched nested case-control design was used to identify cases and controls from a cohort of children aged 5–18 years with physician-diagnosed asthma between 2004 and 2016, in Ontario, Canada. The nest included children prescribed an asthma maintenance medication. In this cohort of children with asthma, 3.3% had been prescribed montelukast. Cases were children with a hospitalization or emergency department visit for a neuropsychiatric event. Each case was matched to up to four controls on birth year, year of asthma diagnosis and sex. The exposure was defined as a dispensed prescription for montelukast in the year prior to the index date. Patients receiving zafirlukast in the year before study entry were excluded. Covariates included other sociodemographic factors and asthma severity. The primary outcome was a first neuropsychiatric event following physician-diagnosed asthma, defined as a hospitalization or ED visit coded for six groups of disorders: substance-related, schizophrenia, anxiety, sleep disturbance, mood and personality disorders, and agitation. Conditional logistic regression was used to measure the unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) for montelukast prescription and neuropsychiatric events.
Results: A total of 898 cases with a neuropsychiatric event and 3497 matched controls were included in this study. The characteristics of cases and controls and neuropsychiatric events of cases at presentation as presented in Table 1. Exposure to montelukast was significantly associated with neuropsychiatric events, after controlling for marginalization quintiles, number of other asthma medication prescriptions, number of corticosteroid prescriptions and number of hospitalizations and ED visits for asthma. Children who had been prescribed montelukast had nearly two times increased odds of a neuropsychiatric event compared to those prescribed other asthma maintenance medications (adjusted OR: 1.91, 95%CI: 1.15–3.18). Almost half of cases presented to hospital for anxiety (48.6%), followed by sleep disturbance (26.1%) (Table 2).
Conclusions: Children prescribed montelukast were almost twice as likely to experience a new-onset neuropsychiatric event, compared to controls on a different asthma maintenance therapy. Our findings echo the 2014 FDA's Pediatric Advisory Committee recommendations, suggesting increased provider awareness and continued monitoring of neuropsychiatric adverse events in patients administered montelukast. Clinicians should be aware of the potential risks of montelukast, as it may inform their prescribing practices and clinical follow-up visits.

Table 1. Descriptive statistics by outcome: cases with a neuropsychiatric event ($N = 898$) and controls ($N = 3497$).

	Cases ($N = 898$) *N* %	Controls ($N = 3497$) *N* %	*p*-Value[a]
Age at asthma diagnosis			
0–5	341 (38.0)	1290 (36.9)	.76
6–12	355 (39.5)	1429 (40.9)	
13–18	202 (22.5)	778 (22.2)	
Age at event date			
6–7	167 (18.6)	591 (17.0)	.71
8–9	123 (13.7)	504 (14.4)	
10–11	103 (11.5)	404 (11.6)	
12–14	221 (24.6)	913 (26.1)	
15–18	284 (31.6)	1085 (31.0)	
Sex: female	476 (53.0)	1874 (53.6)	.78
Urban residence	794 (88.4)	3285 (93.9)	**<.001**
Socioeconomic status quintiles			
Deprivation quintile			
1 Least	67 (7.5)	266 (7.7)	.26
2	96 (10.8)	300 (8.6)	
3	122 (13.7)	506 (14.6)	
4	178 (19.9)	629 (18.1)	
5 Most	430 (48.2)	1774 (51.1)	
Dependency quintile			
1 Least	259 (29.0)	1157 (33.3)	**.02**
2	186 (20.8)	789 (22.7)	
3	156 (17.5)	588 (16.9)	
4	147 (16.5)	481 (13.8)	
5 Most	145 (16.2)	460 (13.2)	
Ethnic concentration quintile			
1 Least	109 (12.2)	274 (7.9)	**<.001**
2	121 (13.5)	318 (9.2)	
3	157 (17.6)	369 (10.6)	
4	195 (21.8)	633 (18.2)	
5 Most	311 (34.8)	1881 (54.1)	
Instability quintile			
1 Least	77 (8.6)	393 (11.3)	.28
2	113 (12.7)	427 (12.3)	
3	152 (17.0)	536 (15.4)	
4	238 (26.7)	933 (26.8)	
5 Most	313 (35.1)	1186 (34.1)	
Asthma severity (hospitalizations and/or ED visits for asthma)			
Median	0	0	**<.001**
Mean (SD)	1.25 (2.54)	0.13 (0.50)	

(*continued*)

Table 1. Continued.

	Cases (*N* = 898) *N* %	Controls (*N* = 3497) *N* %	*p*-Value[a]
Number of other asthma controller medication prescriptions			
Median	6	2	**<.001**
Mean (SD)	10.32 (13.72)	2.63 (2.80)	
Number of other asthma controller medication prescriptions			
0–1	105 (11.7)	1593 (45.6)	**<.001**
2–3	186 (20.7)	1183 (33.8)	
4+	607 (67.6)	721 (20.6)	
Number of corticosteroid prescriptions			
0	528 (58.8)	3022 (86.4)	**<.001**
1	177 (19.7)	363 (10.4)	
2+	193 (21.5)	112 (3.2)	
Number of corticosteroid prescriptions, in corticosteroid users			
Median	2	1	**<.001**
Mean (SD)	3.18 (8.12)	1.44 (1.03)	
N (%)	370 (41.2)	475 (13.6)	
Number of montelukast prescriptions			
0	825 (91.87)	3423 (97.88)	**<.001**
1	17 (1.89)	19 (0.54)	
2+	56 (6.24)	55 (1.57)	
Number of montelukast prescriptions, in montelukast users			
Median	4	2.50	**.001**
Mean (SD)	8.69 (9.96)	3.70 (3.66)	
N (%)	73 (8.1)	74 (2.1)	
Time from most recent (or montelukast) prescription to event date, days			
0–90	381 (42.4)	1392 (39.8)	.15
90–180	199 (22.2)	879 (25.1)	
>180	318 (35.4)	1226 (35.1)	
Time from first known prevalent asthma date to event date, days			
Median	1326	1339	.65
Mean (SD)	1510 (1103.81)	1528 (1103.30)	
First neuropsychiatric event (presenting complaint and/or diagnoses)			
Substance-Related	99 (11.0)	N/A	N/A
Schizophrenia	13 (1.4)	N/A	
Anxiety	436 (48.6)	N/A	
Mood	153 (17.0)	N/A	
Personality	14 (1.6)	N/A	
Sleep Disturbance	234 (26.1)	N/A	
Agitation	12 (1.3)	N/A	

SD: standard deviation; ED: emergency department; N/A: not available.
All percentages are adjusted for missing values.
[a]Determined by a chi-square test (categorical variables) or two-sided *t*-test (discrete variables).

KEYWORDS Asthma; montelukast; adverse events
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2. The changing face of acute liver failure in the wake of the US prescription opioid epidemic: review of 327 cases of acetaminophen-induced acute liver failure over 12 years

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Background: Acetaminophen-induced Acute Liver Failure (Apap-ALF) cases have been steadily rising since 2000 and account for the majority of toxicology consultations and poisoning deaths in our hospital. As the United States prescription opioid abuse epidemic evolved, with it came the hidden danger of acetaminophen-opioid (Apap-Op) combination products and Apap-ALF. We reviewed Apap-ALF cases at a liver transplant center over a 12 year period to characterize these patients and to determine the association of ALF with Apap-Op products.
Method: We retrospectively identified all patients with Apap-ALF from 2001 to 2012, using discharge ICD9 codes for ALF, chronic liver failure, and unspecified hepatitis, who also had AST and ALT elevations greater than 1000 U/l, and received NAC. A total of 526 cases were identified. Standardized chart review by trained abstracters isolated 327 patients who met inclusion criteria. Analysis included descriptive and univariate statistics. Comparisons included analysis between the first 6 years (period 1) versus latter 6 years (period 2).
Results: 327 patients met criteria. Mean age was 39 ± 14 years, 67% were female, 48% were Caucasian, 23% Black. Seventy-two

Table 2. Results of unadjusted and adjusted conditional logistic regression, for the outcome of new-onset neuropsychiatric event (*N* = 4395).

	Unadjusted OR	95% CI	*p*-Value	Adjusted OR*	95% CI	*p*-Value
Montelukast use (*Ref = No*)						
Yes	4.48	3.10–6.46	**<.001**	1.91	1.15–3.18	**.01**
Number of montelukast prescriptions (*Ref =0*)						
1	3.89	1.95–7.73	**<.001**	2.38	0.98–5.77	.06
2+	4.70	3.09–7.14	**<.001**	1.74	0.96–3.16	.07
Socioeconomic status quintiles						
Deprivation Quintile (Ref=1)						
2	1.29	0.91–1.84	.16	1.19	0.76–1.88	.45
3	0.98	0.70–1.37	.89	0.68	0.44–1.08	.10
4	1.13	0.83–1.55	.45	0.88	0.57–1.36	.56
5	0.96	0.72–1.28	.80	0.75	0.49–1.14	.18
Missing	0.95	0.35–1.59	.92	1.50	0.39–5.75	.55
Dependency Quintile (Ref =1)						
2	1.05	0.86–1.30	.62	0.88	0.67–1.15	.34
3	1.20	0.96–1.49	.12	0.77	0.57–1.03	.08
4	1.38	1.10–1.73	**.006**	0.79	0.57–1.09	.16
5	1.39	1.11–1.75	**.005**	0.81	0.58–1.15	.24
Missing	1.05	0.39–2.78	.93	–	–	–
Ethnic Quintile (Ref =1)						
2	0.98	0.71–1.34	.88	1.18	0.78–1.78	.45
3	1.08	0.79–1.44	.67	1.18	0.78–1.79	.43
4	0.79	0.60–1.04	.10	1.00	0.66–1.52	.98
5	0.42	0.33–0.55	**<.001**	0.53	0.34–0.82	**.004**

(*continued*)

Table 2. Continued.

	Unadjusted OR	95% CI	*p*-Value	Adjusted OR*	95% CI	*p*-Value
Missing	0.62	0.23–1.69	.35	–	–	–
Instability Quintile (Ref =1)						
2	1.33	0.97–1.84	.08	1.15	0.75–1.77	.51
3	1.43	1.06–1.94	**.02**	1.36	0.89–2.06	.15
4	1.29	0.97–1.72	.08	1.40	0.93–2.12	.11
5	1.33	1.01–1.76	**.04**	1.80	1.19–2.73	**.006**
Missing	1.19	0.44–3.22	.74	–	–	–
Number of other asthma controller medication prescriptions (*Ref* = 0–1)						
2–3	2.37	1.83–3.06	**<.001**	2.03	1.53–2.68	**<.001**
4+	13.45	10.57–17.11	**<.001**	9.66	7.29–12.81	**<.001**
Number of corticosteroid prescriptions (*Ref* = 0)						
1	2.84	2.30–3.50	**<.001**	0.96	0.72–1.26	.75
2+	10.13	7.75–13.25	**<.001**	1.41	0.99–2.02	.06
Asthma severity (hospitalizations and/or ED Visits for asthma)						
	3.18	2.79–3.63	**<.001**	2.09	1.82–2.40	**<.001**

OR: odds ratio; CI: confidence interval; ED: emergency department.
[a]Adjusted odds ratios were estimated using the model with the binary primary exposure variable (Yes versus No dispensed prescriptions for montelukast). Model was also adjusted for the patient's regional health authority.
*Adjusted odds ratios were estimated using the model with the binary primary exposure variable (Yes vs. No dispensed prescriptions for montelukast). Model was also adjusted for the patient's regional health authority.

percent were admitted as transfers. Chronic pain (45.6%) and alcohol abuse (45%) were common comorbidities. The number of Apap-ALF cases increased from a mean of 12.7 per year in period 1 (2001–2005) to 41.8 per year during period 2 (2006–2012) ($p < .01$). Apap-Op combination pills were responsible for 56% of the cases. Multiple repeat ingestions accounted for 63% of cases versus 30% of single ingestions. For cases with multiple ingestions, Apap-Op combinations accounted for 43% versus 22% for acetaminophen alone. Multiple repeat ingestions increased to 65% and Apap-Op use increased to 61% in period 2, compared to 50% and 28%, respectively, in period 1 ($p < .01$). Misuse (43%) and abuse (26%) were more common motives than suicide (27%). The majority of patients did not receive a liver transplant ($n = 233$) and their overall transplant- free survival to 28-d was 72.7%. Common reasons for transplant denial included improving clinical status (48%), substance abuse (22%), psychiatric (12%) and critical illness (17%), with survival in the latter groups of 71%, 83%, and 31% respectively. Liver transplant occurred in six patients, all of whom survived to 28 d. The overall 28-d mortality was 20.5%. Factors associated with mortality included: age >40 (OR 2.0, 95% CI 1.2–3.4), multiple versus single ingestion (OR 4.0, 95% CI 1.6–9.8), Apap-Op combinations (OR 3.0, 95CI 1.4–6.4), diabetes (OR 2.4, 95% CI 1.1–5.1), and Apap level >40 mcg/ml on the day of admission to transplant center (OR 3.0, 95% CI 1.6–5.8).

Conclusion: The number of Apap-ALF cases increased significantly from 2001–2005 to 2006–2012 in our institution. During this time, Apap-Op combinations accounted for the majority of cases compared to acetaminophen alone, with multiple repeat ingestions more common than single ingestions. The use of Apap-Op products was associated with a higher mortality in this cohort. These data suggest that the prescription opioid abuse epidemic is now a major contributor to Apap- ALF in our transplant center.

KEYWORDS Acetaminophen; liver failure; opioid epidemic

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3. Acetaminophen-protein adducts following acetaminophen overdose

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Objective: Acetaminophen-protein adducts (APAP-CYS) are a specific biomarker of acetaminophen exposure. Previous studies have found that an APAP-CYS >1.0 nmol/ml is both sensitive and specific in identifying patients with hepatotoxicity (ALT >1000 U/l) secondary to acetaminophen. However, less is known about APAP-CYS concentrations early post acetaminophen ingestion or APAP-CYS concentrations in those who do not develop hepatotoxicity. The objective of this study was to characterise APAP-CYS concentrations in patients following acetaminophen overdose.

Method: The Australian Paracetamol Project is a multi-centre prospective observational study, that recruits patients through calls to the Poison's Information Centre and three clinical toxicology units. Patients were recruited from September 2013 until January 2015. Inclusion criteria were any patients assessed for acetaminophen overdose over 14-years regardless of intent or preparation. It was planned to take at least three serum samples in the first 24 h post presentation. Serum samples collected were then analysed for APAP-CYS. Comparison of initial and maximum APAP-CYS concentrations were made using the Mann-Whitney U test.

Results: One hundred and seventy-eight patients were recruited with 790 samples analysed. The median age was 27 years (IQR: 20–41) with 127 (71%) females. One hundred and sixty-two (91%) were acute ingestions (ingestion occurred during a < 8 h time period), 31 (17%) ingested modified-release acetaminophen and seven a combination of products. Median reported ingested dose was 24 g (IQR: 12–40). One hundred and sixty-eight (94%) were treated with intravenous acetylcysteine at a median time of 6 h (IQR: 3.5–10.2) post-ingestion. Twenty-eight (16%) patients developed hepatotoxicity of which all put one received acetylcysteine greater than 8 h post-ingestion. Of those that developed hepatotoxicity, 18 had an ALT <1000 U/l at the time of presentation and these patients had a higher initial APAP-CYS concentration compared with those patients who did not develop hepatoxicity; 1.31 nmol/ml (IQR: 0.71–1.84, $n = 18$) versus 0.27 nmol/ml (IQR: 0.15–0.37, $n = 143$) ($p = < .0001$). Furthermore, six who presented with a normal ALT (< 50 U/l) and developed hepatotoxicity had significantly higher initial APAP-CYS [Median 0.66 nmol/ml (IQR: 0.59–0.75, $n = 6$); Receiver operator characteristic (ROC) AUC 0.96 (95%CI: 0.92–0.99, $p = .0002$) for prediction of hepatotoxicity]. An APAP-CYS concentration of 0.58 nmol/ml was 100% sensitive and 92% specific for identifying which patients would develop hepatotoxicity who presented with a

normal ALT. The maximum APAP-CYS concentration was significantly higher in those with hepatotoxicity 7.69 nmol/ml (IQR: 2.50–16.0, $n = 28$) versus 0.37 nmol/ml (IQR: 0.22–0.60, $n = 150$) ($p = <.0001$) than those who did not. Nine patients who did not develop hepatotoxicity had a peak APAP-CYS concentration of >1.0 nmol/ml, of which six were large (> 48 g) immediate-release acetaminophen ingestions.
Conclusion: As with previous studies, this study showed that an APAP-CYS concentration >1.0 nmol/l occurs in patients with hepatotoxicity secondary to acetaminophen. This study demonstrates concentrations slightly higher than this may be seen in large overdoses without hepatotoxicity and that a lower APAP-CYS concentration threshold (0.58 nmol/l) was superior for predicting which patients who present with a normal ALT will subsequently develop hepatotoxicity.

KEYWORDS Acetaminophen; acetaminophen-protein adducts; hepatotoxicity

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4. Money talks for medical tox: financial impact of the medical toxicology specialty code on a private practice

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Background: On October 1, 2017 the Centers for Medicare and Medicaid Services (CMS) of the Department of Health and Human Services established a unique specialty code for medical toxicology (C8-PHY). CMS based physician specialty codes are utilized to describe the specific types of clinical medicine that providers practice. These codes are used by CMS for programmatic and claims processing purposes. We describe the financial impact following the implementation of this specialty taxonomy code on an established private Medical Toxicology practice.
Methods: A retrospective analysis of quarterly financial data one year prior to Medical Toxicology code implementation (October–December 2016) was compared to financial data following code implementation (October–December 2017). This particular practice encompasses inpatient services at four hospitals and outpatient clinic services at one site. The same provider performed all documentation for both quarters, using the same electronic medical record (EMR) system. The encounters were billed by Current Procedural Terminology (CPT) codes through the same biller and coder during these time periods. Initial claim denial data was tracked throughout the appeals process, and denial data included benefit policy issues, coding irregularities, timely filing, and missing/invalid authorizations.
Results: From all insurance payers, payment per work relative value unit (WRVU) increased almost 70% from $133.98 per WRVU to $227.25 per WRVU. This was likely due in part to a decrease in overall denial rate by 3.4%. An increase in gross collection rate (GCR) by 6% was also seen (see Table 1). The Medicare gross collection rate improved from 41% in 2016 to 48% in 2017 (see Table 2). This was equivalent to an increase of $1.08 Medicare WRVU between the two time periods, and equates to a payment increase of $45.66 per WRVU in 2016 to $46.74 per WRVU in 2017. Medicare CPT code 99205 (new patient-clinic visit) saw the greatest increase in GCR from 8% in 2016 to 32% in 2017. A Medicare conversion factor (CF) increase from $35.8043 in 2016 to $35.887 in 2017 may have accounted for the increase in Medicare payments per WRVU. No Medicare denials occurred after implementation of the specialty code.

Table 1. Reimbursement data for all insurance payors.

Year (final quarter)	CPT count	Charges	Payments	GCR	Denial rate	Payment per WRVU
2016	262	$107,867	$76,543	71%	8.7%	$133.98
2017	139	$89,634	$68,970	77%	5.3%	$227.25

Table 2. Reimbursement data for medicare only.

Year (final quarter)	CPT count	Charges	Payments	GCR	Denial rates
2016	58	$11,685	$4831	41%	3.4%
2017	30	$5798	$2779	48%	0%

Conclusion: Medical Toxicology specialty code implementation had a positive effect on our practice's financial data. This was evident by the substantial decrease in denial rate for all insurance payers. Specialty code implementation also appears to have a positive financial impact on reimbursement of outpatient clinic visits, although other factors such as an increase in Medicare CF may play a role as well.

KEYWORDS Billing; financial impact; toxicology specialty code

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5. Changing nomogram risk zone classification with serial testing following acute acetaminophen overdose

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Objectives: Despite the value of the Rumack-Matthew Nomogram (RMN) for identifying patients at risk of hepatotoxicity, and the fairly consistent pharmacokinetics of acetaminophen (APAP) following overdose, 'line-crossing' (moving from one risk zone into another) does occur. Yet little is known about those who cross risk zones on the RMN. We sought to describe the incidence of patients crossing above or below the RMN treatment threshold after APAP overdose, and to identify risk factors for line-crossing in general.
Methods: We utilized data collected from the Canadian Acetaminophen Overdose Study (CAOS) database, a retrospective medical review of patients hospitalized for APAP poisoning at 34 hospitals between 1980 and 2005. We selected patients in whom at least two serum APAP concentrations could be plotted on the RMN following acute overdose. We defined seven nomogram risk zones using the following cutoffs: < 100, 100–149, 150–199, 200–299, 300–399, 400–499, and > =500 μg/ml (662, 993, 1324, 1986, 2648, and 3310 μmol/l). We classified each subject using every eligible [APAP] into these risk zones to identify line-crossers, and categorized any reported coingestant into distinct, non-exclusive pharmacologic classes. We recorded the greatest increase in nomogram risk zone observed, and the frequency of crossing two or more lines. To identify risk factors we used ordinal logistic regression with a 3-level dependent variable:

patients whose risk increased two or more zones, those remaining in the same or adjacent zone, and those whose risk fell by two or more zones. Potential risk factors studied were age, sex, ingestion type, peak APAP, first 4 + h [APAP], dose reportedly ingested, interval from ingestion to NAC, and coingestants such as ethanol, opioids, antimuscarinics, and NSAIDs.

Results: Of 11,987 unique hospital admissions in the CAOS database, there were 3201 eligible hospitalizations with 7705 APAP concentrations (~2.4/visit), including 124 cases (3.9%) of hepatotoxicity and 10 deaths or referrals for liver transplant. Most (1679, 52.5%) crossed at least one zone (up or down) within 24 h of acute ingestion, including 190 (5.9%) who crossed at least two lines into a higher risk zone, and 516 (16.1%) at least two lines into a lower risk zone (see Table 1). One hundred and thirty-two (4.1%) patients crossed from below to above the RMN treatment line of 150 μg/ml at 4 h postingestion. Being older, male, and coingesting opioids, antimuscarinics, or NSAIDs were associated with line-crossing on multivariate analysis (see Figure 1). The strongest association for line crossing into a higher risk zone was subsequent hepatotoxicity (aminotransferases >=1000 IU/l)

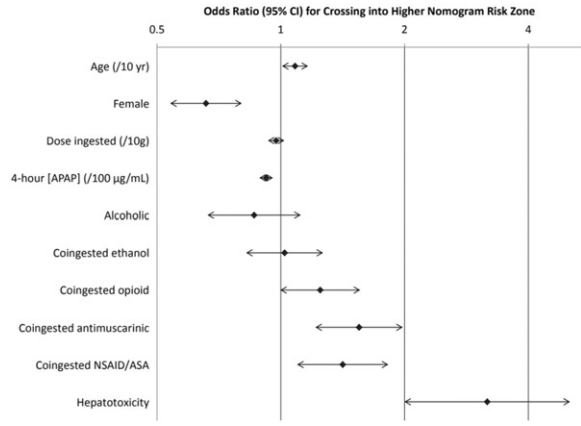

Figure 1. Patient characteristics associated with large changes in nomogram risk zone within 24-h of ingestion on multivariate logistic regression analysis.

Table 1. Number of patients by initial and highest nomogram zone occupied.

	Highest subsequent nomogram zone (μg/ml)							
Initial nomogram zone (μg/ml)	<100	100–150	150–200	200–300	300–400	400–500	≥500	Total
<100	584	24	13	11	4	4	4	643
100–150	251	225	53	24	12	4	3	572
150–200	179	151	199	71	25	4	8	637
200–300	81	115	140	233	75	22	15	681
300–400	18	26	28	78	74	33	40	297
400–500	1	2	12	17	29	35	52	148
≥500	3	0	5	11	14	18	172	223
Total	1117	543	450	445	233	120	293	3201

The highest Rumack-Matthew nomogram zone achieved within 24 h of ingestion is shown along with the initial zone. The primary outcome of *line-crossing* is illustrated by the shading intensity: the heaviest shading shows patients who crossed at least two lines into a higher risk zone, the light shading those who remained within one zone, and unshaded those who decreased by at least two risk zones. No [APAP] below the local assay limit of quantification (LOQ) was used to move a patient into a higher risk zone.

Table 2. Patient characteristics of line-crossers – univariate analysis.

	Greatest increase in nomogram risk zone			
Patient characteristics	≥2 zone increase (*N* = 190)	±1 zone (*N* = 2495)	≥2 zone decrease (*N* = 516)	*p*-Value*
Age, in years	25.6 [18.2, 35.9]	20.9 [16.6, 32.0]	20.9 [16.3, 30.8]	<.001
Sex, female	113 (59.5%)	1814 (72.7%)	404 (78.3%)	<.001
Dose reportedly ingested, in g	20 [10, 33]	15 [7.5, 25]	20 [10, 33]	<.001
First 4+ h [APAP], in μg/ml	133 [75.8, 220]	115 [60.3, 178]	161 [97.3, 199]	<.001
Time of first 4+ h [APAP], in hours from start of ingestion	5.2 [4.3, 6.9]	5.3 [4.3, 7.9]	6.4 [4.7, 8.9]	<.001
4-h equivalent [APAP], in μg/ml	171 [121, 287]	162 [101, 264]	224 [187, 306]	<.001
Time to NAC, in hours from start of ingestion	7.5 [6.0, 10.5]	7.3 [5.8, 9.8]	6.9 [5.5, 9.4]	.03
ψ, in mM·hours	1.52 [0, 3.13]	0.038 [0, 0.987]	0.405 [0, 1.52]	<.001
First [AT], in IU/l	23 [17, 32]	23 [17, 33]	22 [16, 31]	.2
APAPxAT, in mM·IU/l	15.8 [6.60, 33.8]	16.0 [6.10, 31.4]	18.2 [7.10, 33.0]	.42
Alcoholic, Yes versus No/not mentioned	43 (22.6%)	367 (14.7%)	85 (16.5%)	.011
Co-ingested ethanol, Yes	52 (27.4%)	606 (24.3%)	119 (23.1%)	.5
Co-ingested opioid, Yes	48 (25.3%)	499 (20.0%)	77 (14.9%)	.003
Co-ingested antimuscarinic, Yes	36 (18.9)	417 (16.7%)	46 (8.9%)	<.001
Co-ingested NSAID/ASA, Yes	38 (20.0%)	337 (13.5%)	52 (10.1%)	.002
NAC administered, Yes	175 (92.1%)	2000 (80.2%)	508 (98.5%)	<.001
Peak INR	1.2 [1.1, 1.3]	1.2 [1.1, 1.3]	1.1 [1.1, 1.3]	.02
Peak AT, IU/l	27 [18, 59]	26 [18, 42]	25 [19, 40]	.4
Hepatotoxicity, Yes	9 (4.7%)	112 (4.5%)	3 (0.6%)	<.001
Death or liver transplant	0 (0%)	8 (0.3%)	2 (0.4%)	.7

Table Patient characteristics by change in Nomogram Risk Zone within 24 h of ingestion. The columns show the subjects classified by the greatest change in Rumack-Matthew nomogram risk zone compared to their initial risk zone. Continuous characteristics are summarized by the median [25%ile, 75%ile]; binary characteristics by count (% of total). Aminotransferase concentrations ([AT]) and INR (international normalized ratio) were not measured in 18% of cases, most of whom were in the ±1 zone group. Shaded items were used to model the primary outcome using ordered logistic regression. *using the non-parametric Kruskal-Wallis test by ranks for continuous characteristics, and the χ^2 test for nominal characteristics.

(adjusted OR 3.2 [95% CI 2.0, 5.1]) (see Table 2). These findings were robust across several prespecified sensitivity analyses.
Conclusions: Patients commonly cross risk zones within the RMN after an APAP overdose, including from below to above the treatment threshold. Older age, male sex, coingestants and eventual hepatic injury are modestly associated with patients moving into higher risk zones. These findings support recommendations calling for repeat APAP testing in patients after acute APAP poisoning until the individual risk of hepatic injury is clearly established.

KEYWORDS Paracetamol; poisoning; acetylcysteine

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6. Meeting the demand for naloxone: stability of expired naloxone solution

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Background: Naloxone is an opioid receptor antagonist that reverses opioid overdose. In response to the opioid crisis, it has been distributed throughout communities through a variety of programs. Given naloxone's widespread availability, its use by the lay public and first responders with minimal medical training and that seconds matter when deploying naloxone together with administrative issues posed by critical drug shortages and budgetary concerns, the question of whether expired drugs are both safe and efficacious gains increasing importance.
Objective: To analyze the quality and stability of expired naloxone solutions to assess their remaining efficacy and identify potential risks.
Methods: This is an in-vitro study. Expired, unrefrigerated naloxone samples were obtained from first responders with expiration dates ranging from 1980 to 2016. Using liquid chromatography with mass spectroscopy (LCMS), naloxone was quantified from the samples. Possible metabolites, including noroxymorphone, were also quantified.
Results: All tested samples contained >90% of the labeled amount, with degradation correlated with length of storage. Noroxymorphone, a metabolite of naloxone and an opioid agonist, was detected from some older samples; in all samples it comprised less than 1%.
Conclusion: Greater than 90% of labeled naloxone concentrations persisted in expired samples. Accumulation of the potentially harmful opioid agonist noroxymorphone was trivial. Use of expired naloxone, even years after the expiration date, may be safe and efficacious. Further, it may still maintain United State Pharmacopeia-National Foundation (USP-NF) standards.

KEYWORDS Naloxone; medication safety; drug expiry

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7. Acetaminophen metabolites following acute acetaminophen overdose as a biomarker for acute liver injury

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Introduction: Acetaminophen is commonly taken in overdose and is a common cause of acute liver injury (ALI). There has been interest in new biomarkers to detect ALI earlier. Acetaminophen is mainly metabolized into nontoxic glucuronide and sulphate conjugates. A small fraction is metabolized by cytochrome P450 (CYP) enzymes into the reactive metabolite N-acetyl-p-benzoquinone-imine (NAPQI), which subsequently reacts with glutathione to ultimately form cysteine and mercapturate conjugates. NAPQI is responsible for hepatotoxicity when glutathione becomes deplete. Recent studies have shown that CYP metabolites and metabolite ratios are both sensitive and specific for detecting early liver injury (50% increase in ALT). The object of this study was to investigate acetaminophen metabolites as a possible biomarker for ALI.
Method: The Australian Paracetamol Project is a multi-centre prospective observational study that recruits patients through calls to the Poison's Information Centre and three clinical toxicology units. Patients were recruited from September 2013 until January 2015. Inclusion criteria were any patients aged over 14 assessed for acetaminophen overdose, regardless of intent or preparation. It was planned to collect at least three serum samples in the first 24 h post-presentation. A subset of patients was selected who had ingested immediate-release acetaminophen, presented within 24 h of ingestion, and with a serum sample collected prior to acetylcysteine initiation. Serum samples were analysed for acetaminophen and its metabolites by liquid chromatography, tandem mass spectrometry. Metabolites measured included the nontoxic glucuronide (APAP-Glu) and sulphate (APAP-Sul) conjugates and the NAPQI conjugates APAP-cysteine (APAP-Cys) and APAP-mercapturate (APAP-Mer). We calculated the sum of the total CYP metabolites, APAP-Cys/total metabolites and APAP-Cys/APAP-Sul for all patients. We examined their utility in predicting ALI, defined as an ALT >150 U/l. Comparison of ALI and non-ALI patient's metabolites was analysed using the Mann-Whitney U test, and predictive performance using the area under the receiver-operating-characteristic curve (ROC-AUC).
Results: Seventy-one patients were recruited; median age of 26 years (IQR: 19–38) with 53 (75%) females. Median time to presentation of 3.8 h (IQR: 2–7.9) with a median reported acetaminophen dose of 15 g (IQR:10–39). Sixty-five (92%) received intravenous acetylcysteine, at a median time of 6.5 h (IQR: 5–10) post-

Metabolite/Biomarker	Median (IQR)No ALI ($n = 60$)	Median (IQR)ALI ($n = 11$)	p-Value (Mann Whitney)	ROC-AUC (95% CI)
APAP-CYS	2.18 mg (1.38–3.68)	8.2 mg (6.43–15.8)	<.0001	0.87 (0.71–1.02)
Sum CYP Metabolites (APAP-CYS + APAP-Mer)	2.44 mg (1.54–4.15)	9.38 mg (7.64–16.7)	<.0001	0.87 (0.70–1.03)
APAP-Glu	140.5 mg (104–253)	181 mg (134–311)	.1488 (NS)	0.64 (0.47–0.81)
APAP-Sul	18.2 mg (13.2–25.9)	15.6 mg (7.2–23)	.3726 (NS)	0.59 (0.38–0.80)
APAP-CYS/Total Metabolites	1.2% (0.8–1.8)	4.2% (2.7–4.6%)	<.0001	0.90 (0.82–0.97)
APAP-CYS/APAP-Sul	12.7% (7.2–19.2)	99.5% (74.1–119%)	.0004	0.82 (0.62–1.03)
ALT	20 (14–28)	78 (41–158)	.0002	0.84 (0.66–1.01)

ingestion. Eleven patients had a peak ALT >150 U/l of which nine developed hepatotoxicity (ALT >1000 U/l). Of these eleven, four had an ALT <50 U/l on presentation. Results are shown in the table, those who developed ALI had significantly higher APAP-Cys and sum CYP metabolites. CYP metabolites on its own or expressed as a fraction APAP-Sul or total metabolites, all had very good predictive performance (ROC-AUC >0.8).

Conclusion: This study similarly to Vliegenthart et al. 2017, found that patients who developed ALI had higher absolute concentrations and proportion of CYP pathway acetaminophen metabolites compared to those who didn't. All were good predictors of ALI, but data from more patients are required to determine which CYP metabolite marker is the best predictor for ALI. Data is required from more patients who present with a normal ALT and yet develop hepatotoxicity, as early recognition of this group of high-risk patients might lead to improved treatment algorithms.

KEYWORDS Acetaminophen; metabolites; overdose

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8. The effects of activated charcoal (AC) and polyethylene glycol electrolyte solution (PEG-ELS) on bupropion XL concentration *in vitro*

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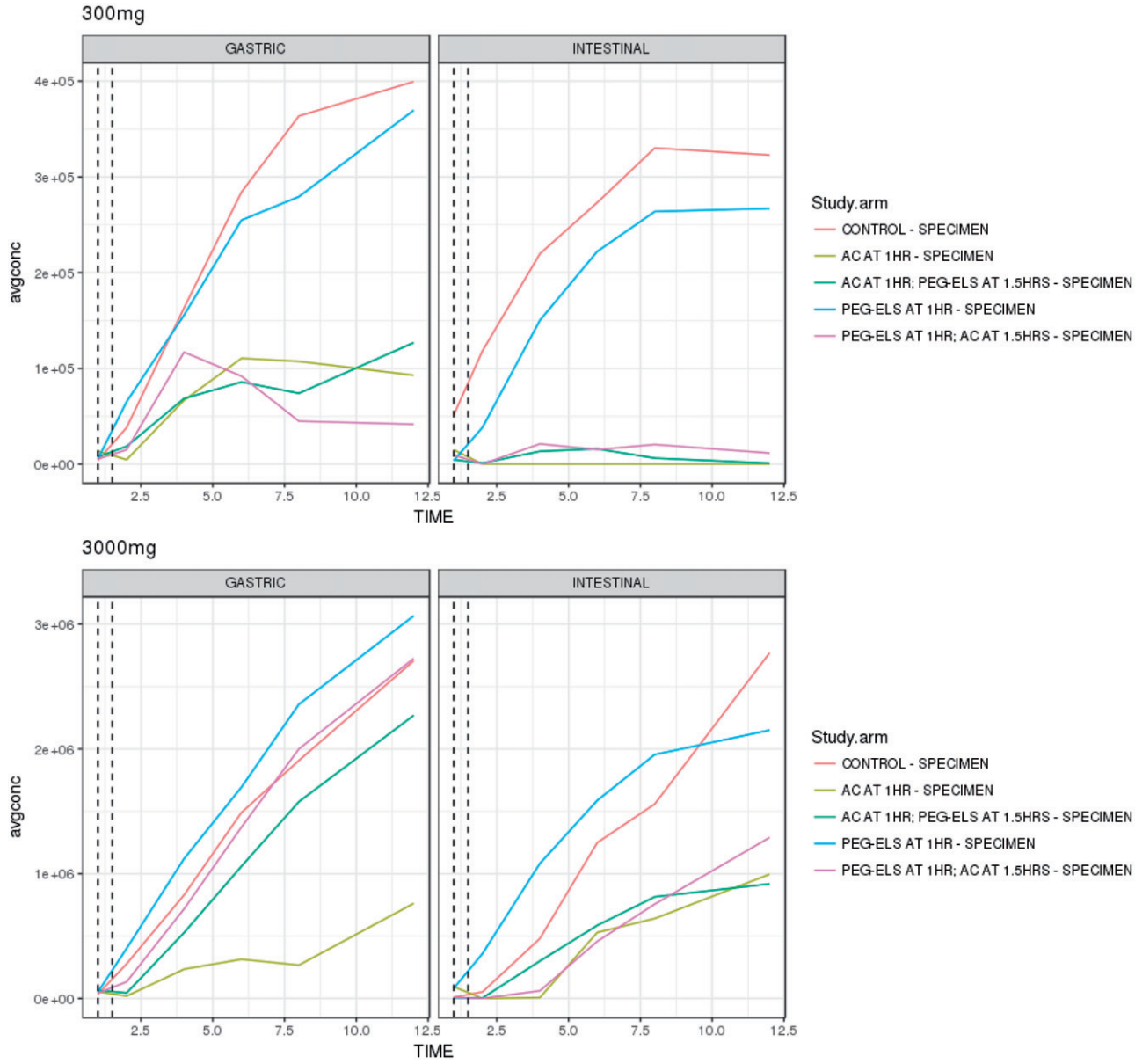

Figure 1 and 2. Time series of the average concentration of bupropion in solution for one of five experimental arms: (1) Control; (2) AC at 1 h; (2) AC at 1 h + PEGS-ELS at 1.5 h; (4) PEGS at 1 h; (5) PEGS at 1 h + AC at 1.5 h. Graphs are presented by bupropion dosage (300 mg and 3000 mg) and medium (gastric or intestinal).

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Introduction: Overdoses of bupropion XL can result in severe morbidity and mortality. Prolonged toxicity may be related to slow drug release through a complex drug delivery system (DDS). Treatment of bupropion toxicity is largely supportive and includes activated charcoal (AC) and/or whole-bowel irrigation (WBI) with PEG-ELS. However, data are lacking on bupropion adsorption to AC, and the effects of PEG-ELS on drug release from the DDS and on AC adsorption.
Aims: The primary aim of this study is to measure the *in vitro* effects of AC and PEG-ELS in a simulated human gastrointestinal model at therapeutic dosing and mimicking an overdose scenario.
Methods: There were two main series; simulated gastric and simulated intestinal contents. Each series had five arms done in triplicate at a final volume of 500 ml at 37 °C, and repeated at two bupropion XL doses; 300 mg and 3000 mg. Study arms were: (1) bupropion only; (2) bupropion plus 50 g AC added at 1 h (AC Only); (3) bupropion plus 250 ml PEG-ELS added at 1 h (PEG Only); (4) bupropion plus 50 g AC added at 1 h and 250 ml PEG-ELS added at 1.5 h; (5) bupropion plus 250 ml PEG-ELS added at 1 h and 50 g AC added at 1.5 h. Samples were collected at 0 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, and 24 h to determine the bupropion concentration using HPLC. Areas under the isotherm curve at 8 h (AUC 8 h) were calculated and overall differences in mean AUC 8 h were tested using analysis of variance; post-hoc pairwise comparisons were performed using Tukey student *t*-tests. All analysis was stratified by initial bupropion concentration.
Results: At the 300 mg dose (Figure 1), compared to control, the study arms (AC, PEG or both) were all associated with differences in the AUC 8 h ($p < .01$) and not altered by fluid pH ($p = .513$). Also at this dose, all experimental arms had a lower AUC 8 h compared to control, though the effect size for the PEG Only arm was smaller ($p = .02$).
At the 3000 mg dose (Figure 2), the mean AUC 8 h was lowest in the AC Only group and highest in the PEG Only group. Compared to control, the AC Only group had the lowest AUC 8 h in both types of fluids ($p < .01$). The experimental arm with PEG added to AC lowered AUC 8 h in intestinal fluid ($p < .01$) but not in gastric fluid ($p = .052$). Both experimental arms that started with PEG were not significantly different compared to control ($p > .05$). Overall, AUC's were higher in gastric fluid compared to intestinal fluid ($p < .01$).
Conclusions: In this *in vitro* model, AC adsorbs bupropion, though that adsorption appears to be affected by the specific media (gastric versus intestinal fluid). These results also suggest that PEG-ELS interferes with AC adsorption of bupropion. The clinical significance of this is unknown. This study was partially funded by a research grant from the American Academy of Clinical Toxicology.

KEYWORDS Bupropion; activated charcoal; whole bowel irrigation

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9. Capillary blood clotting time in detecting venom-induced consumption coagulopathy (VICC)

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Background: VICC is the commonest life-threatening systemic effect of snake envenomation. Early diagnosis of VICC is essential for early administration of antivenom. The international normalised ratio (INR) is the most appropriate test to detect VICC, but is unavailable in most resource poor settings, where snakebites are common. The 20-min Whole Blood Clotting Test (WBCT20) is used in such settings to detect VICC, which is cheap but less sensitive, takes 20 min and still requires venepuncture. The aim of this study is to test the performance of a 10-min capillary whole blood clotting test compared to INR and WBCT20.
Methods: Patients with an authenticated or suspected snakebite admitted to a tertiary care hospital in Sri Lanka during August–October 2017 were enrolled. Capillary blood clotting time, INR, WBCT20 and plasma fibrinogen were serially measured in all patients on 1, 4, 8, 12 and 24 h from the bite and daily thereafter. In each patient, corresponding data from the time point which had the highest INR were taken for diagnosis of VICC. INR >1.5 but <12 was considered partial VICC while INR >12 (uncoagulable blood) with undetectable fibrinogen was considered complete VICC. Capillary clotting time was measured as follows. Following a finger-prick, ~2 cm capillary blood column was collected into a capillary tube. The tube was placed horizontally for 10 min while swiftly turning to the vertical position every 30 s. Time taken for stasis of the blood column was defined as capillary blood clotting time. CBCT of 10 min or more was considered a positive CBCT test. The WBCT20 was done as previously described in standardized tubes by trained research assistants.
Results: There were 92 patients including 31 Russell's viper (Daboia russelii), 27 Merrem's Hump-nosed viper (Hypnale hypnale), 7 non-venomous colubrid, and 5 common krait (Bungarus caeruleus) envenomations; the remainder were unidentified. Of that, 13 (14%) had partial VICC and another 13 (14%) had complete VICC, while the rest had no VICC based on the INR. In comparison, CBCT test was positive in 13/26 VICC (9/13 complete VICC) and the WBCT20 was positive in 14/26 VICC (10/13 complete VICC) patients. Based on 230 serial samples, CBCT had a moderately positive correlation with INR (Pearson's correlation, $r = 0.537$). The median of the highest INR of patients with negative CBCT test was 1.2 (IQR: 1.1–1.3) compared to 13 (IQR: 5.1–13) in positive patients ($p = < .0001$, Mann-Whitney test). In comparison, the median of the highest INR of patients with negative WBCT20 was 1.2 (IQR: 1.1–1.4) while 13 (IQR: 1.6–13) in positive patients ($p = < .0001$, Mann-Whitney test). Sensitivity, specificity, positive and negative predictive values of diagnosing VICC by CBCT test were 50%, 100%, 100%, and 84% respectively, which compared to 54%, 94%, 78%, and 85% respectively for the WBCT20. The CBCT test was slightly better for detecting VICC.
Conclusions: CBCT is a relatively rapid, alternative test for WBCT20 which is as good for detecting VICC in snake envenoming, that does not require venpuncture. Although more accurate bedside tests are required the CBCT appears to be a better option than the WBCT20.

KEYWORDS Envenomation; coagulopathy; capillary clotting time

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10. Phospholipase A2 (PLA2) as an early indicator of envenomation in elapid snakebites (ASP-27)

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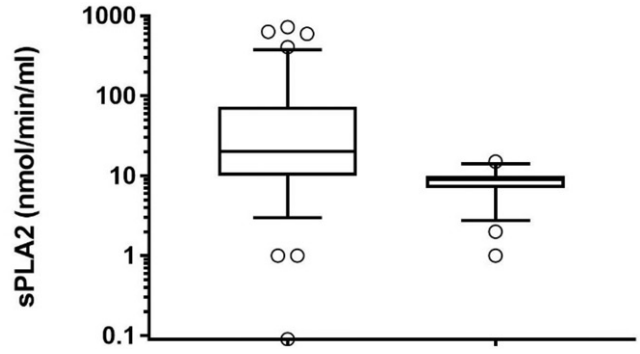

Figure 1.

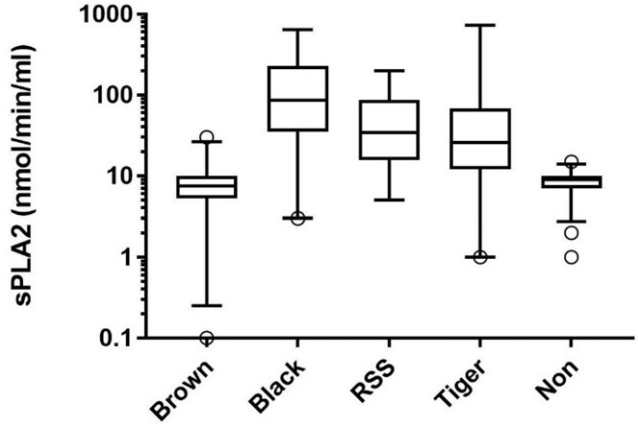

Figure 2.

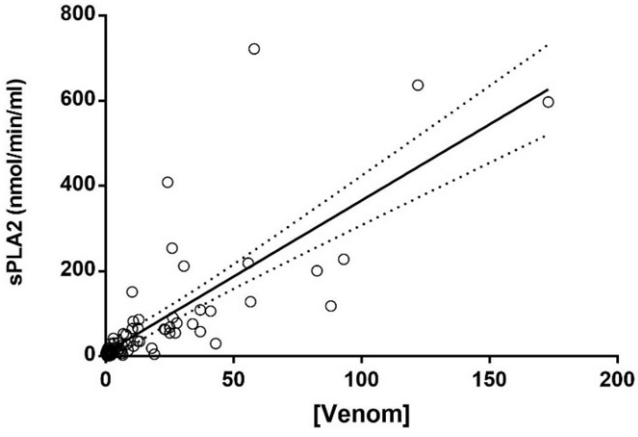

Figure 3.

Objective: Increasing evidence supports the greater effectiveness of early antivenom. Unfortunately determining if a patient is envenomated within hours of the bite is difficult and often relies on the presence of non-specific symptoms. Phospholipase A2 (PLA2) occurs in the venoms of almost all venomous snakes and has been shown to be elevated early in viper envenomation. We investigated the diagnostic value of measuring PLA2 in snakebite patients.

Methods: The Australian Snakebite Project (ASP) is a prospective observational study of snakebite patients across Australia. We included patients recruited from July 2015 to February 2017 with suspected snakebites, in which there was an early blood sample available pre-antivenom. Patient demographics, snake type, timing of the bite and clinical effects were extracted. The first serum sample collected for each patient was analysed for secretory PLA2 activity by Cayman sPLA2 assay kit (#765001Cayman Chemical Company, USA), according to manufacturer instructions. Snake identification was confirmed by expert identification or venom specific enzyme immunoassay, and venom concentration was measured in envenomated patients. PLA2 activity between envenomated and non-envenomated patients was analysed using the Kruskal-Wallis test, and predictive performance using area under the receiver-operating-characteristic curve (ROC-AUC).

Results: From 221 patients recruited to ASP over the 20 month period (median age 38 years [2–81]), 83 had no blood available, 84 were envenomated and 54 were non-envenomated. The most common snake envenomation was brown snake [24], then tiger snake [19], rough-scaled snake [12] and black snake [19]. The median time to first blood sample in envenomated patients was 1.5 h (interquartile range [IQR]:1.1–2.3 h). There was a significant difference in the median PLA2 activity between non-envenomated (9 nmol/min/ml;IQR:7–10) and envenomated patients (20 nmol/min/ml;IQR:10–74, $p < .001$; Figure 1). For the major groups of snake types the median PLA2 activity for brown snakes was 8 nmol/min/ml (3–10), for tiger snake 26 nmol/min/ml (12–68), for rough-scale snake 34 nmol/min/ml (16–88) and black snakes 86 nmol/min/ml (35–228), which were all significantly different to non-envenomated patients except brown snake (Kruskal-Wallis $p < .0001$; Figure 2). There was a highly significant correlation between venom concentrations and PLA2 activity ($R2 = 0.61$; $p < .0001$; Figure 3). PLA2 activity had a good predictive value of envenomation with an AUC-ROC of 0.78 (95% confidence intervals [95%CI]:0.7–0.86), but was excellent when brown snakes were excluded, AUC-ROC of 0.90 (95%CI:0.84–0.97). There was no association between the time from bite and the PLA2 activity.

Conclusion: PLA2 activity was a good early predictor of envenomation in most Australian elapid bites, with high AUC-ROC curves. However, PLA2 activity was not different in brown snake envenomation compared to non-envenomated patients, making it poorly predictive for this snake group. Development of a bedside PLA2 activity test is a potentially useful diagnostic test in elapid bites, similar to viper bites.

KEYWORDS Snakebite; envenomation; phospholipase

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11. Prevalence of hematologic toxicity from copperhead envenomation: an observational study

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Background: Copperhead snakes (Agkistrodon contortrix) are considered the least toxic of the North American pit vipers. The reported incidence of hematologic toxicity from copperhead envenomation is variable and may not take into account regional variation in subspecies and venom toxicity. Coagulation studies are often obtained when evaluating copperhead bites, but the clinical utility of these indices are unclear. Further evaluation of the prevalence of hematologic toxicity among copperheads native to the mid-Atlantic may influence the need for laboratory workups in otherwise stable patients. The aim of this study was to determine the prevalence of hematologic toxicity due to copperhead envenomation from hospitalized patients.

Methods: This was a multi-center, retrospective cross-sectional study evaluating prevalence of hematologic toxicity following copperhead envenomation using electronic hospital data between January 1, 2006 and December 31, 2016. Patients presenting to one of three tertiary care centers with suspected copperhead envenomation were identified using medical billing codes. Cases were excluded if there was no evidence of envenomation ("dry bite"), no laboratory data available, if the encounter was only a follow-up visit, use of anticoagulation or history of liver disease. De-identified patient data including lowest reported coagulation studies were obtained. The primary outcome was to summarize the prevalence of hematologic toxicity including thrombocytopenia, elevated prothrombin or partial thromboplastin times or hypofibrinogenemia. Laboratory cutoffs for defining abnormal values included prothrombin time (PT) > 15 s, activated partial thromboplastin time (aPTT) > 36 s, platelets <140,000/mm^3 and fibrinogen <170 mg/dl.
Results: After excluding 17 patients, there were 235 cases in the final analysis. Prevalence of any hematologic toxicity was noted in 14% (95%CI 10–19%) of cases. Specific indices included: thrombocytopenia 1% (95%CI 0.4–3.7%), hypofibrinogenemia 1% (95%CI 0.1–5.3%), elevated PT 10% (95%CI 7–15%) and elevated aPTT 4% (95%CI 2–8%). All proportions were calculated based on the available data. There was no clinically significant bleeding reported in any case.
Conclusions: Hematologic abnormalities due to copperhead envenomation for patients treated in in the mid-Atlantic region were uncommon and consistent with other regionally reported data. Laboratory abnormalities were clinically insignificant and there were no instances of bleeding.

KEYWORDS Coppperhead; envenomation; coagulopathy

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12. Opioid exposures reported to the National Poison Data System: is the heroin disaster resolving?

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Background: Overuse and abuse of prescription and illicit opioids remains at the apex of US anti-drug policy. Between 2010 and 2016, opioid related overdose deaths more than doubled from 21,089 in 2010 to 42,249 in 2016. The latest data from The Centers for Disease Control and Prevention report heroin use in the United States increased 63% from 2002 to 2013. We examined this epidemic using the current US poison center exposure data for heroin and opioid analgesic exposures reported to the National Poison Data System (NPDS).
Methods: NPDS classifies drugs using a hierarchical, structured categorical system. 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. Descriptive statistics, graphical displays, smoothing spline fits, linear and non-linear regressions were performed using SAS JMP version 12.0.1 (SAS Inc., Cary, NC). To examine recent increases, we examined linear and quadratic regressions of exposures by month for January 1, 2012 to February 28, 2018. We focused on single substance exposures with a more serious outcome (medical outcome = death, major or moderate).
Results: Figure 1 shows serious single substance heroin exposures by month including the resolution of the distinct recent increase (pop) during the end of 2016 and early 2017. This pop had largely resolved by mid 2017. We examined this pop for contributors based on medical outcome, product code, and geography of reports without finding a major contributor. When we excluded the pop, the heroin exposure data were well described by a second order (quadratic) regression (Rsqr = 0.897, $p < .0001$). As shown in Figure 2, the opioids (23 GCs) and combos (10 GCs) were also well described by quadratic regressions. The table shows the number of exposures and rate of increase for each of these for these regressions. Beginning in 2015 opioid exposures began to increase, but heroin exposures were observed to begin a steady increase staring in 2012 with heroin exposure rate clearly outpacing opioids. The quadratic models show this to be

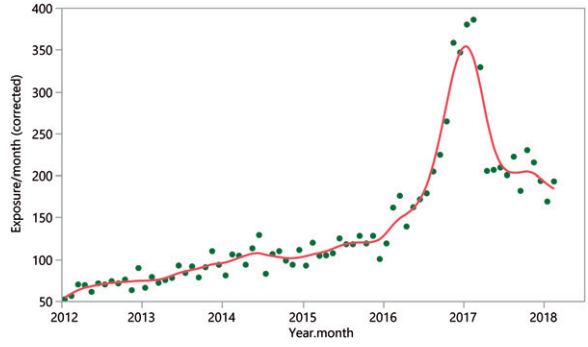

Figure 1. Single substance serious heroin exposures by month, spline fit, lambda = 0.005.

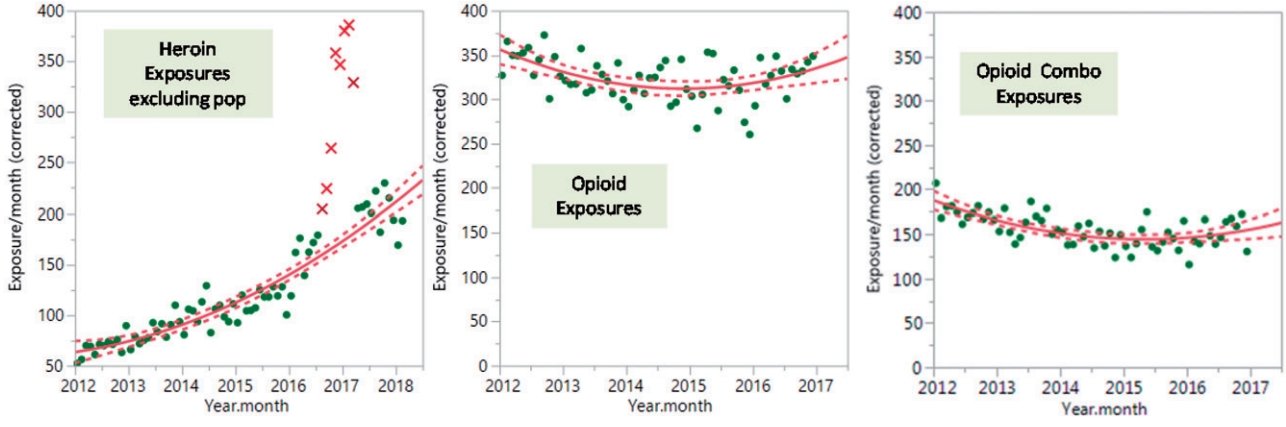

Figure 2. Single substance serious heroin, opioid and combo exposures by month, quadratic regressions and 95% confidence intervals.

	Model Exposure/month (more serious) [95% CI] and Rate of Increase Eposures/month per Year by Drug Group							
	Heroin (All exposures)		Heroin (single substance)		Opioids (single substance)		Combos (single substance)	
Jan 1 of Year	Exposures	Increase	Exposures	Increase	Exposures	Increase	Exposures	Increase
2012	130 [112, 148]	36.3	63.3 [52.4, 74.2]	8.56	356 [340, 373]	-30.5	188 [177, 199]	-26.2
2013	167 [157, 176]	37.1	74 [68.2, 79.8]	14.0	331 [323, 339]	-20.0	166 [161, 171]	-18.3
2014	204 [196, 212]	38.0	90.3 [85.3, 95.2]	19.5	316 [308, 324]	-9.51	151 [146, 156]	-10.5
2015	243 [234, 252]	38.8	112 [107, 118]	25.0	312 [304, 320]	0.97	145 [140, 150]	-2.60
2016	282 [273, 291]	39.7	140 [134, 145]	30.5	318 [310, 326]	11.5	146 [141, 151]	5.25
2017	322 [312, 332]	40.5	173 [167, 179]	36.0	335 [318, 352]	22.0	155 [145, 166]	13.1
2018	363 [346, 380]	41.4	211 [201, 222]	41.5	362 [329, 396]	32.4	172 [151, 194]	21.0
2019	405 [374, 435]	42.2	256 [237, 274]	47.0	400 [343, 457]	42.9	197 [161, 234]	28.8
2020	448 [399, 496]	43.1	305 [276, 335]	52.5	448 [361, 535]	53.4	230 [174, 286]	36.7

the case, but such is predicted to change in 2020 with opioids outpacing heroin.

Conclusions: Evaluation of change over time for heroin and opioid exposures demonstrate how NPDS data can be predictive as well as historical. Although heroin exposures were clearly higher than opioids, the data suggest this trend may reverse by 2020. Therefore, both heroin and opioids are expected to be a continuing exposure problem for the US. NPDS data is not only a barometer of exposures with its 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, but also has predictive properties when well described by simple regression models.

KEYWORDS Heroin; opioid epidemic; National Poison Data System

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13. Serious loperamide exposures and cardiotoxicity, 2000–2017

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Background: Loperamide, an over-the-counter antidiarrheal, exerts its therapeutic effect via mu-opioid receptor agonism, calcium channel blockade and calmodulin inhibition. Due to its high extraction ratio and p-glycoprotein drug efflux, loperamide exerts minimal central opioid effects at therapeutic doses. Increasing abuse may reflect its low cost and relative accessibility. In addition to opioid toxicity, loperamide abuse also causes cardiac conduction disturbances including QRS and QTc prolongation and fatal arrhythmias. We examined loperamide exposure change over time and cardiotoxicity compared to heroin, propoxyphene, and other opioids.

Methods: We extracted National Poison Data System (NPDS) single substance exposure data for 35 generic codes (22 opioids, 10 opioid-combinations, heroin and loperamide) for January 1, 2000 to December 31, 2017 for exposures categorized as serious (medical outcome = moderate, major or death). We extracted individual clinical effects and defined cardiotoxicity as a patient with one or more of: asystole, bradycardia, cardiac arrest, conduction disturbance, other arrhythmia, or VT/VFib. StatsDirect (3.1.14) provided Forest plots and odds ratios; SAS JMP (12.0.1) provided data handling, descriptive statistics, graphs and regressions.

Results: Serious exposures for 2000–2017 numbered 99,236 including: 762 loperamide, 2857 propoxyphene, 14,866 heroin, 54,154 opioids, and 26,366 opioid-combos. Figure 1 shows the increase in loperamide exposures, particularly in the last 24 months. Figure 2 shows the proportion of cardiotoxicity and 95% confidence intervals by generic code. Based on a similar rate of

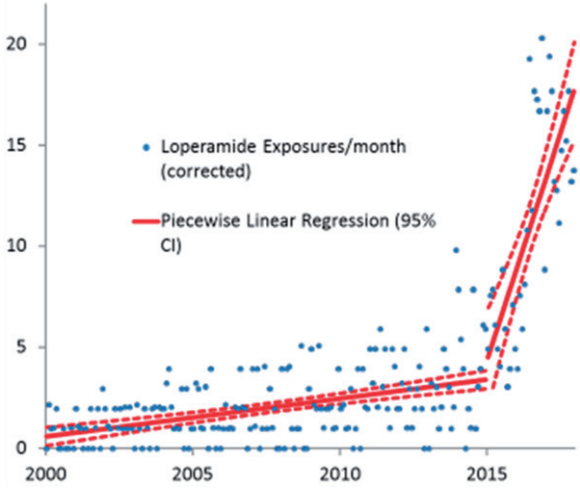

Figure 1. Single substance serious loperamide exposures by month.

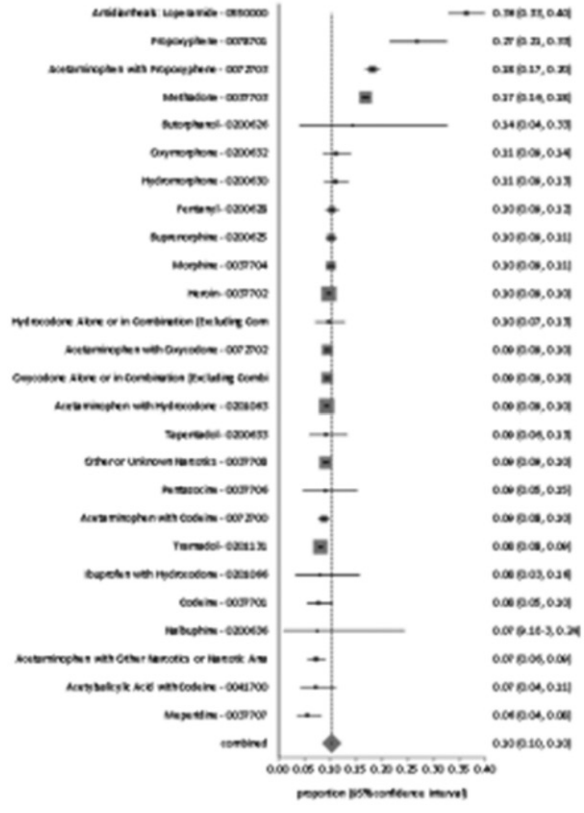

Figure 2. Proportion of cardiotoxicity by generic code.

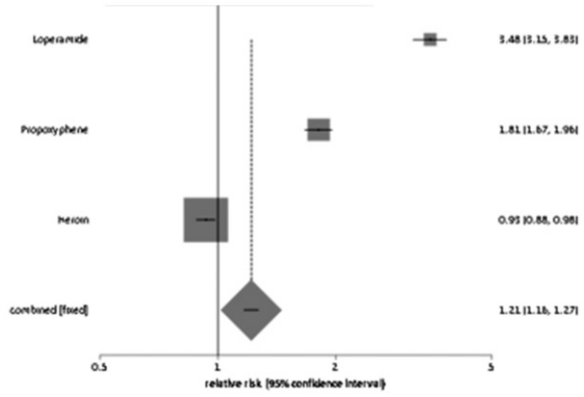

Figure 3. Relative risk of cardiotoxicity by drug group.

cardiotoxicity among the opioids and opioid-combos we combined them into a control group. Figure 3 shows the relative risk of cardiotoxicity.

Conclusion: These data demonstrate the increasing incidence of serious loperamide exposures reported to poison centers and most importantly, corroborate that loperamide is a cardiac toxin and results in more significant cardiovascular outcomes compared to other opioids including methadone. The FDA has recently begun to evaluate and restrict package size and quantity for over the counter sales of loperamide and this data will help in describing the severity of risk of toxicity. Our data demonstrates this higher risk of loperamide cardiotoxicity compared to other opioids and we believe that further limitations including the placement of loperamide behind the counter should be considered.

KEYWORDS Loperamide; cardiac toxicity; opioids

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14. Outbreak of coagulopathy associated with synthetic cannabinoid use

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Table 1. Sites of bleeding.

Site	*n*
Hematuria	98
Epistaxis	35
Mucocutaneous	24
Hematemesis	23
GI tract	19
Hemoptysis	18
Ecchymoses	16
Hematoma	8
Vaginal	6
Laceration	2
Intracranial	1

Background: In the spring of 2018 a regional poison center (RPC) became aware of a large cohort of patients with coagulopathy and associated bleeding after smoking synthetic cannabinoids (SCs). We describe the characteristics of this unusual outbreak and our experience managing these cases.

Methods: We performed a retrospective review of RPC cases from March 11 to April 18, 2018 of cases coded as exposures to THC homologs. Our case definition is suspected SC use, international normalized ratio (INR) >3, and no alternative explanation of coagulopathy. Trained investigators abstracted the following data: history of SC use, presenting health care facility, presenting INR, presenting hemoglobin (hgb), gender, age, reported bleeding site, blood products administered (fresh frozen plasma [FFP], 4-factor prothrombin complex concentrate [4-PCC], cryoprecipitate [cryo], factor eight inhibitor bypassing activity [FEIBA], packed red blood cells [PRBC]), SC product name, duration of hospitalization, dosing of vitamin K1 recommended upon case closure, and confirmatory testing for anticoagulants and SCs.

Results: A total of 168 cases were searched with 135 cases meeting inclusion criteria. One hundred thirty-three (133) cases had complete data and were analyzed. The outbreak was centered around two distinct metropolitan areas 130 miles apart (area 1 $n=78$, area 2 $n=52$). On presentation 91% of cases had an INR of >10. The median initial hgb was 14.9 g/dl (range 3.8–19). Seventy-four percent (74%) of cases were male. Most patients were 18–44 years (77%), while 19% of cases were 45–60 years and 2% were >60 years. There were no pediatric (<18 years) exposures. Reported sources of bleeding are listed in Table 1. Blood products administered are listed in Table 2. A specific product name was only available in 21.8% of cases. Patients identified use of 18 different products and no single product has emerged as a common source of exposure. Cases were typically followed from admission until discharge for a median of 3 d (range 0–13); however, 27 left against medical advice, 6 were lost to follow-up, and 1 expired. The divided daily dose of oral vitamin K1 recommended upon discharge varied (median 100 mg, range 20–200 mg) depending on trend of INR, reliability of outpatient follow-up, and if the patient had left against medical advice. Qualitative high-performance liquid chromatography/tandem mass spectrometry confirmation for coumarin anticoagulants on serum and SCs on serum and urine were obtained and presented in Table 3 (0406SP, 4282SP, 4283U NMS Labs, Willow Grove, PA).

Conclusion: We report a large-scale outbreak of bleeding complications associated with SCs. Patients presented with bleeding from varied sites, often required blood products, factor replacement, and high dose vitamin K1 for stabilization. Confirmatory

Table 2. Blood products transfused.

Blood product	Cases	Units transfused (median, range)
PRBC	7	2 (1–4)
FFP	56	3.5 (1–6)
4-PCC	5	
Cryo	3	
FEIBA	1	

Table 3. Confirmatory testing.

Patient	Anticoagulant panel	Urine SC panel	Serum SC panel
1	Brodificoum	AMB-FUBINACA metabolite	AMB-FUBINACA, FUB-APINACA
2	Brodificoum, difenacoum	AMB-FUBINACA metabolite	FUB-APINACA
3	Brodificoum, difenacoum	AMB-FUBINACA metabolite	AMB-FUBINACA, FUB-APINACA
4	Brodificoum, difenacoum	None detected	None detected
5	Brodificoum, difenacoum	AMB-FUBINACA metabolite	FUB-APINACA
6	Brodificoum, difenacoum	AMB-FUBINACA metabolite	FUB-APINACA
7	Brodificoum, difenacoum	5F-AMB-PINACA metabolite	–
8	Brodificoum, difenacoum	AMB-FUBINACA metabolite	–
9	Brodificoum, difenacoum	–	–
10	Brodificoum, bromadialone	–	–

testing revealed more than one synthetic cannabinoid and three long-acting anticoagulants with the most common being brodifacoum.

KEYWORDS Synthetic cannabinoid; brodifacoum; rodenticide

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15. Bystander naloxone administration for undifferentiated opioid overdose in the era of non-pharmaceutical fentanyl: a retrospective study of a regional poison center data

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Background: Various organizations have implemented bystander naloxone (BNAL) programs to combat the opioid epidemic. However, opioid misuse and opioid-overdose deaths continue to increase annually. Currently, a growing supply of heroin is adulterated with non-pharmaceutical fentanyl (NPF) or other synthetic opioids. Intranasal administration of naloxone (2 mg) is sufficient to reverse heroin-induced ventilatory depression. However, it is unclear if higher doses are required to reverse the ventilatory depression induced by NPF and its analogs. Therefore, the purpose of this study was to estimate the trend of BNAL dose required to reverse undifferentiated opioid-induced ventilatory depression. We hypothesized that larger naloxone dose was administered to reverse undifferentiated opioid-induced ventilatory depression between 2015 and 2017.
Methods: This is a retrospective study of suspected opioid overdose patients who received BNAL. Bystanders were defined as non-medical or non-EMS providers. All reported cases of BNAL administration to the regional poison control center for suspected opioid overdose were systematically identified from January 1, 2015 to August 30, 2017. Research members abstracted data from the case narrative of all identified cases. Descriptive analysis was performed to determine the frequencies. ANOVA with Tukey test and Cochran-Armitage trend test were performed to compare the change in means and frequencies between 2015 and 2017. Our primary outcome was the mean BNAL dose required to reverse the opioid-induced ventilatory depression. Secondary outcomes were the reversal rate of opioid-induced ventilatory and central nervous system (CNS) depression, transport to health care facility (HCF), and patient disposition.
Results: One thousand one hundred and fifty-eight BNAL cases were identified. The male cases were 68.8% ($n = 797$) and the mean age was 34.3 years. The largest age group to receive BNAL was 20–29 years ($n = 478$; 43.1%). One thousand and twenty-one cases (88.2%) had ventilatory depression while 1114 (96.2%) were unresponsive. Additional 41 cases had depressed mental status. One hundred and sixteen cases were in cardiopulmonary arrest prior to BNAL administration. Law enforcement administered 91.6% ($n = 1061$) of the BNAL and the most common route was intranasal ($n = 1075$; 92.8%). The majority of the cases received single BNAL dose (81.6%; $n = 924$); an additional 179 cases (15.9%) received a second dose. The overall reversal rate of opioid-induced ventilatory or CNS depression by BNAL was 77.3% ($n = 887$). Between 2015 and 2017, administered BNAL dose (mean) increased from 2.16 mg to 3.66 mg ($p < .05$) while clinical reversal rate decreased from 84.2% to 72.7% ($p = .0003$). Ventilation improved or normalized in 86.7% ($n = 740$) while 646 (55.8%) cases regained normal mental status. Nine hundred and eighteen cases were transported to a HCF while 197 were treated at the scene only. Of those transported to a HCF, 651 (70.9%) were treated and released from a HCF while 100 (10.9%) were hospitalized. Disposition data on 154 transported cases were not available. Twenty-nine cased died at a HCF while 35 died at the scene.
Conclusions: BNAL administration reversed the majority of undifferentiated opioid intoxication. Between 2015 and 2017, increasing doses of BNAL was administered while the reversal rate of opioid-induced ventilatory and CNS depression decreased. This change in trend is likely due to the increasing availability of NPF.

KEYWORDS Bystander naloxone; opioid overdose; non-pharmaceutical fentanyl

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16. Comparison of pediatric buprenorphine and methadone exposures reported to The U.S. Poison Centers, 2013–2016

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Background: Buprenorphine and methadone are used for treating opioid use disorder. Buprenorphine prescriptions have increased dramatically in the last decade within the United States while methadone continues to be used widely. The risk of accidental exposures to these medications, although preventable, does occur among the pediatric population. We investigated the trends and characteristics of buprenorphine and methadone exposures in this population.
Methods: We identified pediatric exposures, defined as individuals aged ≤19 years, to buprenorphine and methadone reported to the National Poison Data System (NPDS) from 2013 to 2016. Descriptive statistics were used to compare the characteristics of pediatric buprenorphine and methadone exposures. Poisson regression models were used to evaluate the trends in the number and rates of exposures with the year as the independent variable. The percentage changes during the study period were reported for each exposure agent, further stratified by select characteristics. Case fatality rates were calculated for both medications. Incidence (per 100,000 pediatric populations) for pediatric buprenorphine exposures at the state- and national-level was calculated.
Results: Pediatric buprenorphine exposures increased by 11.8% (95% CI: 3.1%, 21.2%, $p = .03$) from 2013 (1097) to 2016 (1226). Pediatric methadone calls decreased by 18.6% (95% CI: −28.6%, −7.0%, $p = .01$) from 2013 (486) to 2016 (396). Children <=5 years constituted the highest percentage of exposures for both buprenorphine and methadone in the pediatric age group (84.1% and 59.1%, respectively). Most exposures occurred in a residence (95.6% and 92.6%, respectively) and via ingestion (95.2% and 92.8%, respectively). Unintentional exposures accounted for the majority of the buprenorphine (86.9%) and

methadone (62.4%) exposures. Abuse (6.3% versus 13.2%) and suspected suicide (2.5% versus 12.5%) were less common in the buprenorphine exposures. Buprenorphine demonstrated a higher proportion of single substance exposures (89.8% versus 69.4%). Major clinical effects were demonstrated in 2.3% of buprenorphine exposures and 6 deaths were reported, 4 of which occurred in children <=5 years. Major clinical effects (13.0%) were more frequent with methadone, with the case fatality rate being higher in methadone exposures (1.0% versus 0.1%). Approximately 25.0% of the buprenorphine and 52.0% of methadone exposures with major effects were teenagers. A greater proportion of methadone cases were admitted to the critical care unit (CCU) (23.2% versus 35.4%). Unintentional buprenorphine exposures increased by 18.8% and there was a significant increase in patients admitted to the CCU (34.8%). Within the methadone group, exposures among teenagers decreased by 31.9% while intentional abuse declined significantly (50.0%). Suboxone film was the most common product reported for buprenorphine exposures. West Virginia demonstrated the highest incidence of buprenorphine exposures.

Conclusions: Pediatric buprenorphine exposures increased from 2013 to 2016, but demonstrated less severe effects compared to methadone exposures which decreased during the study. The observed increase in the buprenorphine exposures in our study parallels the changing prescribing practices and growing efforts to increase the patient access. Pediatric exposures and fatalities further highlight the need for greater attention to managing prescriptions and increasing patient awareness regarding the safe storage and adverse effects of these medications.

KEYWORDS Buprenorphine; methadone; pediatrics

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17. Renal injury or lab error? Interpretation of renal function studies following a massive dosing error of Vitamin C in sepsis

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Background: The Marik Protocol1 is a recently described protocol for sepsis treatment that involves administration of hydrocortisone, thiamine, and high doses of vitamin C intravenously. The authors of the Marik Protocol state a total daily dose of 6 g (1.5 g q6h) of vitamin C should be sufficient to see a mortality improvement but not increase the risk or precipitating oxalate crystals that lead to kidney injury. We report a case of a significant dosing error involving the Marik Protocol that led to an apparent reversible kidney injury.

Case report: A 58-year-old woman with a history of emphysema was admitted to the intensive care unit with a diagnosis of community acquired pneumonia, hypoxic respiratory failure requiring intubation, and sepsis. She was treated with vancomycin, gentamycin, as well as hydrocortisone, thiamine, and 225 g (instead of 1.5 g) of Vitamin C intravenously due to a dosing error. She did not have any hypotension and had a normal creatinine. The following day she developed hypernatremia (Na 172 meq/l), hypokalemia (2.2 meq/l), hyperchloridemia (11 meq/l) and acute kidney injury (BUN 22 mg/dl, Cr 3.1 mg/dl). Urine output was maintained. Her Vitamin C, vancomycin, and gentamycin were discontinued. The following day her creatinine decreased to 1.3 and other electrolytes began to normalize. On the following day her creatinine returned to 0.9 and her vancomycin and gentamycin were restarted. She was extubated and recovered with no additional kidney injury.

Case Discussion: High doses of intravenous vitamin C have been associated with oxalate nephropathy, though this adverse event associated with the use of a newly introduced sepsis protocol has not been well delineated. Additionally, high doses of Vitamin C have been noted to interfere with some chemistry analyzers, resulting in elevated sodium, potassium, calcium, and creatinine, and reported decreases in chloride, total bilirubin, uric acid, total cholesterol, triglyceride, ammonia, and lactate concentrations. This is thought to be due to interference with the redox reactions involved with these tests. Although our case is confounded by the potentially nephrotoxic antibiotics Vancomycin and Gentamycin, peak and trough measurements were within normal limits in this patient and she maintained normal urine output. The diffuse laboratory abnormalities and her rapid return to baseline suggest this was most likely instrument interference.

Conclusions: Physicians and pharmacists should be aware of the potential for oxalate nephropathy as well as potential interference with laboratory analyzers dependent on redox reactions when interpreting laboratory findings associated with high concentrations of Vitamin C. This is especially important in sepsis populations in which kidney injury and significant electrolyte abnormalities are often encountered and treatment decisions based on laboratory interference can have profound impacts.

KEYWORDS Vitamin C; ascorbic acid; renal failure

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18. Adverse effects associated with adult uninttional ingestions of bupropion reported to four US Poison Centers

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Background: Bupropion is a frequently used psychoactive medication that in excessive doses causes altered mental status (AMS), seizures and dysrhythmias. Daily doses of more than 450 mg/day have been reported to have a marked increase in the incidence of seizures. Guidance for home management of bupropion therapeutic accidents is lacking. Specifically, there is a need for estimate of seizure risk and determination if minor symptoms are harbingers of more concerning clinical effects.

Methods: A retrospective review of adult, non-chronic, unintentional therapeutic error, single substance bupropion ingestions with known outcome reported to four poison centers from January 1, 2004 to 31 December, 2016. Cases where the error dose was taken over more than 4 h and cases with incorrect reason or route were excluded. All case notes were reviewed by two researchers who reached agreement on all fields. Data included age, gender, single error dose, total bupropion dose over 18 h, PMHx, management site, observation time, presence of an out-of-hospital concerning event (defined as a clinical effect that was unexpected, concerning or caused harm), jittery/anxious/agitated (a grouped clinical effect), AMS, tachycardia/palpitations, seizures, dysrhythmias and time to develop seizures and/or dysrhythmias. The total error dose used in the analysis was the total bupropion dose over 18 h if it was an extended release

preparation; otherwise the single error dose was used. Continuous variables were expressed as ±1 standard deviation; Student t and Fisher's exact tests were used for statistical significance.
Results: There were 642 included cases; 151 cases were excluded after review. Median age was 42 years and 76% were female. Cases were predominantly managed at home (55.9%); outcomes were no effect (49.8%), minor (45.6%) and moderate (4.5%). The average reported dose for no effect/minor was 692 (±296) mg, and for moderate was 1231 (±808) mg; this difference was significant ($p < .001$). Mean observation time was 13.2 (±11.8) h. Seizures occurred in four patients with mean onset time of 9.6 h [range 2–21.5 h]; one patient had 2+ seizures and none had any PMHx believed contributory. Patients were jittery/anxious/agitated in 75% of cases that developed seizure(s) and only 28% of cases that did not have a seizure; this difference was not significant ($p = .07$). The median reported dose in patients who seized was 900 mg [range 600 mg–3000 mg]. The probability of developing seizures in patients with dose of 600 mg–1200 mg was 0.6% [95% CI 0.1%–1.8%]. The probability of having an out-of-hospital concerning event (including seizure) with reported dose of 600 mg–1200 mg was 1.6% [95% CI 0.7%–3.2%]; of note, there were two out-of-hospital concerning events with doses ≤450 mg. Tachycardia/palpitations was reported in 12% of cases; more serious dysrhythmias were not reported.
Conclusions: Outcomes from unintentional adult ingestions of bupropion are overall mild and appear to be at least in part, dose related. Depending on how risk-averse the caregiver and the patient are, home management may be an option with doses up to 1200 mg in an appropriate patient population.

KEYWORDS Bupropion; medication error; seizure

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19. Inadvertent ocular exposures secondary to e-liquid misuse

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Background: "Vaping fluids" are often purchased in refill bottles with varying concentrations of nicotine that are used to fill the electronic cigarette cartridge. There are no standardized tip or dropper for e-liquid refill bottles. Most manufacturers make refill bottles with either a needle tip or dropper cap that can easily fill a variety of vaping devices. Vaping refill bottles may physically appear similar to ophthalmic drops. There is little published data on ocular exposures to concentrated nicotine-containing fluid.
Methods: A single Poison Center database was queried from July 1, 2014 to December 31, 2017 for cases with "nicotine" listed in the exposure data field. Inclusion criteria: ocular exposure to e-cigarette nicotine refill bottle.
Case reports: Seven cases of e-liquid ocular exposures were reported to the poison center in this 3.5 year period. In all seven cases, a drop of e-liquid was inadvertently administered into their eye thinking it was their own eye drops. One individual mistook the e-liquid refill bottle for their saline eye drops. Another individual mistakenly administered e-liquid thinking it was their antibiotic eye drops recently prescribed for suspected bacterial conjunctivitis. In the remaining five cases, the eye drop product was not reported. Reported symptoms included eye redness ($n = 4$), pain ($n = 5$), and blurry vision ($n = 2$). One individual was asymptomatic after the exposure. Four individuals were wearing contact lenses at the time of the exposure. All individuals irrigated their eyes with water ($n = 6$) or saline ($n = 1$) soon after realizing their mistake. Those wearing contact lenses immediately removed them following the exposure. Symptoms resolved or significantly improved after irrigation.
Discussion: This retrospective review describes six incidents of mild ocular chemical injury caused by inadvertent administration of e-liquid into the eye instead of eye drops. One individual in this series was asymptomatic following the ocular exposure. All patients were managed at home, suffered only minor and temporary symptoms which resolved with water or saline irrigation. These cases suggest that individuals who wear contact lenses and those using therapeutic eye drops may be at risk of inadvertent ocular injury from e-cigarette liquid. The similarities between the size and shape of the eye drop bottles and e-liquid refill bottles is likely the main contributing factor. These bottles contain no warnings about the risk of unintentional ocular exposure or safety advice if the liquid comes into contact with the eyes.
Conclusion: We would like to increase awareness of this potential risk that may lead to inadvertent ocular chemical injury. Mechanisms to reduce the likelihood of ocular exposures, such as regulation of the mechanism of refill containers and product warning labels, may mitigate this potential hazard.

KEYWORDS E-cigarette liquid; ocular exposure; misuse

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20. Inadvertent administration of intrathecal tranexamic acid

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Background: Tranexamic acid (TXA) is a commonly used medication to treat or prevent excessive bleeding. It is typically administered for a variety of medical indications such as trauma, surgery, menorrhagia and dental bleeding by intravenous (IV), topical or oral routes depending on its use. Side effects are rare with appropriate usage. This case report details the inadvertent administration of tranexamic acid into the intrathecal space, a rare but significant cause of morbidity and mortality.
Case report: A 63-year-old male with history of sclerosing cholangitis and osteoarthritis was scheduled for an elective total knee replacement. During spinal anesthesia, 200 mg of tranexamic acid was inadvertently infused into the intrathecal space instead of the intended bupivicaine. The patient exhibited significant uncontrolled full body myoclonic jerking motions but was able to follow commands when these were occurring. The patient was initially given 2 doses of 2 mg midazolam IV, which temporarily improved his symptoms. The patient at this time had a heart rate ranging from 150 to 190 bpm, blood pressure 180–194/89–109 mmHg, respiratory rate greater than 20 breaths per min and oxygen saturations as low as 75%. The patient was intubated using rapid sequence induction due to hypoxia and need for chemical sedation to control his neuromuscular agitation. He received 4 mg of midazolam IV, 50 mg of propofol IV and 100 mg of rocuronium IV for intubation. He was admitted to the ICU and maintained on propofol infusion starting at 100 mcg/kg/h to control the myoclonic jerking and fentanyl at 50 mcg/h to control pain from the muscle contractions. He was also given intermittent labetalol doses to control hypertension. The patient was seen by neurology who believed the myoclonic jerks were due to the tranexamic acid due to the patient's lack of prior neurologic history and temporal association of symptom onset; an EEG was not performed. The patient demonstrated gradual improvement over the following 3 d as evident by

decreasing full body myoclonic jerking and eventually full neurologic recovery as sedation was weaned.
Case Discussion: The literature shows that TXA is both a glycine and GABA antagonist. This can lead to both seizure activity and significant myoclonic contractions with minimal stimulation. Case reports have reported death from intrathecal TXA, which appear to be due to cardiovascular collapse that occurs after extremely elevated heart rate and blood pressure of unclear mechanism. Often these patients have demonstrated episodes of ventricular fibrillation, which is resistant to standard medications and cardioversion. Some early bench research shows that propofol decreases the GABA excitation caused by tranexamic acid and the case reports with survivors all had large doses of propofol, benzodiazepines or prolonged courses of volatile anesthetics. Our patient did not exhibit any malignant arrhythmias and symptoms were controlled with intensive supportive care. Many case reports with good outcomes shared similar features of intensive supportive care and symptom control.
Conclusions: This is an infrequent cause of complications due to intrathecal administration of TXA which demonstrated survival and excellent neurological outcome with early intubation and chemical sedation.

KEYWORDS Tranexamic acid; intrathecal; seizure

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21. Reasons for calls from nursing homes to a national poisons centre

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Background: The number of calls from nursing homes to our national poisons centre has been increasing during the last decade. The needs of such institutions when calling for poisons information are expected to be specific for the caring staff and their patients. In order to better understand the needs of nursing home staff we aimed to analyse the reasons for their calls to enable the poisons centre to improve its service for this caller group.
Methods: All calls from nursing homes to the national poisons centre from January to December 2016 were included in the analysis. Nursing homes are defined as non-hospital institutions where medical care is provided, mostly long-term. The analysis included the circumstances of exposure and the agents exposed with.
Results: In 2016 the national poisons centre received 566 inquiries from nursing homes (1.4% of all calls). Forty-four of these were calls without exposure, and the remaining 522 calls concerned 509 individual patients, mostly adults (86.8%, sex ratio f:m = 1.07). Of the 67 children 19 were <6-years-old, 14 between 6 and 12-years-old, and 29 between 12 and 16–years-old. Fifty percent of inquiries came in during out-of-office hours (17:00–07:00) irrespective of the day of the week. Three hundred and forty of these 509 cases (66.8%) were unintentional ($n = 279$) or intentional ($n = 61$) toxic exposures caused by the patients themselves, 167 cases were medication errors by the nursing home staff, and 2 cases were other medication issues. Medication errors included: wrong dose administered ($n = 8$), inadvertent repeated administration of the same dose ($n = 18$), administration to the wrong patient ($n = 45$), administration of the wrong medication ($n = 92$), wrong route ($n = 2$), administration of a medication with outdated shelf-life ($n = 1$), and adverse drug reactions ($n = 1$). In 13 cases the exposed individuals were members of the staff. The involved agents included medications ($n = 304$), chemicals ($n = 114$), cosmetics ($n = 40$), plants ($n = 23$), illicit and recreational drugs ($n = 10$), mushrooms ($n = 5$), food ($n = 8$) and other agents (5). The route of exposure in these 509 cases was oral ($n = 471$), ocular ($n = 13$), inhalation ($n = 8$), other ($n = 17$). Theoretical inquiries (without exposure, $n = 44$) concerned mostly questions how to proceed with a medication outside office hours when the treating physicians were not available. Other questions were dealing with toxic risks of various agents including plants, food, and biocides.
Conclusions: Besides accidental and intentional poisoning, medication issues including mediation errors were a major reason for calls from nursing homes in 2016 in our country. A considerable percentage of calls were received outside office hours. Poisons centres can provide valuable assistance to nursing home personnel in case of toxic exposures and for problems with the administration of pharmaceuticals, particularly medication errors.

KEYWORDS Nursing homes; medication errors; poison center

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22. Unintentional therapeutic errors involving dofetilide reported to NPDS

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Background: Dofetilide (Tykosyn®) is an orally administered Class III antiarrhythmic approved by the United Stated Food and Drug Administration in 1999 for chemical cardioversion and heart rhythm control of atrial fibrillation. For 17 years, prescribers and pharmacies were required to enroll in a Risk Evaluation and Mitigation Strategy (REMS) drug safety program to ensure safe prescribing and monitoring of dofetilide. A retrospective case series of consecutive dofetilide overdoses reported to a poison center stated that small unintentional overdoses were not associated with significant clinical effects and suggested safe home management for some. The objective of this study is to analyze unintentional therapeutic errors involving dofetilide reported to the National Poison Data System (NPDS).
Methods: A retrospective analysis of unintentional therapeutic errors with dofetilide reported to the NPDS from January 1, 2007 to December 31, 2016 (10 years) was conducted. Inclusion criteria were (1) human exposures to dofetilide, (2) reason for exposure: unintentional therapeutic error (3) single substance only. Exclusion criteria were confirmed non exposure or not followed to known outcome.
Results: A total of 73 cases met inclusion criteria. Twenty-five cases were excluded leaving 48 cases for analysis; most were excluded because of failure to follow to known outcome. Sixty percent are male. Mean age was 70 years. Of the 48 cases, 19 (40%)had documented clinical effects, 24 (50%) had none, and 5 (10%) had unrelated clinical effects. Of the 19 with documented clinical effects, the majority had at least one cardiovascular effect: conduction disturbances 25%, bradycardia 17%, tachycardia 4%, ventricular tachycardia/ventricular fibrillation 2%, ECG change (other) 2%, dysrhythmia(other) 2%, and hypertension 2%. Of the 19 patients who experienced symptoms,53% were treated/released from the emergency department, 26% were admitted to non-critical care, and 21% admitted to critical care. No patients died.
Conclusion: This is the first large case series of unintentional therapeutic errors involving dofetilide. Fifty percent of patients remained asymptomatic. Among symptomatic patients, cardiovascular effects predominated (89%). Forty-seven percent of cases were admitted for cardiovascular toxicity. No patients died.

Prospective study of unintentional therapeutic errors involving dofetilide is needed to further assess risks.

KEYWORDS Dofetilide; therapeutic error; National Poison Data System

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23. The others: characterizing other dosing errors reported to a poison center

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Background/Objectives: Therapeutic errors are costly and result in unplanned hospital visits. Recent studies on therapeutic errors have focused on coded data from either the National Poison Database System (NPDS) or individual poison centers. Approximately 30% of therapeutic errors reported to NPDS are coded as "other incorrect dose" (OI) or "other/unknown therapeutic error" (OU). The purpose of this study was to characterize those errors coded as OI or OU reported to a single poison center.
Methods: Retrospective, single-poison center chart review of therapeutic error exposures with at least one scenario coded as OI or OU from January 1, 2000 to September 30, 2017. Patients were either referred to healthcare facility (HCF) by poison specialist or already in/enroute to HCF. All cases were reviewed and re-coded to pre-defined scenarios or recoded to newly defined scenarios as appropriate.
Results: A total of 3413 cases were identified as having met inclusion criteria. Mean age was 40 years (range: 1 d–99 years); 53% female; mean number of cases per year was 181 (range: 130–239). There were 726 cases assessed as not therapeutic errors and were recoded as either intentional misuse (430), adverse reaction drug (209), or other non-therapeutic errors (87). Of the remaining cases, 1723 cases were re-coded to one of the 16 existing therapeutic error scenarios. The four most common re-codings were to: wrong medication taken or given (488), inadvertent took or given other's medication (283), doses taken too close together (274) and inadvertent took or given medication twice (247). After re-coding there remained 964 coded as OI or OU. Most of these were due to double, triple, quadruple, or higher than recommended dose (477/964); an additional common error was mistaken strength (81/964). The remaining scenarios occurred in fewer than 50 cases each with greater than 40 different possible scenarios such that additional coded scenarios would not be feasible. Based on review of free text notes, common scenarios for coding as OI or OU were: taking more than recommended in effort to treat pain, presenting to the hospital with a high drug level but no known therapeutic error, taking a full day's medication at once, confusing two medications, errors associated with pill boxes, pill dumpers, and mistaken strength.
Conclusions: This study was intended to describe the OI or OU that were managed in an HCF. Most cases coded as OI or OU could be re-coded as one of the NPDS pre-defined therapeutic error scenarios or non-error reasons for exposure. Considering the large proportion of double dose cases and the unique errors associated with mistaken strengths of tablets, these scenarios would be appropriate to add as new pre-defined coding scenarios, which would aid in future research and patient counseling. A prospective study evaluating the incidence of pill-box errors, pill dumpers, and mistaken strength of medications may be worthwhile to clinicians for focused counseling of patients.

KEYWORDS Therapeutic error; other errors; chart review

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24. I thought it was my vitamin drops: mistaking liquid medications for vitamin D drops

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Objective: Medication errors are an important issue in patient safety, and look-alike bottles are a well-known risk factor for confusing liquid pharmaceuticals [1]. Monthly dosing of vitamin D with ingestion of the contents of a whole bottle instead of daily dosing is becoming popular. Glass medicine bottles normally contain the x-fold of a therapeutic dose, and therefore confusing the vitamin D bottle with another medicine bottle might lead to serious symptoms of overdose. The aim of this study was to investigate these particular incidents.
Methods: Retrospective review of cases with ingestion of the contents of a whole bottle or part of a bottle of medications mistaken for vitamin D reported to our poisons centre from 1995 to 2017 with a reliable history of exposure. For analyzing severity of poisoning only cases with written feedback from a physician and high causality were included. The severity of observed symptoms was graded according to the Poisoning Severity Score (PSS).
Results: Twenty-two cases were reported from 1995 to 2017: none until 2011, one in 2012, two in 2013, three in 2014, two in 2015, six in 2016, and eight in 2017. All patients (16 females, 6 males) were adults, age was known in 18 patients with a mean

Table 1. Active ingredient erroneously taken, ingested dose and reported dose for serious toxicity ($n = 22$).

Active ingredient	Number of cases	Dose ingested [mg] (number of cases)	Part of a whole bottle (number of cases)	Reported dose for serious toxicity in adults
Metamizole (5 g or 10 g bottle)	12	5000 (11) 9000 (1)	0.5 (1) 0.9 (1) 1 (10)	5000 mg
Trimipramine	3	600 (1) 1200 (2)	0.5 (1) 1 (2)	750–1000 mg
Tramadol	2	750 (1) 1000 (1)	0.75 (1) 1 (1)	500 mg
Codeine	2	100 (1) 200 (1)	0.5 (1) 1 (1)	5–7.5 mg/kg
Diphenhydramine	1	1200 (1)	1 (1)	1000 mg
Atropine	1	10 (1)	1 (1)	10 mg
Japanese mint oil	1	unknown	0.5 (1)	unknown

Table 2. Clinical effects and severity in the cases with written feedback ($n = 11$).

Active ingredient	Dose [mg]	Age [years]	Sex	Clinical effects	Severity (PSS)
Metamizole	5000	70	m	None	No effects
Metamizole	5000	69	m	None	No effects
Codeine	100	60	f	Vertigo	Minor effects
Metamizole	5000	62	f	Drowsiness	Minor effects
Metamizole	5000	49	f	Abdominal pain	Minor effects
Tramadol	750	53	f	Vertigo, drowsiness, vomiting	Minor effects
Trimipramine	600	76	f	Drowsiness, ataxia	Minor effects
Atropine	10	67	f	Agitation, vertigo, dry mouth	Moderate effects
Tramadol	1000	61	m	Bradycardia (40/min), vomiting, miosis	Moderate effects
Trimipramine	1200	25	f	QRS widening (125 ms), somnolence (GCS 13), disorientation, slurred speech	Moderate effects
Trimipramine	1200	73	f	Coma (GCS 6), tachycardia (125/min), QTc prolongation (464 ms), extrapyramidal symptoms	Major effects

age of 60.0 years (median 61.5 years, range 25–90 years). The details of the substances involved with ingested doses and reported doses for serious toxicity are listed in Table 1. In most cases ($n = 20$) the medication error occurred at home, in one case in a nursing home, and in one case the circumstances of exposure were unknown. Clinical outcomes were known in 11 cases. Two patients had no effects, five had minor effects, three had moderate effects, and one had major effects. The clinical effects are listed in Table 2.

Conclusions: This case series shows that ingesting a whole bottle of a liquid medication due to confusion with vitamin D drops in a look-alike bottle can lead to moderate to severe toxicity. This particular medication error seems to have increased over the past few years, and elderly people are at particular risk. Proper information for patients, physicians and nurses in hospitals and retirement homes, and better labelling and distinctive design of the vitamin D bottles for monthly use to prevent this potentially dangerous medication error are very important.

Reference

[1] Wittich CM, Burkle CM, Lanier WL. Medication errors: an overview for clinicians. Mayo Clin Proc. 2014;89(8):1116–1125.

KEYWORDS Medication error; look-alike bottles; vitamin D

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25. Shock and lactic acidosis due to inadvertent intravenous albuterol

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Background: We present a patient who was administered 12 mg albuterol intravenously instead of nebulized inhalation. This is the highest dose of intravenous albuterol administration reported in the literature.

Case report: A 76-year-old man with prior renal transplant was being evaluated for acute renal failure and suspected graft rejection. He developed hyperkalemia, for which the treating physician ordered nebulized albuterol. Inadvertently, 12 mg of albuterol solution for inhalation was administered intravenously. The patient developed anxiety and tremors, but denied chest pain. The patient's heart rate subsequently rose from 76 to 136 bpm, though he initially maintained a normal blood pressure at 124/73 mmHg. Soon after, he developed shock, with blood pressure 96/54 mmHg and heart rate 128 bpm. Electrocardiogram had non-specific ST segment changes in the lateral leads. Troponin remained negative. Venous blood gas showed: pH 7.20, pCO_2 30.3, pO_2 83.3, HCO_3 11.7, lactate 7.0. Potassium corrected from greater than 6 to 4.9 mEq/l. Hypotension continued, reaching 80 s/40 s mmHg, which was initially treated with 2 l crystalloid bolus. A phenylephrine drip was started. Over the next 2–3 h, the patient's blood pressure improved to 110/80 mmHg and heart rate decreased to 78 bpm. He was admitted for continued care of his acute renal failure and graft rejection.

Case Conclusions: Albuterol solution is beta adrenergic agonist that comes as 0.083% (0.83 mg/ml) isotonic aqueous solution with sodium chloride. While typical route is inhalational, IV administration has been used in severe asthma (15 μg/kg in pediatrics) or hypercapnic respiratory failure in severe acute asthma (0.5 mg IV over 1 h in adults). Our patient presented with a significantly larger intravenous load than has been studied. We postulate that his initial tachycardia and lactic acidosis are direct effects of the beta-2 adrenergic agonism. Beta-2 adrenergic receptors are present in arterioles supplying skeletal muscle, and we suspect his hypotension may have been mediated by vasodilation of these arterioles, decreasing systemic vascular resistance.

Discussion: Treatment for hypotension should include IV crystalloid bolus. Phenylephrine can be used as a first line agent to increase vascular tone. Esmolol (0.025–0.1 mg/kg/min IV) or propranolol (0.01–0.02 mg/kg IV) can also be used. Esmolol may be preferred, as it is easily titrated due to its short half-life.

KEYWORDS Albuterol; iatrogenic; medication error

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26. Poison centres and active pharmacovigilance: focus on causes of medication errors

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Background: The primary role of poison centres is to give specialized assistance when exposure to a hazardous substance occurs; nevertheless, calls to poison centres contain valuable information

for pharmacovigilance purposes. Generally, due to the emergency nature of the calls and the need for prompt intervention, this information is only partially collected by the healthcare professionals handling incoming calls. Through a national project based on the collaboration of various poison centres and the national medicines regulatory agency, an active pharmacovigilance system was developed to delve deeper into "what happened" and better analyse medication errors (MEs) and adverse drug reactions (ADRs). We present a synthesis of this active pharmacovigilance experience from May 1, 2017 to February 28, 2017, particularly with respect to MEs and observed critical issues.
Methods: The National Project provides for a follow-up call of all incoming emergency calls related to medication exposures. Poison centres subsequently enter all collected information into a shared national database through the compilation of appropriate forms. The data collected include: demographics, details on the medication taken (i.e. active substance, dose, frequency and route of administration), symptoms, concomitant therapies, investigations and treatments undergone by the patient, comorbidities, and outcome. For MEs, the type (i.e. wrong dose, medication or route of administration) and cause (i.e. distraction, similar packaging) of ME was asked.
Results: In the period considered, the poison centres managed a total of 2900 calls related to medication exposures, of which 2643 (91.1%) were related to MEs and 257 (9.1%) were related to ADRs. The age group with higher risk of MEs is children, especially under 10-years-old (43.5% of all cases). In all age groups, the main cause of MEs is distraction (38.6%) with the only exception of people aged 80–89-years-old, where age-related confusion has a comparable influence. Interestingly, the overall second cause of MEs (14.9%) is the misunderstanding of medical prescription: it represents 26% of MEs in children under 10-years-old, and it is the number one cause of MEs related to incorrect route of administration or incorrect preparation of the medicinal product. When considering posology errors and errors related to administration of the incorrect drug, which are the most common types of MEs (90%), the most common cause for both is distraction, whilst the second causes are the misunderstanding of medical prescription and similar packaging, respectively.
Conclusions: Although accurate follow-up is a time-consuming activity that needs dedicated personnel and the collaboration of healthcare professionals and individuals who utilized poison centres services, it enables a better understanding of the root causes of MEs so as to address preventive measures. It is clear from our data that distraction and misunderstanding of medical prescription are the main causes of MEs. We believe that treating physicians should be aware of the importance of clear communication with their patients, including encouraging patients to avoid distractions during drug administration and ascertaining that all details of the prescription are understood.

KEYWORDS Medication errors; pharmacovigilance; poison centre

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27. The changing poison center- baby boomers calling for themselves and not for their kids

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Background: In the past, today's grandparents called the poison center about their children with accidental exposures. Now, they are calling for themselves, resulting in what appears to be a paradigm shift for poison center (PC) utilization. The older adult population today are living longer and taking more medications, increasing the potential for adverse reactions and errors. Consequently, emergency department visits for these adverse drug events are escalating along with healthcare costs.
Objective: To describe the trend in utilization patterns of a poison center in adults 60 and older (60+)
Methods: Reviewed toxiCALL™ data for all human exposure calls from 1999 to 2017 in a single poison center. Call reason, management site with referral patterns, and substance data for 2017 for adults 60+ were analyzed.
Results: Human exposure call volume decreased 34% from 1999 to 2017 while calls regarding adults 60+ increased 4.8% (peaking at 8.5% in 2017), with an 18% increase in calls for adults 60+ classified as medication errors or adverse reactions (32% in 1999–50% in 2017). The top three reasons for medication error calls were double dose (29%), wrong drug (20%), and other wrong dose (17%). The top substances involved in errors were cardiovascular medications (21%) and insulin (4%), accounting for 25% of total errors. Seventy-nine per cent of medication errors in adults 60+ were managed at home, regardless of caller site. However, when the poison center was called first, 95.3% of medication errors were kept at home.
Conclusion: In the last 18 years, medication error calls to the poison center have increased in adults 60+, despite overall human exposure calls declining. By calling the poison center first, the majority of these medication exposure reasons in adults 60+ could be managed at home, therefore decreasing the risks associated with hospitalization as well as saving health care dollars. Specific education targeting management strategies that involve poison center utilization and specific errors with specific medication is needed in this population, especially with U.S Census projecting that seniors will outnumber those under age 18 by 2030. It is imperative to invest in the poison center with the changing public health landscape to provide a resource in prevention and management of these errors in adults 60+.

KEYWORDS Seniors; older adult; therapeutic error

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28. Impact of legislation legalizing recreational Marijuana sales on cannabis exposure calls to poison centers 2008–2017

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Background: During the past decade, nine states and the District of Columbia have legalized recreational (retail) cannabis. Each jurisdiction previously had a period where medical marijuana was legalized prior to legislation allowing legal adult recreational use. The purpose of this study was to examine the change over time in exposures to cannabis reported to poison centers, for any relation to legislation related to the legalization status of marijuana by state and across states.
Methods: We collected dates of legal status changes by state including: decriminalization, medical use, and recreational use. Following approval by the AAPCC Data Access Committee, we examined the case logs for the 15 generic codes associated with marijuana/THC, and extracted all closed, human, single substance

State	Date	Marijuana Encounters (2008-2018)
Vermont (10)	1/22/2018	30
California (9)	1/1/2018	3311
Alaska	2/25/2015	61
Colorado	11/6/2012	993
District of Columbia	2/26/2015	92
Maine	11/9/2016	213
Massachusetts	11/8/2016	271
Nevada	11/8/2016	175
Oregon	7/1/2015	809
Washington	2/26/2015	1160
	Total (10 states)	7115
	Total (9 states)	7085
	Total (8 states)	3774

Figure 1. Exposures reported to poison centers 2008–2018 for ten states with legalization of recreational cannabis.

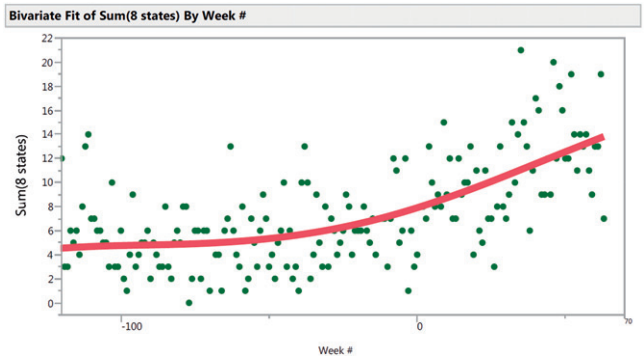

Figure 2. Exposures reported to poison centers by week 2008–2018: spline fit (lambda = 100) for eight states with legalization of recreational cannabis before 2018.

exposures from January 1, 2008 to February 28, 2018. Changes in exposure groups over time were examined by day, by week and by month (28 d period). Data management, descriptive statistics, graphical summaries, and the relationships (correlations and multivariate analyses) by state and across states were via SAS JMP 12.0.1. After screening analyses, exposure data for states with recreational laws were aligned by specific legal action day to examine the dynamics of the effect.

Results: Between January 1, 2008 and February 28, 2018 there were 45,184 single substance exposures related to a cannabis product reported to US poison centers. Male to female ratio of cases was 2.23:1. There was a spike in exposures ~ month 100 (April, 2016) for all states taken together. Principal contributors to this spike were THC/homologs, most heavily reported from Mississippi, New York, New Jersey and Pennsylvania. Since our focus was changes in the effect of marijuana product laws, subsequent analyses excluded THC/homologs. Multivariate statistical modeling of exposures by month by state showed statistically significant effects related to recreational cannabis legislation in four states (medical in three, decriminalization in one). An across state multivariate model assigned relative importance (LogWorth) of 1154 to recreational, 2.53 to medical and none to decriminalization. We aligned the exposure data for the 10 states with recreational laws (see Figure 1) by date of recreational cannabis law enactment to examine the profile of change in calls to poison centers. Figure 2 shows the exposures by week with a spline fit. The statistical model which best described this eight state response (Figure 3) included an overall increase in exposures (increase/year, [95% CI]) of 0.230 [0.058, 0.401] and the post-recreational slope (increase) of 1.42 [0.909, 1.93], a six-fold increase after recreational law enactment.

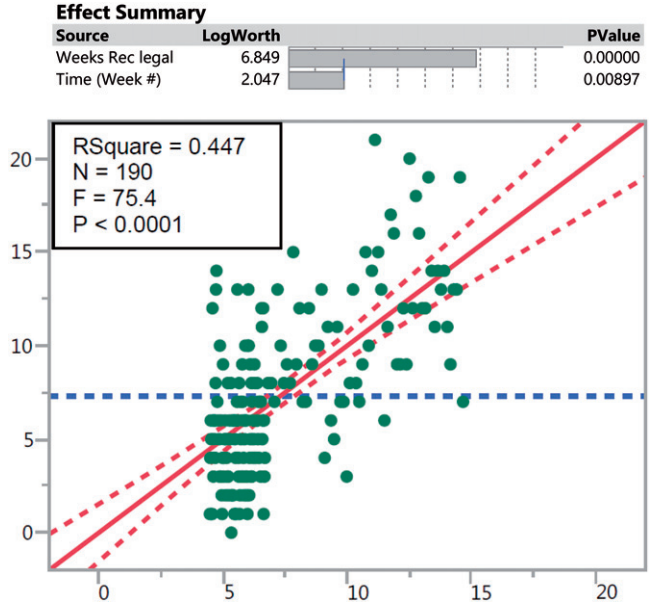

Figure 3. Actual (*Y*-axis) by predicted (*X*-axis) plot for cannabis exposures reported to poison centers 2008–2018 for eight states with legalization of recreational cannabis before 2018.

Conclusions: We restricted these exposures to single substance, and have relatively little data after enactment of recreational laws, as well as relatively small numbers by state. Despite these limitations, these preliminary analyses indicate a strong relationship between the number of exposures to cannabis products that were reported to Poison Centers and the regulatory statutes for recreational ≫ medical > decriminalization. As more states change their regulatory status and time passes, exposure profiles will likely change and can be better assessed.

KEYWORDS Cannabis legalization; Poison Control Center; cannabis exposure

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29. Clinical prediction rule for torsade de pointes in patients with drug-induced QT prolongation

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Introduction: Torsade de pointes (TdP) is a serious complication in patients who develop QT prolongation (QTP) from drugs. However, only a few cases with QTP progress to TdP. Using multivariate analysis to identify risk factors and develop prediction models for TdP has not been performed before.

Objective: To develop clinical prediction models that help clinicians to estimate the probability of TdP occurring from drug-induced QT prolongation.

Methods: The study population was derived from two datasets. All cases aged over 18 years with an exposure to QT prolonging drugs. Group-1 was obtained from systematic review of 230 cases from Medline since its establishment until 10 December 2015, everyone in this group developed TdP. Group-2 (291 cases) dataset was extracted from a chart review of three medical

Table 1. Multivariate analysis of the two prediction models.

	Model with QT nomogram				Model with QTcRTH			
Variable	Adjusted OR	95% CI	Coefficient	Score	Adjusted OR	95% CI	Coefficient	Score
1. Age (years)								
<40	1		0.00	0	1		0.00	0
40–65	1.80	0.96–3.39	0.59	1.0	1.65	0.81–3.38	0.50	1.0
> 65	12.52	3.38–46.43	2.53	4.5	16.01	4.27–60.01	2.77	5.5
2. Sex								
Male	1		0.00	0	1		0.00	0
Female	2.43	1.32–4.48	0.89	1.5	1.83	0.92–3.62	0.60	1.0
3. Cardiac disease								
No	1		0.00	0	1		0.00	0
Yes	4.10	1.73–9.72	1.41	2.5	2.82	1.07–7.41	1.04	2.0
4. Heart rate (/min)								
60–100	1		0.00	0	1		0.00	0
>100	0.09	0.04–0.18	−2.44	−4.0	0.61	0.28–1.36	−0.49	−1.0
<60	2.30	0.79–6.71	0.83	1.5	3.94	1.24–12.49	1.37	3.0
5.1 QT-Nom								
Below the line	1		0.00	0				
Above the line	36.07	17.75–73.27	3.59	6.0				
5.2 QTcRTH (sec)								
<0.477					1		0.00	0
0.477–0.500					7.73	2.62–22.82	2.04	4.0
>0.500					66.18	31.73–138.06	4.19	8.5
Area under ROC		0.9490 (0.9285–0.9695)				0.9596 (0.9421–0.9770)		
Sensitivity		88.3% (83.4%–92.1%)				90.4% (85.9%–93.9%)		
Specificity		92.8% (89.2%–95.5%)				92.8% (89.2%–95.5%)		

Table 2. Clinical prediction scores and outcome probability of the two models.

	Model with QT nomogram				Model with QTcRTH			
Probability categories	Score	Case ($N = 230$)	Control ($N = 291$)	LR (95% CI)	Score	Case ($N = 230$)	Control ($N = 291$)	LR (95% CI)
Low	≤3	13 (5.7%)	242 (83.2%)	0.07 (0.04–0.12)	≤3	11 (4.8%)	268 (92.1%)	0.05 (0.03–0.09)
Moderate	3.5–7.0	59 (25.7%)	42 (14.4%)	1.78 (1.25–2.54)	3.5–8.0	12 (5.2%)	14 (4.8%)	1.08 (0.51–2.30)
High	≥7.5	158 (68.7%)	7 (2.4%)	28.56 (13.67–59.68)	≥8.5	207 (90.0%)	9 (3.1%)	29.10 (15.27–55.44)
Discrimination of the two models								
AUROC			0.9490 (0.928–0.970)				0.9683 (0.952–0.985)	
p-Value			.0006					

Net reclassification index (NRI):
- Additive NRI = 10.97 (Patients with TdP had higher risk prediction and patients without TdP had lower risk prediction using the QTcRTH model compared with using the QT nomogram based model)
- Absolute NRI = 3.84% (The overall reclassification by the model using the QTcRTH improved the risk prediction in 3.8% of the patients compared with using the QT nomogram based model)

centers from 2008 to 2010. These patients overdosed on QT prolonging drugs, but did not develop TdP. Risk factors of TdP and QT prolongation status (prolonged/not prolonged) classified by QT nomogram (QT-Nom), QT corrected by Dmitrienko's formula (QTcDMT = QT/RR 0.413, cut-off 0.475 s), and QT corrected by Rautaharju's formula (QTcRTH = QT*(120 + heart rate)/180, cut-off 0.477 s) were included for univariate analysis. Several models were developed and studied using multiple logistic regression, only two models ([risk factors + status of QTP based on QT-Nom] and [risk factors + status of QTP defined by QTcRTH]) are presented here for comparison. The coefficient from each variable was converted to a score. A scoring system with three categories was developed for each model to predict outcome probability (low, moderate, high). Discrimination between the two models was tested using area under the receiver operating characteristic curve (AUROC) and the net reclassification index (NRI).

Results: Univariate analysis revealed that low serum potassium, magnesium and calcium were not significant risk factors for TdP. However, older age, female sex, bradycardia, and heart disease were significant and these variables were included for the multivariate analysis of the two models (one with the QT nomogram, and the other with QTcRTH). Results of the multivariate analysis of the two models are presented in Table 1. Each coefficient of each variable was converted to a score. Performance of the model using QTcRTH was better than the nomogram based model, according to the AUROC. We further developed the clinical prediction model by stratifying the score as low, moderate, or high for each model according to probability of outcome (Table 2). Discrimination tests were applied to determine the two risk prediction scores. The AUROC (0.9683 versus 0.9490; *p*-value = .0006) and the NRI revealed that prediction score performance of the model using QTcRTH was significantly better than the model with QT nomogram (Table 2). Using the QTcRTH

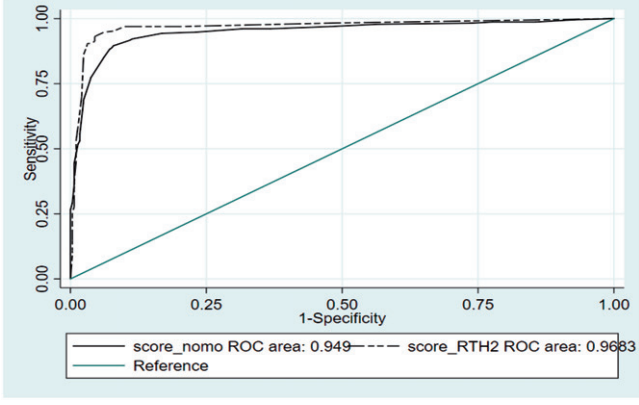

Figure 1. Area under the ROC curves of the two models.

model, 96% (268/279) of those with a low score were correctly classified as no TdP, and 96% (207/216) with a high score were also accurately predicted to develop TdP.
Conclusions: We revealed that those with drug-induced QTP were at increased risk for TdP the more risk factors they had. In addition, the two clinical prediction rules developed from those risk factors demonstrated high performance in predicting TdP.

KEYWORDS Torsade; QT prolongation; risk factors

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30. A comparison of resource utilization and adverse events related to the management of antimuscarinic delirium between physostigmine and non-antidote therapy

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Background: Antimuscarinic delirium is associated with significant in-hospital morbidity and its management often requires substantial resource allocation, including intubation, physical restraint, and intensive care unit (ICU) placement. There is some controversy over the ideal management of these patients. Physostigmine, a centrally acting acetylcholinesterase inhibitor, can rapidly reverse antimuscarinic delirium but has been associated with adverse effects, including cholinergic excess and seizures. This study aims to assess the effects of physostigmine use on resource allocation and adverse events in this patient population.
Methods: This is a retrospective chart review of patients diagnosed with an antimuscarinic toxidrome at a single tertiary hospital with an inpatient toxicology service. Charts were abstracted by a single blinded abstractor using a standardized form and protocol. Demographics were obtained, including age, gender, and heart rate. Whether the patient was given physostigmine within the first 24 h or not was recorded. Presence or absence of intubation, restraint use, and critical care admission were recorded. Adverse events were recorded including seizure, vomiting, and bradycardia. The primary aim was to compare frequency of intubation between those that received physostigmine and those that did not. Secondary aims included determining the association between physostigmine administration and restraint use, ICU placement, vomiting, bradycardia, and seizures. Comparisons were made between the groups with regards to these variables using appropriate statistical methods.
Results: There were 141 patients identified after applying inclusion and exclusion criteria. The results indicated no statistically significant difference between the groups with regard to age, gender, or initial heart rate. Overall, 65 patients (46%) received physostigmine, 45 (32%) were admitted to the ICU, and 29 (20%) were intubated. Using a logistic regression model, patients who received physostigmine in the first 24 h were less likely to be intubated (9% versus 23%, OR 0.241, $p = .00306$), and less likely to be admitted to an ICU (23% versus 39%, OR 0.476, $p = .04811$). Patients in the physostigmine group showed a trend toward being restrained less often (29% versus 44%, OR 0.524, $p = .082$). Overall, the instance of bradycardia ($n = 16$), vomiting ($n = 27$), and seizures ($n = 7$) was relatively limited and there were no significant differences between the groups. Using a logistic regression model, there were no significant associations noted between physostigmine administration and adverse events.
Conclusions: This study showed that in patients diagnosed with an antimuscarinic toxidrome, physostigmine use is associated with a lower incidence of intubation and ICU placement without having a significant association with the incidence of bradycardia, vomiting, or seizures. Results are limited by the nature of retrospective chart reviews and their inherent biases.

KEYWORDS Physostigmine; anticholinergic; antimuscarinic delirium

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31. Exposures through breastmilk: an analysis of exposure and information calls to US Poison Centers, 2001–2017

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Background: Breastfed infants may be at risk for exposure to a drug or other substance present in breastmilk. Lactating women may become concerned about potential exposures to their infant through breastmilk, and may consult a poison center for information, or a potential exposure via lactation. There is a paucity of published descriptions of the patients or substances involved in breastmilk exposure or information calls to United States poison centers.
Methods: This study analyzed reports to the National Poison Data System (NPDS) for exposure with Scenario of 'Exposure through breastmilk' or information call for 'Drug use during breastfeeding' (Info Calls) from 2001 to 2017. Descriptive statistics for these calls including substances involved, effects, and disposition were carried out using SAS JMP 12.01.
Results: Between 2001 and 2017, U.S. Poison Centers received 76,416 Info Calls and 2319 exposure reports related to breastmilk. Exposures to substances in breastmilk included 1184 females (51%) 948 males (41%), 186 unknown sex (8%). Most common caller locations were: 1758 own residence (76%); 360 healthcare facility (15.5%); 15 workplace (0.6%). One thousand eight hundred and two of the exposure calls were managed on site (78%); 297 were en route to healthcare facility (HCF) when poison center was called (12.8%); and 169 were referred to a HCF (7.3%). There were 466 exposures (20.1%) managed at a HCF: 269 were evaluated and released (58%); 38 were admitted to ICU (8.2%); 53 were admitted to floor (11%); 86 were lost to follow up or left against medical advice (18%). Medical outcomes included: 1 death (0.04%); 8 major effect (0.3%); 43 moderate effect (1.9%); 170 minor effect (7.3%); 390 no effect (16.8%). The death was a 4-month-old male with a possible exposure to benzodiazepines, opioids, and an SSRI via breastmilk, however the death was deemed unrelated to exposure. The substances associated with major effects among breastfed infants included opioids, benzodiazepines, ethanol, cyclobenzaprine, insulin, and amphetamines (See Table 1). Exposure calls were most commonly in reference to antibiotics, antifungals, benzodiazepines, opioids, and SSRIs. Figure 1 shows the substances (by generic code) most commonly reported in exposures. For comparison, data on Information Calls for those same substances are shown. Information calls were most commonly in reference to systemic antibiotics, SSRIs, antihistamines, corticosteroids, and benzodiazepines. One thousand one hundred and ninety-two exposures (51.4%) had reported signs/symptoms. The most common signs/symptoms were drowsiness, agitation, rash, and vomiting/diarrhea (Figure 2).

Table 1. Poison center cases 2001–2017 for infants with exposures to substances via breastmilk with death or major effect.

Medical outcome	Age	Gender	Substance	Level of care	Clinical effect
Death	4 months	Male	Methadone, Benzodiazepines, SSRI	Admitted to ICU	Deemed unrelated to exposure: Cardiac arrest, Respiratory arrest
Major effect	16 d	Male	Cyclobenzaprine, Acetaminophen with Oxycodone	Admitted to noncritical care unit	Bradycardia, Hypotension, Respiratory arrest
Major effect	1 month	Male	Methadone	Admitted to ICU	Agitated/irritable, Tremor, Respiratory arrest, Diarrhea, Drowsiness/lethargy
Major effect	13 months	Male	Methadone	Admitted to ICU	Respiratory depression
Major effect	14 d	Male	Acetaminophen with Oxycodone	Treated/evaluated and released	Cyanosis
Major effect	16 d	Male	Ethanol, Benzodiazepines	Admitted to ICU	Cardiac arrest, Respiratory arrest
Major effect	6 months	Female	Benzodiazepines, Methadone	Admitted to ICU	Drowsiness/lethargy, Seizure, Tremor
Major effect	17 months	Male	Fentanyl, Morphine, Oxycodone, Benzodiazepines	Admitted to ICU	Tachycardia, Agitated/irritable, Confusion, Drowsiness/lethargy, Miosis, Respiratory depression, Acidosis, Hyperglycemia

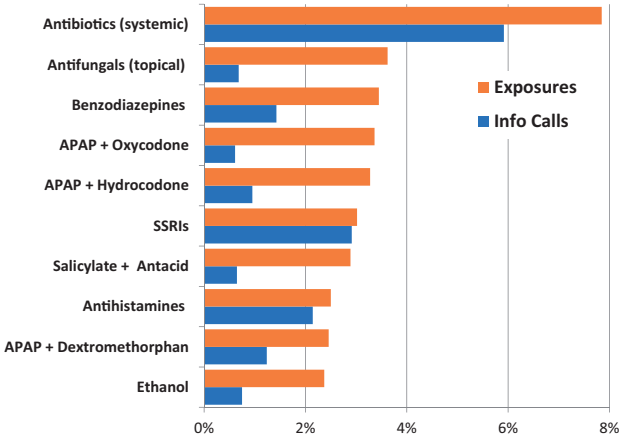

Figure 1. Generic codes, exposures through breastmilk: % of 2319 info calls for drug use during breastfeeding: % of 76, 416 NPDS 2001–2017.

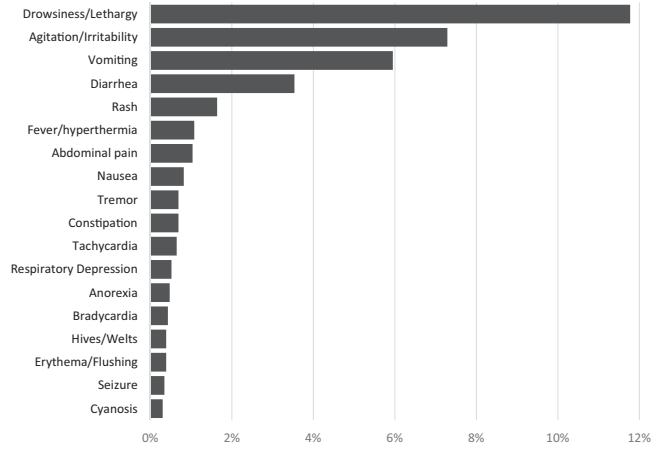

Figure 2. Clinical effects as percent of 2319 exposures via breastmilk NPDS 2001–2017.

	Percent of calls Info calls	Exposures
Ethanol	0.007485	0.023717
APAP + Dextromethorphan	0.01238	0.02458
Antihistamines	0.021448	0.025011
Salicylate + Antacid	0.006478	0.028892
SSRIs	0.029143	0.030185
APAP + Hydrocodone	0.009527	0.032773
APAP + Oxycodone	0.006111	0.033635
Benzodiazepines	0.014264	0.034498
Antifungals (topical)	0.006831	0.036223
Antibiotics (systemic)	0.059176	0.078482

Clinical effect	Number of exposures
Cyanosis	0.003018542
Seizure	0.003449763
Erythema/Flushing	0.003880983
Hives/Welts	0.003880983
Bradycardia	0.004312204
Anorexia	0.004743424
Respiratory Depression	0.005174644
Tachycardia	0.006468305
Constipation	0.006899526
Tremor	0.006899526
Nausea	0.008193187
Abdominal pain	0.010349288
Fever/hyperthermia	0.010780509
Rash	0.016386373
Diarrhea	0.035360069
Vomiting	0.059508409
Agitation/Irritability	0.07287624
Drowsiness/Lethargy	0.117723157

Conclusions: Substances common to both exposures via breastmilk and information calls concerning drug use during breastfeeding included antibiotics, benzodiazepines, and SSRIs. Most cases of severe toxicity included potential exposures via breastmilk to benzodiazepines and opioids. These data should help inform educational outreach and bedside care for breastfeeding mothers. Further study into exposures via breastmilk may help inform an understanding of the potential risks of substance exposure to breastfed infants.

KEYWORDS Breastmilk; exposure through breastmilk; information call drug use during breastfeeding

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32. Etched in stone: a case of fatal ammonium bifluoride poisoning

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Background: Ammonium bifluoride and hydrofluoric acid are potent toxins with severe local and systemic toxicity due to high permeability coefficient and binding of divalent cations with disruption of the Na-K-ATPase pump.
Case report: A 52-year-old developmentally delayed deaf and mute male with known pica was attending a craft workshop involving glass etching. When the teacher was distracted, he swallowed about 3 ounces of Armour Etch cream. On the initial call to the poison center the patient had vomited, but otherwise appeared well. Immediate transport was requested and he arrived approximately 1–2 h post-ingestion ingestion[c1]. The first SDS stated the product was a proprietary formula with ammonium bifluorides and 1–2% hydrofluoric acid. A more specific SDS was located and which showed 21–27% ammonium bifluoride and a small amount of barium sulfate in the product. This corresponds to 17–23 g of ammonium bifluoride in a 3 ounce ingestion. The patient's presenting vital signs were BP: 126/91, HR: 86, RR: 18, Temperature: 36.6, SpO_2: 94% RA. He was reportedly asymptomatic on arrival per ED notes. Initial laboratories were significant for magnesium of 1.7, calcium of 6.8, and potassium of 3.9. An NG tube placement was attempted without success due to agitation. The patient received 3 gm of $CaCl_2$ IV and 2 gm $MgSO_4$. One hour post ED arrival, the patient was sedated and NG tube was placed with clear aspirate obtained. Two hour post ED arrival the patient had respiratory distress, was intubated, and had widening QRS on EKG and rising troponins (ultimately peaking at 89). By 6 h post arrival, transfer arrangements were made and the patient was started on a sodium bicarbonate infusion, antibiotics, and PPI. He was given an additional 5 gm $CaCl_2$. The patient's calcium continued to drop as low as <5 and potassium rose as high as 5.3 8 h post arrival. The patient arrested as helicopter transport was packaging for travel. He was unable to be resuscitated despite receiving 5 gm $CaCl_2$, epinephrine, bicarbonate, and amiodarone over a 20 min resuscitation attempt. In total, he received 10–12 g of $CaCl_2$ and 2 g of magnesium during his ED stay. Post-mortem showed gastric perforation with barium staining of the peritoneum and mediastinum.
Case discussion: Most patients who ingest these products will die; those who survived reportedly received 25–50 g of calcium in the first 24 h. Early decontamination is a challenge because of vomiting. Oral calcium products or lavage with calcium gluconate should be considered. Aggressive calcium and magnesium replacement, correction of acidosis, and CV support are critical management steps. For severe cases, hemodialysis may be considered with case reports demonstrating successful clearance of fluoride ions, although it is unclear if this is helpful in patients with normal renal function.
Conclusion: Significant fluoride and hydrofluoric acid ingestions are extremely deadly and management is very challenging. The severity and rapidity of deterioration of patients may be underappreciated.

KEYWORDS Hydrofluoric acid; ammonium bifluoride; accidental overdose

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33. Accuracy of product identification for acetaminophen products in the National Poison Data System

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Background: The accuracy of product identification (ID) within the National Poison Data System (NPDS) is known to vary. The objective of this analysis is to characterize product ID inconsistencies for single ingredient acetaminophen product exposures by comparing NPDS product ID with product ID data systematically collected via a follow-up survey.
Methods: A follow-up survey was done at six US poison centers (PCs) to collect additional information including product-specific details for medication errors and accidental ingestions of single ingredient acetaminophen in children <12 years of age. Each product reported in the survey was matched to a specific product in Poisindex® using a product ID code. Product ID codes were selected by reviewing the survey information and comparing it to the NPDS record. If details in the survey differed from the NPDS product, a more accurate product was identified based on product ID components (dosage formulation (e.g., liquid versus solid), age formulation (e.g., adult versus pediatric), brand) identified in Poisindex®. Product ID code, generic code, and product ID components extracted from exposure call data in NPDS were compared to survey product ID information for cases reported in 2016 and 2017. The consistency between product ID variables was summarized for cases with only one product identified in the survey and NPDS.
Results: One thousand four hundred and twenty-one survey cases with corresponding NPDS data were completed. In 1401 (98.6%), the survey and NPDS record each had one product reported, in 5 (0.4%) the survey and NPDS record each had the same number of multiple products, and in 15 (1.1%) the number of products was discrepant. In 1401 cases with only one product, 677 (48.3%) identified the correct product ID code. Among the 724 (51.7%) with incorrect product ID code, 625 (86.3%) identified the correct generic code. Within specific product ID components, dosage formulation (74.2%) was most accurate, followed by age formulation (49.4%) then brand (6.1%). Of cases with the incorrect product ID code identified, 76.8% identified at least one of the three product ID components, 52.2% identified at least two of the three product ID components, and 0.7% identified three of the three product ID components. Among all cases, 12.0% ($n = 168/1401$) identified none of the correct product ID components.
Conclusions: This analysis shows that single ingredient acetaminophen products are often incorrectly identified using the Poisindex® product ID code. Though the accuracy of product ID code selection was limited, generic code ID was relatively precise. For analyses of NPDS data dependent on product characteristics, considerations for the variability in product ID are important and alternative methods of accurate product ID (e.g., follow-up survey) may be necessary. Additional understanding of the barriers to accurate product ID selection should be encouraged to improve the functionality of NPDS.

KEYWORDS Product; identification; NPDS

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34. Completeness of National Poison Data System (NPDS) scenario identification in pediatric exposures to acetaminophen

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Background: Scenario data collected in the National Poison Data System (NPDS) are intended to standardize the collection of contributing factors that lead to exposures. The accuracy of these data are unknown. The aim of this study is to assess the completeness of the NPDS scenario data by comparing these data to root causes collected through a survey follow-up process.

Methods: Follow-up surveys were conducted at six U.S. poison centers to collect additional information, including root causes (contributing factors to exposure), for accidental unsupervised ingestions (AUIs) and medication errors (MedErrs) involving single ingredient acetaminophen products among children <12-years-old. NPDS scenarios were matched to individual root causes collected via the survey where an individual scenario matched to an exact root cause. Of 47 AUI root causes captured via the survey, 12 were matched to 18 NPDS scenarios. Of 35 MedErr root causes captured via the survey, 4 were matched to 14 NPDS scenarios. NPDS cases from 2016 and 2017 with completed follow-up surveys were analyzed. The completeness of scenario reporting is summarized as the number and percentage of times a survey-identified root cause was also identified in NPDS.

Results: A total of 1191 AUI follow-up surveys were completed, of which 99.9% identified at least one root cause. At least one scenario was identified by 31.4% of the corresponding AUI NPDS cases. A total of 553 MedErr follow-up surveys were completed, of which 99.8% identified at least one root cause. At least one scenario was identified by 97.3% of the corresponding MedErr NPDS cases. Tables 1 and 2 display the number and percentage of times a survey-identified root cause was identified as a NPDS scenario for AUI and MedErr cases, respectively. The most common survey-identified AUI root cause was "product mistaken for candy or food or desirable product taste" ($n = 500$), which was not captured as a scenario in any of the corresponding NPDS cases (0.0%). "Storage in a purse or other bag" was also commonly identified by the survey ($n = 208$) and was captured as a scenario in 10.1% of NPDS cases. The most common survey-identified MedErr root cause was "doses given too close together" ($n = 210$), which was captured as a scenario in 32.4% of cases. "Wrong product" was the root cause most commonly correctly identified among MedErr cases ($n = 46$) and was captured as a scenario in 58.7% of NPDS cases.

Conclusions: This analysis shows that the NPDS scenario data infrequently capture some root causes of exposure. Scenarios were more complete among MedErr cases, likely due to the NPDS requirement to record a scenario for MedErr cases. Regardless of exposure type, the completeness was lacking and alternative methods for identifying root causes of exposures may be necessary to use NPDS data for the purposes of detecting preventable factors that contribute to exposures.

Table 1. Number and percentage of follow-up survey-identified root causes also captured as scenarios for AUI cases.

	N	Identified as a scenario n (%)
Medication Container Storage or Access	349	29 (8.3%)
Medication stored in purse or other bag	208	21 (10.1%)
Medication in use or product left out after recent use	133	8 (6.0%)
Medication stored on top of or in refrigerator	8	0 (0.0%)
Child Resistant Closure (CRC) Issues	283	11 (3.9%)
Medicine bottle left open	11	1 (9.1%)
CRC left unsecured	171	8 (4.7%)
No CRC mechanism present	101	2 (2.0%)
Product Packaging / Containment	80	1 (1.3%)
Medication contained in plastic baggie	38	1 (2.6%)
Medication contained in other container	42	0 (0.0%)
Presence of Another Child	45	3 (6.7%)
Administered by other child	30	3 (10.0%)
Product opened, left out, or made accessible by other child	15	0 (0.0%)
Other	528	1 (0.2%)
Mistaken for candy or food or desirable product taste	500	0 (0.0%)
History of behavioral or mental health disorder	28	1 (3.6%)

Table 2. Number and percentage of follow-up survey-identified root causes also captured as scenarios for MedErr cases.

	N	Identified as a scenario n (%)
Dose Volume Error	233	79 (33.9%)
Multiple products containing acetaminophen	23	11 (47.8%)
Doses given too close together	210	68 (32.4%)
Other	64	29 (45.3%)
Wrong product	46	27 (58.7%)
Given to wrong patient	18	2 (11.1%)

KEYWORDS Scenarios; root cause; National Poison Data System

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35. Extracorporeal membrane oxygenation (ECMO) for refractory shock due to poisoning: experience and trends from a Regional Poison Center

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Background/objectives: Extracorporeal Membrane Oxygenation (ECMO) can support gas exchange and perfusion in patients with cardiorespiratory failure. ECMO support can rescue patients with refractory shock due to poisoning, however data on the use of ECMO for poisoning are sparse in the United States. This study sought to characterize this patient population, evaluate regional trends in the use of ECMO for poisoning, assess the feasibility of ECMO if transfer to an ECMO center is needed, and describe related complications.

Methods: This was a retrospective study from a single poison center covering multiple medical centers across three states. Cases were identified by querying our electronic patient database (Toxicall®) for the therapy code "ECMO" from 2000 to 2018. Cases were abstracted by two board-certified medical toxicologists for the following data: indication for and duration of ECMO,

Table 1. Clinical characteristics and substances ($n = 22$).

Exposure reason	
Intentional – Suspected suicide	$n = 9$ (41%)
Intentional – Abuse	$n = 6$ (27%)
Unintentional – General	$n = 2$ (9%)
Unintentional – Therapeutic error/Misuse	$n = 2$
Adverse reaction – Drug/Other	$n = 2$
Adverse reaction – Other/Unknown reason	$n = 2$
Initial vital signs, median (range)	
Pulse rate, (beats/min, $n = 19$)	109 (0–180)
Systolic blood pressure (mmHg, $n = 19$)	90 (0–200)
SpO_2, (in %, $n = 8$)	97 (50–100)
Temperature (°C, $n = 11$)	36.9 (26.3–40)
Year of encounter ($n = 22$)	
2006	$n = 1$ (4%)
2012	$n = 1$ (4%)
2013	$n = 1$ (4%)
2014	$n = 1$ (4%)
2016	$n = 5$ (23%)
2017	$n = 8$ (36%)
2018	$n = 5$ (23%)
Reported substances/poisons	
Cardiac medications	$n = 11$ (50%)
Calcium channel blockers	$n = 5$
Beta blockers	$n = 2$
Flecainide	$n = 2$
Vasodilators	$n = 2$
Antidepressants	$n = 8$ (36%)
Cyclic antidepressants	$n = 2$
Desvenlafaxine/bupropion	$n = 2$
Trazodone	$n = 2$
Sertraline/mirtazapine	$n = 2$
Ethanol	$n = 6$ (27%)
Opioids	$n = 5$ (23%)
Sympathomimetics	$n = 5$ (23%)
Phenethylamines	$n = 3$
Cocaine	$n = 2$
Sedative/hypnotics	$n = 3$ (14%)
Other substances	
Valproate/lamotrigine	$n = 2$
Amanita bisporigera	$n = 1$
Cobalt	$n = 1$
Skin lightening cream (aspiration)	$n = 1$

Table 2. Selected other therapies.

Alkalinization	$n = 7$ (32%)
Anti-arrhythmic	$n = 8$ (36%)
Calcium	$n = 8$ (36%)
Cardioversion	$n = 2$ (9%)
CPR	$n = 11$ (50%)
Epoprostenol (inhaled)	$n = 4$ (18%)
Glucagon	$n = 3$ (14%)
Hemodialysis	$n = 6$ (27%)
Intra-aortic balloon pump	$n = 1$ (4%)
Intravenous fat emulsion	$n = 3$ (14%)
Insulin (high dose)	$n = 4$ (18%)
Intubation & mechanical ventilation	$n = 22$ (100%)
Methylene blue	$n = 2$ (9%)
Pacemaker	$n = 2$ (9%)
Surfactant	$n = 1$ (4%)
Vasopressors & Inotropes	$n = 17$ (77%)
Norepinephrine	$n = 16$
Epinephrine	$n = 14$
Vasopressin	$n = 13$
Dopamine	$n = 9$
Dobutamine	$n = 6$
Phenylephrine	$n = 5$
Milrinone	$n = 2$
Max # of vasopressors, median (IQR)	4 (3–5)

whether transfer to an ECMO center occurred, drug/substance exposures, complications related to ECMO, concomitant therapies, clinical effects, and outcomes.

Table 3. Selected clinical effects.

Clinical effects	
Acidosis	$n = 17$ (77%)
Adverse drug reaction to treatment	$n = 5$ (23%)
Bradycardia	$n = 5$ (23%)
Cardiac arrest	$n = 12$ (54%)
Coma	$n = 10$ (45%)
Cough/choke	$n = 3$ (14%)
Drowsiness/lethargy	$n = 5$ (23%)
Dysrhythmia (V-Tach/V-Fib)	$n = 9$ (45%)
Hyperthermia	$n = 5$ (23%)
Hypothermia	$n = 4$ (18%)
Hypotension	$n = 17$ (77%)
Lab abnormalities	
AST, ALT >1000	$n = 6$ (27%)
CPK elevated	$n = 10$ (50%)
Creatinine increased	$n = 9$ (45%)
Electrolyte abnormalities	$n = 12$ (54%)
PT prolonged	$n = 3$ (14%)
Oliguria/anuria	$n = 7$ (32%)
Pulmonary edema	$n = 3$ (14%)
Pneumonitis	$n = 2$ (9%)
Renal failure	$n = 3$ (14%)
Respiratory arrest	$n = 3$ (14%)
Respiratory depression	$n = 5$ (23%)
Rhabdomyolysis	$n = 4$ (18%)
Seizure	$n = 4$ (18%)
Tachycardia	$n = 15$ (68%)
X-ray finding (+)	$n = 7$ (32%)

Results: Twenty-nine patients had ECMO coded as "recommended" or "performed"; a total of 22 patients received ECMO for poisoning and were included in final analysis. Median age was 34 years (range 1–69, 68% female, including two children ages 1 and 10). Sixteen of these (73%) survived, all coded as "Major Effect." Specific substances and additional clinical data are displayed in Table 1. The most common poisons were cardiac medications (50%) followed by antidepressants (36%). Indications for ECMO were cardiogenic shock ($n = 16$, 73%), refractory hypoxemia ($n = 2$, 9%), refractory ventricular dysrhythmias ($n = 1$, 4%), or a combination of these ($n = 3$, 14%). Definitive ECMO was performed at seven different hospitals. Transfer to an ECMO center occurred in 14 cases (64%); in 5 cases (36%), cannulation occurred prior to interfacility transfer. Median duration of ECMO treatment was 5 d (range 1–10). Veno-arterial ECMO ($n = 20$, 91%) was more prevalent than veno-venous ECMO ($n = 2$, 9%). Selected other therapies are displayed in Table 2. Seventeen patients (77%) received vasopressors or inotropes with a median of 4 (IQR: 3–5) vasopressors/inotropes per patient. Ten patients (45%) experienced a complication attributed to ECMO including limb ischemia and/or thrombosis ($n = 5$, 23%), blood transfusion ($n = 4$, 18%), hemolysis ($n = 2$, 9%), intracerebral hemorrhage ($n = 1$, 4%), disseminated intravascular coagulation ($n = 1$, 4%), and compartment syndrome resulting in fasciotomy ($n = 1$, 4%). Cardiac arrest occurred in 12 cases of which seven survived (58%). Additional clinical effects are displayed in Table 3.

Conclusions: The use of ECMO for poisoned patients reported to our Poison Center increased over the study period. ECMO cannulation prior to transfer to an ECMO center was common, suggesting this process may be a feasible recommendation for Poison Centers that cover large geographic areas. Significant complications related to ECMO were observed in almost half of patients. These data suggest that ECMO is a viable therapy for patients in refractory shock due to poisoning, however further study is needed to assess the balance of benefits and complications in this critically ill patient population.

KEYWORDS ECMO; shock; poison center

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36. Studies with enucleated rabbit eyes exposed topically to 10% phenol and decontaminated with amphoteric solutions or tap water: EVEIT and OCT findings

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Background: Phenol (carboxylic acid) is considered a weak acid and has had a wide variety of uses over many years, including as a disinfectant, for chemical skin peels, and many industrial uses. Various recommendations exist for decontamination of phenol skin splashes, but most are not appropriate for eye splashes. Because phenol is poorly water soluble, water eye irrigation may be ineffective.
Methods: In the EVEIT (*Ex Vivo* Eye Irritation Test), freshly enucleated rabbit eyes obtained from an abattoir were exposed for 20 s to a 10 mm filter paper patch saturated with 10% saturated phenol solution in water. Immediately after exposure, the eyes were rinsed with tap water (15 min at 66.7 ml/min), or two slightly different water-based amphoteric solutions (500 ml for 3 min). Experiments were evaluated in triplicate using OCT (Optical Coherence Tomography) and fluorescein staining. Eyes were monitored with photography and then were examined histologically by a blinded observer.
Results: In untreated control eyes, phenol solution caused corneal epithelial and stromal damage with further tissue penetration after removal of the saturated patch. Significant damage was found with tap water rinsing. Much less damage was found after rinsing with amphoteric solutions.
Conclusion: In these studies, tap water rinsing after enucleated rabbit eyes were exposed to 10% phenol, water rinsing was less efficacious than rinsing with amphoteric solutions.

KEYWORDS Phenol; eye decontamination; amphoteric solutions

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37. Shaken not stirred, an assessment of residual charcoal after administration

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Background: Activated charcoal (AC) is one of the most commonly used interventions in toxicology. It is used to help adsorb xenobiotics in the gastrointestinal tract to prevent absorption or interrupt enterohepatic and enteroenteric recirculation. AC forms hard sediment at the bottom of the container, resulting in partial dose administration. Appropriate preparation and administration of activated charcoal is necessary to ensure adequate delivery to adsorb xenobiotics in the gastrointestinal tract. This study sought to characterize the percentage of the AC dose actually administered in clinical practice and during high fidelity simulation with and without administration instructions.
Methods: We conducted a two-phase, prospective non-interventional assessment of charcoal administration in the emergency department (ED) at a single academic medical center. The study was approved by the SUNY Upstate Medical University institutional review board. Prior to initiating the study, ten containers of charcoal were weighed to determine the average mass of a 25 g charcoal dose based on the initial mass and mass of the empty container after washing. The average total mass was used to determine the proportion of residual charcoal in each dose for phase one and two of the study. During phase one of the study, a convenience sample of used 25 g AC containers were collected over 3-months during time periods when one of the researchers was present in the ED. The residual mass of charcoal remaining after administration was determined for each collected dose. During phase two, nurses completed a high fidelity simulation requiring them to triage an overdose patient and prepare a 25 g dose of AC. The nurses were then randomized to undergo video-based education for proper charcoal preparation using either a 30 s shaking method or a 30 s shaking followed by stirring method and then prepared an additional dose as instructed. The residual charcoal mass was determined for each dose. The percentage of AC administered was calculated using the residual mass and pre-determined average dose mass.
Results: Eight AC containers were collected during phase one of the study period and eight ED nurses completed the high fidelity simulation during phase two of the study. All AC containers were from the same manufacturer [Kerr Insta-Char, VistaPharm, Birmingham, AL] but were from different lot numbers. The average percent AC dose administered per container ± standard deviation (SD) from the ED, high fidelity simulation without instruction, and high fidelity simulation with instruction was 59.1 ± 17.7%, 85.8 ± 14.3%, and 97.2 ± 2.1%, respectively. The average percent AC dose administered ± SD when the nurse was instructed to shake the bottle during preparation compared to shaking followed by stirring the preparation was 95.8 ± 1.9% and 98.6 ± 1.1% respectively.
Conclusions: AC administration in the ED resulted in less than 60% of the total dose being administered. Direct observation and, more importantly, education improved the percent of the AC dose prepared for administration. Further research is required to identify the method for optimal charcoal preparation and administration.

KEYWORDS Activated charcoal; GI decontamination; medication dosing

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38. Adsorptive capacity of OTC activated charcoal compared to standard hospital formulation activated charcoal

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Introduction: The adsorptive capacity of various OTC activated charcoals (AC) were compared to two brands of AC commonly used in hospitals.

Method: A stock solution was made by adding 76 ml of green food colouring to 19 l of distilled water. To the 250 ml of the green stock solution, 0.7 g of AC was added. OTC AC products in capsule form had the gelatin capsule removed before adding the AC to the stock solution. The AC-stock solution was stirred for 30 s and then allowed to stand undisturbed for 5 min. The AC was filtered off and the filtrate was scanned with a spectrophotometer. Each AC product was run in triplicate. Adsorption by an OTC AC over time was determined by following the above procedure for seven different samples of one bulk powder OTC AC and filtering off the AC at 0, 5, 10, 15, 20, 25, and 30 min. Using the spectrophotometer, a standard curve was created using dilutions from 5% to 100% (no dilution) of the stock solution. A best-fit polynomial trend line was obtained and the percent of food colouring adsorbed by each AC was calculated. Each sample was measured in triplicate.
Results: Thirteen OTC ACs and two standard hospital formulation (SHF) ACs, one aqueous and one powder, were tested. Eleven OTC AC products adsorbed between 20.2% and 95% of the colouring. Of the eleven, five bulk powder OTC ACs adsorbed between 20.2% and 50.1% of the colouring. Another four OTC AC products sold in capsule form adsorbed between 85.4% and 95% of the colouring. Two additional OTC AC products used for tooth whitening adsorbed 33.%5 and 38% of the colouring. The two remaining OTC products labeled as AC were primarily bentonite. These bentonite products required repeated filtering to adequately remove the bentonite. The bentonite powders adsorbed 7.6% and 9.9% of the colouring.The percent of colouring adsorbed by the SHF ACs was 45.4% for the powdered AC and 39% for aqueous AC. Regarding AC adsorption over time, the amount of colouring adsorbed at the times listed in "Methods" were 15.1%, 15.8%, 15.1%, 18.0%, 18.7%, 31.8%, and 39.9%. Using an OTC capsule AC, the amount of colouring adsorbed at time 0 min was 65.2% and at five min was 88.3%.
Discussion: The SHF AC's adsorptive capacity was similar to that of the adsorptive capacity of the bulk powder and tooth-whitening ACs. The OTC AC capsules, sold specifically as dietary supplements, had the best adsorptive capacity, over twice that of the SHF AC. The labels on three of the four OTC AC capsules read "Caution: Not to be taken at the same time as medications or other dietary supplements … This product is not intended as a treatment for accidental poisoning." While adsorption increased over time in the one product tested, all samples were handled in a similar manner.
Conclusion: Some OTC AC products have potent adsorptive capacity and could affect the body's absorption of medications if the AC and medications are taken at or near the same time.

KEYWORDS Activated charcoal; OTC activated charcoal; spectrophotometry

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39. Efficacy of isosorbide dinitrate in cyanide poisoned swine

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Objective: To evaluate the efficacy of isosorbide dinitrate in cyanide poisoned swine.
Methods: A comparative study was conducted using domestic swine. Animals were intravenously poisoned with potassium cyanide, either 2 mg/kg or 4 mg/kg dose. Two control groups (one for each cyanide dose) were not further treated. Other groups were treated within 1 min after poisoning with isosorbide dinitrate in different doses (50–400 mcg/kg) and routes of administration (intravenous injection and oral spray). The study outcomes were survival, time to death, clinical score, and blood tests including pH, lactate, and methemoglobinlevels.
Results: All the animals started to convulse within 20–30 s after poisoning, then became unresponsive after another 20–30 s. Survival rates were not significantly different between untreated and isosorbide dinitrate treated animals. Clinical scores of the treated swine were significantly better compared to the untreated animals after poisoning with the lower cyanide dose. No significant difference was evident in the clinical scores after the higher cyanide dose. After the lower cyanide dose, acidosis was significantly more pronounced in the untreated animals. In contrast, no significant difference was observed between the study groups after the higher poison dose. Methemoglobin levels were below 1% at any time point in all animals.
Conclusion: Limited efficacy of isosorbide dinitrate was observed only after poisoning with a lower dose of cyanide. Further research using updated study outline may lead to better evaluation of the efficacy of isosorbide dinitrate in cyanide poisoning.

KEYWORDS Cyanide; poisoning; isosorbide dinitrate

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40. Fatal calcium channel blocker poisoning: practice variations in gastrointestinal decontamination

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Background: The combined effects of new pharmaceuticals, novel delivery systems, and recent research shed doubt on the validity of existing practice guidelines for gastrointestinal decontamination (GID). We sought to examine the practice variability of GID in severe calcium channel blocker (CCB) poisoning.
Methods: We performed a secondary analysis of a subset of fatal poisonings reported to the National Poison Database (NPDS). The original dataset comprised over 400 cases from 2010 to 2015 in which intravenous lipid emulsion was recommended or given. In order to provide a more robust analysis, only cases in which a CCB was listed as the primary toxin were included; the largest category in the dataset. Demographics, ingestion history, clinical effects, and therapy were abstracted on a standardized form by one of the authors with >80% verified by a second author. Cases were then assigned to one of three categories: GID was performed; GID was not performed but the patient had an accepted contraindication to GID; GID not performed and there were no reported contraindications. Accepted contraindications in this context included: Non-oral poisoning; altered mental status without a protected airway; and cardiovascular instability requiring major resuscitative efforts. No value judgement was made regarding the indications for GID. Descriptive statistics were used to compare the results.

Results: There are 179 cases of CCB ingestion were identified; 38 diltiazem, 55 verapamil, 77 amlodipine, 6 nifedipine, and 3 unspecified CCB. The majority of cases involved sustained release preparations. Forty-seven percent were male with a mean age of 49 years (range 17–71). Forty-three cases had a documented contraindication to GID, 54 cases received some form of decontamination leaving 82 cases without GID and no reported contraindications. Activated charcoal alone was administered in 31 cases, gastric lavage alone in one, whole bowel irrigation alone in 6 cases. Sixteen cases received mixed GID procedures including gastric lavage in 10 cases, 2 of which returned pill fragments. In 30 cases that received GID, the time of ingestion was reported as unknown. In 16 cases, the delay from ingestion to presentation was reported <6 h, among those, 6 were less than 2 h and 6 others were less than 1 h. In cases that did not receive GID and had no specific contraindications, the reported delay between ingestion and presentation was <6 h in 12 cases (2 of which were <1 h, 2 others between 1 and 2 h) and 53 cases had an unknown time of ingestion. In two cases the poison centre had recommended GID but it was not performed by the local treating teams.
Conclusions: In this dataset derived from the most thoroughly documented part of NPDS we observed a significant heterogeneity in GID for severe CCB poisonings. Despite the limitations of potential miscoding and reporting bias, this highlights either a lack of applicability and/or acceptance of existing guidelines. We hypothesize that an overestimation of the benefits of lipid emulsion therapy and other "antidotal therapies" may have contributed to the abandon of GID in some of these patients.

KEYWORDS Calcium channel blocker; gastrointestinal decontamination; fatality
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41. Acetaminophen immediate release pharmacokinetics in iatrogenic overdose

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Background: Iatrogenic overdose with immediate release (IR) acetaminophen (APAP) has been evaluated several times as a treatment for malignancy. These studies provide a more precise, reliable, and quantifiable database to determine APAP toxicokinetics than case reports, case series, or retrospective studies of APAP overdose.
Methods: We analyzed the concentration data from a clinical study in which APAP 10–20 g/m^2 (15.5–40.5 mg/70 kg) was administered orally and carmustine was administered intravenously to patients with metastatic melanoma. Neither malignant melanoma nor carmustine have been reported to affect APAP pharmacokinetics. Most patients received multiple APAP courses. Intravenous acetylcysteine (NAC) rescue began 6–8 h following the APAP dose. Serum sampling was sparse so the pharmacokinetic (PK) data were fit to a single compartment model with first order absorption. The data were combined across courses for each patient – 1 patient received 8 courses, 5 received 1, 2 received 3, 12 received 2, and 8 received a single course. Individual model fits were via Microsoft Excel 2010 using Solver (GRG Nonlinear). All other data handling and statistics used SAS JMP (12.0.1).

Dose group (g/m^2)	10	15	20
Number of patients	3	19	5
C-max (μ/ml)			
Mean ± SD	195 ± 17.7	290 ± 88.0	355 ± 110.3
Median [min, max]	199 [176, 210]	266 [89, 448]	380 [229, 473]
T-max (h)			
Mean ± SD	1.95 ± 1.28	2.71 ± 0.91	3.65 ± 1.7
Median [min, max]	1.53 [0.93, 3.39]	2.69 [1.48, 5.11]	3.95 [1.31, 5.37]
Half-life (h)			
Mean ± SD	4.11 ± 0.92	3.34 ± 1	4.79 ± 2.18
Median [min, max]	3.85 [3.35, 5.13]	3.65 [0.96, 4.62]	3.73 [2.89, 8.35]
Double peaks			
Number of patients	0	2	0

Results: The table summarizes the maximum APAP serum concentration (C-max), time of C-max (T-max) and elimination half-life from each model fit. C-max shows the expected increase with dose, but concentrations do not quite double with a doubling of dose. T-max mean and median values increase with dose group though this relationship is not statistically significant across this two-fold dosage range. Elimination half-life was greater than 4 h in 9 of 27 (33%) cases. A double peak was observed in two instances.
Conclusion: As the APAP dose increases from 10 to 20 g/m^2, T-max is delayed, elimination half-life is prolonged and double peaks appear. Substantive APAP body burden may thus be evident for more than 24 h. Compared to studies of a therapeutic dose of IR APAP, T-max and elimination half-life all appear longer and similar to toxicokinetics of the extended release (ER) APAP product available in the United States and Canada in contrast to the ER formulation used in other countries. Further studies should be undertaken to evaluate the toxicokinetic profiles after overdose of large non-modified and modified release APAP formulations.

KEYWORDS Acetaminophen pharmacokinetics; immediate release acetaminophen; acetaminophen overdose
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42. B17: not just a vitamin

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Background: Amygdalin, marketed misleadingly by the misnomer "Vitamin B17", is a cyanogenic glycoside found in certain seeds (apricot, bitter almond, etc.). When swallowed, it is hydrolyzed in the small intestine into cyanide, and absorbed systemically. Despite a ban from the U.S. FDA and a Cochrane Review concluding no benefit to treat cancer, amygdalin is still available for purchase over the internet in 500 mg capsules, each containing up to 30 mg of cyanide. Thus, an estimated adult LD50 is as few as four capsules. We present a massive intentional overdose of amygdalin, with delayed recurrent hyperlactatemia, and successful combination antidotal therapy.
Case report: A 33-year-old woman presented to the ED approximately 5 h after intentionally ingesting 40 capsules of 500 mg

amygdalin (20 g). On arrival, her vital signs were: HR 127/min, BP 112/65 mmHg, RR 25/min, SpO_2 98%. She was in agitated delirium, diaphoretic and mydriatic with an ECG notable for QTc 538 ms. Lorazepam 2 mg and magnesium sulfate 2 g were administered for agitation and prolonged QTc, respectively. Within 30 min of sedation, she became comatose, more tachypneic/diaphoretic, and hypotensive; therefore, 5 g hydroxocobalamin was empirically administered. Her pre-treatment venous blood gas showed: pH 7.27, pCO_2 17.1 mmHg, HCO_3 7.7 mmol/l, and lactate 14.1 mmol/l. After initial treatment, she was noted to have oral foaming and hypoxia, so was intubated with sodium bicarbonate pre-treatment and another 5 g of hydroxocobalamin was given along with 25 g of sodium thiosulfate. Her BP normalized, QTc shortened, and lactate fell to 0.9 mmol/l. Approximately 12 h later, her BP decreased to 60 s/40 s, her lactate increased to 8.1 mmol/l and her QTc prolonged to 547 ms. Norepinephrine and vasopressin were started, activated charcoal was given and magnesium sulfate, sodium bicarbonate, hydroxocobalamin and sodium thiosulfate were redosed as previously with an improvement in vital signs, decrease in QTc and clearance of lactate. Her course was complicated by pneumonia, requiring continued sedation and ventilation, but she was extubated with no neurologic deficits on hospital day 9. Initial serum cyanide concentration was found to be 400 mcg/l.

Case discussion: Given that each 500 mg capsule of amygdalin contains up to 30 mg of cyanide, this patient ingested as much as 1.2 g of cyanide. The first-line antidote, hydroxocobalamin, has a binding ratio of 50:1 by molecular weight. So, for every 5 g of hydroxocobalamin, only approximately 100 mg (4–5 capsules) of hydrogen cyanide will be sequestered. As might be expected, toxicity recurred due to ongoing absorption and/or decreased motility to the distal gut, where the majority of cyanide absorption may occur. Finally, we demonstrate the need to redose hydroxocobalamin and sodium thiosulfate in the case of recurrent cyanide toxicity from massive amygdalin overdose.

Conclusions: Amygdalin remains a significant threat to human life with no role as a clinical therapeutic. Internet marketers should be held accountable by government authorities. We present a case of severe, recurrent cyanide toxicity secondary to massive amygdalin overdose, requiring multiple staggered doses of hydroxocobalamin and sodium thiosulfate.

KEYWORDS Amygdalin; cyanide; supplement

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43. Wide alternating QRS complexes from herbal poisoning

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Case presentation: A 44-year-old male, with a history of hypertension and chronic kidney disease presented to the Emergency Department after an out-of-hospital cardiac arrest. The patient had an unknown down-time prior to paramedic arrival and initiation of cardiopulmonary resuscitation. The first rhythm noted on the automatic external defibrillator was pulseless electrical activity. Laboratory tests revealed hyperkalemia and metabolic acidosis. In addition to the immediate medical management, an urgent hemodialysis was started. Despite improvement in metabolic abnormalities following hemodialysis, the patient continued to have ongoing ventricular tachydysrhythmias, which were refractory to electrical cardioversion and intravenous amiodarone. An electrocardiogram (ECG) was obtained and showed wide QRS complexes and left bundle branch block with alternating inferior and superior axes, consistent with a diagnosis of bidirectional ventricular tachycardia (BDVT). This patient's ECG has an unusual pattern for BDVT, which is usually characterized by: (1) alternating left and right bundle branch block, or (2) right bundle branch block with alternating left-and-right axis deviation.

Clinical course: The ECG findings prompted empiric treatment with DigiFab® (digoxin-immune FAB antidote). However, there was no clinical response and, once available, the pretreatment serum digoxin level was undetectable. Further history from the family revealed that earlier in the day, the patient had ingested a large amount of raw aconite root. After 24 h, the ventricular dysrhythmias resolved with eventual improvement in the hemodynamic status. However, despite ongoing supportive care, the neurologic exam and neuroimaging findings were consistent with brain death secondary to anoxic brain injury. The family subsequently decided to withdraw care.

Discussion: Bidirectional ventricular tachycardia is a rare ventricular dysrhythmia characterized by beat-to-beat variation in QRS axis. The differential diagnosis for this dysrhythmia is limited to severe digitalis/digoxin toxicity, familial catecholaminergic polymorphic ventricular tachycardia (CPVT), and herbal aconite poisoning. Importantly, if BDVT is recognized on ECG, digoxin toxicity should always be at the top of the differential diagnosis as it is this poisoning alone that has antidotal treatment. Consideration should be given to CPVT and aconite toxicity as possible etiologies once digoxin toxicity has been ruled out. Aconite is a highly toxic plant that contains aconitine and related alkaloids. It has been used in traditional Chinese medicine, and homeopathy for its analgesic, anti-inflammatory and cardiotonic effects. Aconite poisoning is more common in East Asia. Recognition of this entity may pose a considerable challenge in both diagnosis and management particularly in parts of the world where aconite use is less common. Aconite is a potent sodium channel opener and induces persistent activation of the voltage-sensitive sodium channels in the myocardium and the nervous system. The mainstay of treatment is supportive care and management of ventricular dysrhythmias with standard Advanced Cardiac Life Support protocols. There is no antidote, but there have been anecdotal reports of successful restoration of sinus rhythm with anti-dysrhythmics, specifically those with sodium channel blocking properties.

Conclusion: This case highlights the ECG findings of BDVT. Emergency physicians should be aware that the differential diagnosis of this unmistakable rhythm is digoxin toxicity, CPVT, and herbal aconite poisoning.

KEYWORDS Aconite poisoning; herbal poisoning; bidirectional ventricular tachycardia

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44. The mineral miracle disaster: accidental poisoning after use of 28% sodium chlorite solution resulting in methemoglobinemia and mild hemolytic anemia

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Background: Mineral Miracle Supplement is a concentrated solution of 28% sodium chlorite that has been purported to bestow

numerous health benefits. Toxicity associated with sodium chlorite solutions have only been reported in three individuals in the literature1,2,3. We present a case of sodium chlorite toxicity without the development of significant hemolytic anemia or acute kidney injury.
Case report: A healthy 27-year-old woman presented to the ED after accidentally ingesting approximately 2.5 ounces (75 ml) of 28% sodium chlorite solution mixed in water. The patient's daughter had mixed 2.5 ounces instead of two drops of the solution as instructed on the bottle. Within minutes she developed diaphoresis and intractable vomiting. Upon arrival to the ED, vital signs were: P-132bpm, R-24bpm, BP-99/63 mmHg, SpO_2-80% on room air. Initial arterial blood gas showed pH 7.55, pCO_2 24torr, pO_2 90torr and HCO_3 21 mmol/l (room air) and she was placed on oxygen. Methemoglobin analysis was unavailable. She was intubated and was given a single 50 mg (0.7 mg/kg) dose of methylene blue for suspected methemoglobinemia. Complete metabolic panel, including liver function tests were normal. Hematocrit was normal at 41. Acetaminophen, salicylate, ethanol, and urine drug screens were undetectable. Her oxygen saturation improved and she was transferred to a tertiary care center. Her repeat methemoglobinemia 2 h after methylene blue was 5.3%. During her hospitalization, her hematocrit decreased to 28 and she developed hypotension that briefly required vasopressors. She did not develop acute kidney injury. She was extubated on hospital day two and had an uneventful recovery.
Case Discussion: Only three case reports of exposure to sodium chlorite solution have been previously described in the literature. The three case reports describes: (1) ingestions of 10 g, (2) an unknown amount of 28% solution in water, and (3) $<$ 28 g, that all resulted in methemoglobinemia, hemolysis, disseminated intravascular coagulation, and renal failure. Treatments have included methylene blue, n-acetylcysteine, RBC transfusion and exchange transfusion, and hemodialysis. Previous studies suggest a dose-related response in toxicity and it is possible that our patient ingested less than what was reported (21 g of sodium chlorite). Nonetheless, our report adds to the literature describing this rarely encountered toxin and describes a large dose that was not associated with severe hemolysis or renal toxicity requiring intervention.
Conclusions: Solutions of 28% sodium chlorite solution, such as the marketed Miracle Mineral Supplement, appear to continually be associated with severe toxicity, even in accidental dosing scenarios. Physicians and pharmacists should be aware of the spectrum of sodium chlorite toxicity and advise patients of the potential dangers associated with its use.

KEYWORDS Sodium chlorite; methemoglobinemia; mineral miracle

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45. Large ingestions of melatonin safely tolerated by toddlers

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Introduction: Melatonin is widely used as an over-the-counter sleep aid. While generally regarded as being very safe at commercially available doses, overdose data are limited. We present the case of two pediatric patients that ingested a combined total of 425 mg with minimal adverse effects.
Case presentation: The Poison Center was contacted in regards to two 3-year-old males that reportedly ingested up to 85 Melatonin 5 mg gummies 20 min earlier. The bottle contained 90 gummies when new, and the caller had taken four the night before and was only able to find one on the floor. It was unknown how many gummies each child ingested. The children appeared asymptomatic during the initial call to the Poison Center. Both weighed 14.9 kg, were healthy with no prior medical history and no known allergies. Based on the wide safety profile of melatonin, the decision was made to manage the toddlers at home with close monitoring and hourly follow-up calls throughout the day. On subsequent follow-up calls to the home, both children were noted to be more irritable than normal and both took longer naps than normal, one for 3.5 h and the other for 2.5 h. Otherwise no other changes or symptoms were reported in the 8 h after ingestion. Additionally, no other gummies were found in the home.
Discussion: Besides signs and symptoms commonly associated with CNS depression, other reported adverse effects from melatonin include nightmares, hypotension, sleep disorders, and abdominal pain. Doses of up to 80 mg orally and 100 mg intravenously have been used safely in pharmacokinetic studies. Admittedly our decision to monitor the patients at home ran against the information posted in databases routinely utilized by the Poison Center which recommended home observation for accidental ingestions of 80 mg or less.
Conclusion: Recognizing the limitations incumbent with Poison Center data, these cases demonstrate the low risk generally associated with melatonin and the effective use of Poison Center services to safely avoid unnecessary healthcare utilization.

KEYWORDS Melatonin; pediatric; ingestion

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46. Severe rattlesnake envenomation in a patient with impaired lymphatic flow after double mastectomy

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Background: In the United States, there are an estimated 8000 pit viper bites occurring each year. Pit Viper venom is complex and depending on the species involved, may cause any combination of local tissue injury, coagulation abnormalities, and neurotoxicity. The venom is thought to be absorbed into the blood capillaries and lymphatic system once injected into the tissues, after which it is distributed systemically. Thus, it can be postulated that an individual with impaired lymphatic drainage, local injury may be more severe. We report a case of an individual with an impaired lymphatic drainage status post lymph node dissection with severe local tissue damage in the envemonated limb.
Case report: An 80-year-old female with a history of double mastectomy with lymph node dissection and CHF; was bitten in her right wrist by a rattlesnake. At the scene, the swelling was localized around the bite site. However, when she arrived at the emergency department 1 h later, the swelling had extended to the shoulder with ecchymosis to the elbow. Her initial labs showed PT of 17.4 s, PTT of 34 s, INR 1.4, platelets 82 $\times$ 109/l, and D-dimer was 0.91 mg/l. Patient received six vials of Crotalidae Polyvalent Immune Fab (AV) and she was transferred to a tertiary care facility. She had significant local injury with bullae already

forming at and around the bite site. A second dose of 6 vials (Total 12) was given. On reevaluation, edema and induration had progressed into the axilla, so a third loading dose of 4 vials was given (Total 16). Day 2, the patient had significant third-spacing with pronounced edema and ecchymosis extending into the mid chest wall with several bullae present, another 4 vials (Total 20) was given before starting maintenance doses (Total 26). Day 3, patient received another 4 vials (Total 30) due to increased edema. Day 4 and 5, the swelling had improved. Days 6 and 7, her hemoglobin had trended down to 7.4, so she was given one unit of pRBCs and an additional 4 vials of AV (Total 34). Day 8, the patient was discharged home and she was doing well at follow-up appointment 2 d later.

Case discussion: Antivenom has been shown to halt progression of local effects, setting-up a paradigm of 'time is tissue'. Paniagua et al. showed that the lymphatic system has an important role in the absorption of snake venom. After subcutaneous injection in a sheep model of envenomation, the highest concentration of venom was found in the lymph, and it was more than 25-fold higher than in the blood. Another animal model of rattlesnake envenomation using pressure immobilization bands, which inhibit lymph flow, showed worse local tissue injury. In our patient, with double mastectomy and lymph node dissection, her severe local effects may be explained by her impaired lymphatics. It suggests that aggressive administration of AV in patients with a history of lymph impairment in the affected limb may minimize morbidity.

KEYWORDS Rattlesnake; lymphatics; envenomation

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47. Burning coral causing multiple palytoxin exposures

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Background: Palytoxin is one of the most potent toxins found in the world. Produced by some microalgae, sea anemones, and zoanthid coral, it poses a risk to humans by dermal, ingestion, or inhalational exposure. The exact mechanism of toxicity is unknown. It is theorized that palytoxin effects the Na+/K+ATPase pump causing the depolarization of cells leading to multiple organ dysfunction. Deaths have been reported. Inhalational exposure is reported to occur with boiling or pulverizing coral. We report four cases from one high school science class of palytoxin exposure. This is the first documented event of palytoxin exposure from burning coral.

Case report: Case 1 – 48-year-old female teacher with a history of asthma cleaned out her classroom aquarium and proceeded to burn zoanthid coral. Within 30 min she developed shortness of breath and wheezing. She then developed myalgias and reportedly had an elevated temperature and atrial fibrillation with a rapid ventricular rate though specific vitals were not documented in the Poison Center database. Patient was treated with bronchodilators.

Case 2 – 17-year-old male student with a history of chronic kidney disease experienced headache, abdominal pain, and palpitations 30 min after exposure. On arrival to the emergency department, patient had a heart rate (HR) of 133 bpm, blood pressure (BP) of 135/95 mmHg, and temperature of 37.5 °C. Within 1 h he developed a temperature of 39 °C. A comprehensive metabolic panel and creatinine kinase were normal other than a creatinine of 7 mg/dl which is baseline for the patient.

Case 3 – 16-year-old male student developed chills, chest pain, headache, and back pain 3 h after exposure. The patient was found to have a HR of 118, BP 127/49 mmHg, oxygen saturation 95% on room air, respiratory rate (RR) 20, and a temperature 38.1 °C after receiving 1 g of acetaminophen.

Case 4 – 15-year-old male student presented to a pediatric emergency department with bronchospasm, myalgias, hyperthermia, and fatigue 45 min after exposure to burning coral. Initial HR was 175 bpm, BP 142/60 mmHg, O_2 saturation 98%, RR 26, and temperature 39.2 °C. He had diffuse bilateral wheezing on bedside toxicology consult exam. Patient received acetaminophen, normal saline, and bronchodilators. All labs other than stated including comprehensive metabolic panels, complete blood counts, and creatinine kinases were normal.

Cases 1 and 3 were observed for 6 h.

Cases 2 and 4 were admitted for observation overnight. All patients were discharged with normal vitals and feeling well.

Case discussion: Palytoxin is known to be heat stable in the setting of boiling water. These cases suggest that palytoxin may be stable at much higher temperatures also. Reported symptoms from inhalation exposure including rhinorrhea, cough, bronchospasm, nausea, vomiting, headache, and abdominal pain. There is no antidote to palytoxin and treatment is mainly supportive care. While we recognize smoke inhalation may present with similar symptoms, the documented fevers and abdominal pain is suggestive of another mechanism.

Conclusion: These are the first reported cases of likely palytoxin exposure from burning coral.

KEYWORDS Palytoxin; coral; inhalation

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48. Fatality after *Abrus precatorius* ingestion with severe neurologic symptoms

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Background: *Abrus precatorius* is an ornamental plant indigenous to tropical regions including areas of the southern United States. The seeds are known by various names including rosary pea and jequirity bean and have a characteristic bright red color with a black end. The seeds contain the toxin Abrin that irreversibly binds the 60 s ribosomal subunit which inhibits protein synthesis. We present a fatal case of Abrin toxicity after ingestion of 1000 ground seeds.

Case report: A 20-year-old man presented to an emergency department with 36 h of nausea, vomiting, and diarrhea that had progressed to hematemesis and hematochezia. He admitted to purchasing a 1000 jequirity beans online, crushing them and ingesting them 2 d prior to presentation in a self-harm attempt. The patient was neurologically normal on presentation. He had previously attempted suicide with castor beans. His family found the packaging from his online purchase of the Abrus seeds as

well as a pill grinder that he used to process them. He had progression of gastrointestinal symptoms for 2 d which improved with supportive care. He developed confusion and agitation with tremors and abnormal eye movements. His head CT was normal. His symptoms progressed to obtundation and he developed choreoathetoid movements of his extremities. EEG was significant for mild background slowing. MRI showed bilaterally symmetric signal abnormalities in the basal ganglia, brainstem, corpus callosum and corona radiata with diffuse leptomeningeal enhancement. Supportive care was continued. Abrine was detected (8.84 ng/ml) in the patient's urine approximately 61 h after the ingestion. He developed a tonic clonic seizure followed by pulseless electrical activity. His family ultimately chose to discontinue resuscitation and aggressive interventions due to presumed poor neurologic outcome and he died 5 d after his ingestion despite aggressive supportive care.
Case Discussion: There are case reports of Abrin toxicity with neurologic symptoms including seizures and demyelination. This severe case of Abrin toxicity was associated with choreoathetoid movements of the extremities as well as seizures and diffuse leptomeningeal enhancement on MRI. Urine samples confirmed exposure to Abrin toxin by confirmation of Abrine in the urine which was present almost 3 d after exposure.
Conclusion: Large ingestions of Abrin can be lethal and associated with neurologic symptoms as well as abnormalities on MRI.

KEYWORDS Abrin; abrus precatorius; plants

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49. Acute expressive aphasia after intravenous ozone gas therapy

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Background: Ozone therapy is a type of alternative medicine that has been purported to aid in the treatment of various ailments including herpes, acne, AIDS, Parkinson Disease, cancer, and multiple sclerosis. It can be administered by topical, oral, intramuscular, and intravenous (IV) routes. When infused IV, it can be mixed with a patient's blood to dissolve in solution and then reinjected, or administered directly into a vein as a gas. Although the U.S. Food and Drug Administration (FDA) reports ozone is a toxic gas with no known useful medical applications, proponents of this therapy tout the safety of ozone therapy and note few if any complications.
Case report: A 69-year-old woman without significant past medical history was administered ozone (O_3) gas 28 ml intravenously at an alternative medicine clinic. Within one min she became confused and lightheaded. She was observed for approximately 5 h in the clinic and was administered glutathione before being transferred to the ED. There, she had normal vital signs and expressive aphasia without other focal neurological deficits. Laboratory data were without significant abnormality. A CT scan of her head showed no acute abnormalities and no air embolus was noted. An MRI brain revealed a left temporal lobe infarction. Over the course of 6 d, with supportive care, she improved and was able to converse with limited difficulty and was discharged home with persistent confusion and home health services. The case was reported to the South Carolina Department of Health and Environmental Control for further investigation.
Discussion: Air emboli are reported as a complication of manipulation of central venous, hemodialysis, or arterial access. Cerebral air emboli are described in cases with aterio-venous connections, such as patent foramen ovale or atrial septal defect, but even without connection between venous and arterial circulations. The described patient was infused with a relatively large volume of gas. She did not have a large cerebral air embolus on imaging, which guided her further workup for other causes of cerebral infarction rather than transfer for emergent hyperbaric oxygen therapy. There was also significant delay to seek medical care between the onset of symptoms as the patient was being observed until resolution of her symptoms. It is unclear whether CT imaging would have been able to diagnose an air embolus if it was performed closer to the onset of symptoms. Given the temporal relationship between the administration of ozone and the onset of symptoms it is likely that was the causative agent.
Conclusion: Ozone therapy in an alternative medicine clinic administered directly IV was associated with acute expressive aphasia and left temporal infarction.

KEYWORDS Ozone; CVA; gas embolism

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50. Is it *Amanita phalloides*? what is the value of a clinical diagnosis?

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Background: Although silibinin reportedly improves mortality in patients with cyclopeptide-containing mushroom poisoning, such as Amanita Phalloides, randomized controlled data in humans are lacking. In fact, an ongoing uncontrolled trial of silibinin will likely compare cyclopeptide-associated mortality to historical controls. The purpose of this study was to examine the mortality rate of patients with suspected cyclopeptide-containing mushroom ingestions reported to a single poison control center (PCC) using the same clinical criteria as the current silibinin trial.
Methods: This was a retrospective review of patients with presumed amanita phalloides ingestion using the same definitions as the current silibinin trial (NCT00915681): History of eating foraged mushrooms, gastrointestinal symptoms within 48 h of mushroom ingestion, and liver function tests (asparate transaminase (AST) or alanine transferase (ALT)) above the upper limit of normal within 48 h after mushroom ingestion. Toxicall data were searched for all human exposures reported from health care facilities between January 1, 2000 and December 31, 2017 in which ingestion of mushrooms were reported and the inclusion criteria previously mentioned were met. Case fatality rate and final diagnosis were recorded.
Results: There were 1498 cases of human mushroom exposures reported to our PCC, of which 662 were from a health care facility and 36 met inclusion criteria. Demographics of the study population included: age range between 7 and 76 years and 26 (72%) were male. The AST and ALT ranged between 30–10,000 and 33–9000, IU/l, respectively. Three patients died resulting in a mortality rate of 8.3%. None of the three fatalities had laboratory confirmation of amanita phalloides. One patient in the study had an unconfirmed case of amanita phalloides who received silibinin and survived. There was one mycologist confirmed case of amanita phalloides who survived with supportive care alone.

Additionally, there were two mycologist confirmed cases of chlorophyllum molybdites, as well as a woman ultimately diagnosed with choledocholithiasis. Although neither case involved amanita phalloides, both met inclusion criteria and survived.
Conclusion: This retrospective review demonstrates a very low mortality rate in patients who meet the current criteria for enrollment in the silibinin trial. It also highlights the significant limitation of clinical inclusion criteria to confirm cyclopeptide mushroom ingestion. The presence of gastrointestinal symptoms within 48 h includes patients who had symptoms within the first 6 h of ingestion, making amanita phalloides ingestion less likely. Additionally, any abnormality in AST or ALT may lead to false positive inclusion secondary to rhabdomyolysis, a history of hepatic disease or concurrent alcohol use. Yet even with these major limitations, the mortality rate of presumed amanita phalloides ingestion is likely overestimated because many survivors had to be excluded for lack of AST or ALT reporting. In conclusion, using the current clinical criteria of the silibin trial, the mortality rate from presumed cyclopeptide containing mushroom ingestion is lower than previously documented. Using these flawed definitions, in order to demonstrate a 50% reduction in mortality from a conservative 10% mortality, the current silibinin trial would have to include over 200 patients to reach statistical significance with an alpha of 0.05 and a beta of 0.2.

KEYWORDS Amanita phalloides; mushroom; silibinin

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51. Angioedema, cricothyrotomy and continuous antivenom infusion after rattlesnake envenomation

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Background: Venom-induced respiratory compromise is rare after rattlesnake envenomation, requiring emergent intubation in only 0.7% of cases. Repeat envenomation may cause IgE-mediated anaphylaxis with dyspnea, wheezing and angioedema. Prior work suggests that dermal exposure to snake proteins results in the formation of antibodies against snake venom. Therefore, it is postulated that anaphylaxis may occur without previous envenomation. Alternatively, it has been proposed that respiratory compromise without prior envenomation may be due to anaphylactoid reactions or direct venom microangiopathic toxicity.
Case report: A 57-year-old male without prior envenomation was bitten on the hand by a decapitated rattlesnake, likely *Crotalus oreganus* by geography. He rapidly developed facial swelling, respiratory distress, and altered mental status. Paramedics found him with SpO_2 of 83% and blood pressure of 140/76 mmHg. They administered albuterol, epinephrine and diphenhydramine, and summoned air medical transport. Oral intubation with video laryngoscopy failed due to profound angioedema of the lips, tongue, and hypopharynx. A cricothyroidotomy was performed, resulting in significant bleeding. A norepinephrine (NE) infusion was initiated en route to our hospital. In the emergency department, six vials of Crotalidae polyvalent immune Fab (CroFab®) were administered. No skin rashes or pulmonary wheezes were present. NE was discontinued. Initial lab values were: INR 1.92, fibrinogen 66 mg% and, platelets 5000/mm^3. Twelve additional vials of CroFab®, 1 unit fresh frozen plasma, and 2 units packed red cells were given. Repeat lab values were: INR 1.49, fibrinogen 71 mg%, and platelets 179,000/mm^3. The cricothyrotomy was then converted to tracheostomy. Over subsequent days, his extremity edema stabilized but he had recurrent thrombocytopenia and bleeding. He received two vials CroFab® three times as well as a continuous CroFab® infusion (one vial over 4 h for 12 h) based on hypothesized venom and CroFab kinetics. His angioedema resolved and his tracheostomy was decannulated. He then left against medical advice. He was advised to abstain from work or dangerous activities. Discharge lab values were: platelets 73,000/mm^3, INR 0.91, fibrinogen 301 mg%. Two days later, the patient presented for lab testing. Findings were: platelets 23,000/mm^3, fibrinogen $<$50 mg%, INR 1.50. He had no bleeding or bruising and declined admission for treatment. Three days later, he was evaluated in clinic. Labs values were: platelets 60,000/mm^3, fibrinogen 86 mg%, and INR 1.04. He again declined treatment. At 2-week follow-up his lab values had normalized.
Discussion: Our patient had no prior crotalid envenomation. He regularly handled and ate rattlesnakes but denied associated urticaria, tearing, wheeze, or diarrhea. We believe his presentation is inconsistent with an anaphylactic or anaphylactoid reaction as he did not demonstrate hypotension, urticaria or wheeze and did not require vasopressor therapy after CroFab® administration. Additionally, his angioedema improved after antivenom but not with epinephrine. This patient is also unique in that he had severe, delayed coagulopathy which was managed without additional antivenom or blood products and he had no adverse outcomes.
Conclusion: We present an unusual case of severe angioedema not clearly due to anaphylaxis or anaphylactoid reaction, requiring emergent surgical airway, in a patient with first crotalid envenomation.

KEYWORDS Crotalid; angioedema; antivenom

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52. Alpha-lipoic-acid (ALA) toxicity with seizure, lactic acidosis, and agitation; another supplement to make you healthy

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Background: ALA is an antioxidant gaining use in the treatment of diabetes, cancer, hepatic, and Alzheimer disease. There is minimal human efficacy data. Toxicity and adverse events are described as rare. We present a case of ALA overdose with associated metabolic acidosis, seizure, and agitation requiring intubation.
Case report: A 34-years-old male presented to the ED after ingesting approximately 10,800 mg of ALA that he took for malaise. He felt ill afterwards, called his father who advised him to go to the ED. Father did not believe this was suicide attempt based on discussion and recent status. In the ED, initial mental status was normal, and he complained of nausea and vomiting. VS: Hr 104, BP 120/67, RR 28, temp 94.3, and SpO_2 99% on RA. Pill count was consistent with report. Over the next couple hours, he became increasingly agitated with upper and lower extremity myoclonus with minimal improvement with IV benzodiazepines. He was increasingly diaphoretic with tachypnea. Initial labs showed an acidosis with pH 7.2, pCO_2 39, pO_2 475, and HCO_3 15.

Chemistry showed HCO_3 of 19 with an anion gap of 19. Lactate was elevated at 5.4 mmol/l. ASA and APAP were undetectable. CK was elevated at 4114 U/l. Agitation worsened and he was intubated to facilitate increased sedation and for concern of worsening metabolic status. Sedation was maintained with propofol and fentanyl. He developed a petechial, non-blanching rash across his back and chest. With hypothermia, rash, and encephalopathy antibiotics were started and LP done which showed no organisms, normal glucose, and protein. In the next few hours he had tonic-clonic seizure activity. It lasted about 2–3 min and spontaneously resolved. He was loaded with levetiracetam. He had no further seizures. Vital signs remained stable and hypothermia resolved. Over the next 24–48 h, CK peaked at 6288 U/l and lactate peaked at 6.2 mmol/l. He received supportive care including sedation and hydration. Over the following day, labs trended towards normal. Sedation was lightened, and he was extubated. Mental status normalized. Psychiatric consult agreed that although a bad decision, ingestion was not suicidal. He was discharged home with PCP follow-up on HD#3.
Discussion: ALA is an over-the-counter antioxidant. Although not well studied in humans, it is utilized in the treatment of diabetic and chemotherapeutic-induced neuropathy. ALA has also been used for heavy metal poisoning and Alzheimer disease, though again studies are lacking. Doses range from 600 to 2000 mg/day. ALA is reported as safe, though there are rare cases of acute toxicity from overdose reported in the literature. Described clinical effects include altered mental status, abnormal muscle movement, tachycardia, hypotension, metabolic acidosis with elevated lactate, seizure, and ventricular dysrhythmias. One death was reported in a 14-year-old girl after suicidal ingestion of at least 6 gm. Although we were unsuccessful in getting a concentration, we have no other cause for clinical presentation and course is consistent with prior description of toxicity.
Conclusions: Although uncommon, clinicians need to be aware of the potential neurologic and metabolic toxicity associated with over-the-counter ALA as use appears to be increasing.

KEYWORDS Alpha-lipoic-acid; supplement; toxicity

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53. Sago cycad (*cycas revoluta*) exposures: it's more than just ingestion

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Background: Sago cycad or palm (*Cycas revoluta*) is an ornamental plant in the United States and used as an inexpensive, readily available food starch in underdeveloped parts of the world. In the U.S., exposures are most likely after confusing as a food source, accidental, or exploratory ingestions. All parts of the plant are toxic, with the seeds containing the greatest concentration of cycasin and beta-methylamino l-alanine and can be harmful if ingested. It is possible for cycasin toxin on the seeds to survive vigorous repeated washings. Clinical symptoms of ingestion will develop within 12 h and include vomiting, diarrhea, abdominal pain, tachycardia, headache, dizziness, weakness, seizures, and liver failure. This study aimed to characterize clinical effects after *C. revoluta* exposures reported to poison centers.
Methods: Cases were *C. revoluta* exposures reported to a statewide poison center network during 2000–2017. The distribution of cases was determined for various factors related to patient demographics, exposure circumstances, management, and outcome.
Results: Of 164 total *C. revoluta* exposures, the patient age distribution was 46 (28%) 5 years or less, 24 (14.6%) 6–12 years, 7 (4.3%) 13–19 years, and 84 (51.2%) 20 years or more; 89 (54.3%) were male. The most common exposure routes were ingestion ($n = 92$, 56.1%) and dermal ($n = 58$, 35.4%). The exposure reason was unintentional in 150 (91.5%) of the exposures and occurred at the patient's own residence in 155 (94.5%). The patient was managed on site in 127 (77.4%) of the cases, already at/en route to a healthcare facility in 20 (12.2%) and referred to a healthcare facility in 16 (9.8%). Medical outcomes were reported as 44 (26.8%) no effect, 24 (14.6%) minor effect, 3 (1.8%) moderate effect, 12 (7.3%) not followed-judged nontoxic, 70 (42.7%) not followed-minimal effects possible, 10 (6.1%) unable to follow-potentially toxic, and 1 (0.6%) unrelated effect. No deaths were reported. The most common reported clinical effects were dermal ($n = 41$, 25%), particularly puncture/wound ($n = 28$, 17.1%), dermal irritation/pain ($n = 26$, 15.9%), and edema ($n = 17$, 10.4%), followed by gastrointestinal ($n = 19$, 11.6%), particularly vomiting ($n = 13$, 7.9%) and nausea ($n = 10$, 6.1%).
Discussion: Most of the patients exposed to *C. revoluta* were adults. The exposures tended to be unintentional and occurred at home. Although most of the *C. revoluta* exposures involved ingestion, 35% were dermal, and the most frequently reported clinical effects were dermal followed by gastrointestinal. Most of the exposures were not severe and were managed outside of a healthcare facility.
Conclusion: *C. revoluta* exposures resulted in mostly minor dermal and gastrointestinal clinical effects.

KEYWORDS Cycas revoluta; sago palm; plant toxicity

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54. *Melia azedarach* ingestions reported to a statewide poison center network

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Background: *Melia azedarach*, also known as the chinaberry tree, is native to Southeast Asia and Northern Australia but has become an invasive species in the United States. *M. azedarach* contains limonoid tetranortriterpenes, found in highest concentrations in its berries. The toxins are meliatoxin from the fruit and toosendanin from the bark. They may act like insecticides. Ingestion has been reported to result in adverse clinical effects of the gastrointestinal, cardiovascular, respiratory, and neurological systems, and even death. This investigation describes *M. azedarach* ingestions reported to a statewide poison center network.
Methods: Cases were *M. azedarach* ingestions reported to a statewide poison center network during 2000–2017. We describe patient demographics, ingestion circumstances, management, and outcome for these cases.
Results: Of 961 total *M. azedarach* ingestions reported, 836 (87%) involved the berry. Of these, 558 (66.7%) were reported to involve only one berry. There was a seasonal pattern with 42.8% of exposures reported during March–May. The patients were male in 55% of cases, and 86% of the patients were aged 5 years or less. The ingestion occurred at the patient's residence in 83% of cases and school in 9%. Patients were managed outside of a healthcare facility in 90% of the cases. Ninety-five percent of the ingestions resulted in no or at most minor clinical effects, and no deaths were reported. The most frequently reported clinical effects were gastrointestinal (11.4% – vomiting 5.3%, diarrhea 2.4%, nausea

1.6%, abdominal pain 1.6%, other) and neurological (2.3% – drowsiness/lethargy 1.5%, agitated 0.3%, seizures 0.2%, other) in nature. The most common treatments were dilution (67%) and food/snack (16%).
Discussion: *M. azedarach* ingestions reported to Texas poison centers tended to involve berries, usually a single berry. Most of the patients were young children. The intakes often occurred in March–May and at the patient's home or school. The ingestions typically were managed outside of a healthcare facility and did not result in severe outcomes. The most common clinical effects were gastrointestinal and neurological.

KEYWORDS Melia azedarach; chinaberry; plant toxicity

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55. *Euphorbia tirucalli* exposures reported to a statewide poison control network

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Background: *Euphorbia tirucalli*, commonly known as pencil cactus, is not a true cactus but a member of the Euphorbiaceae family that produces a milky white latex that can cause problems if ingested or comes in contact with the skin or eyes. This study characterized *E. tirucalli* exposures reported to a large, statewide poison center network.
Methods: Cases were *E. tirucalli* exposures reported to the poison center network during 2000–2017. The distribution of cases was determined for various factors related to patient demographics, exposure circumstances, management, and outcome.
Results: Of 668 total *E. tirucalli* exposures, the patient age distribution was 16.9% 5 years or less, 7.6% 6–12 years, 1.6% 13–19 years, and 72.3% 20 years or more; 56% were male. The most common exposure routes were ocular (61.1%), ingestion (31.7%), and dermal (17.2%). The exposure reason was unintentional in 97.5% of the exposures and occurred at the patient's residence in 94.5%. The patient was managed on site in 66.8% of the cases, already at/en route to a healthcare facility in 22.0% and referred to a healthcare facility in 9.6%. A potentially severe outcome (moderate effect, major effect, unable to follow-potentially toxic) was reported in 16.9% of the cases; no deaths were reported. The most commonly reported clinical effects were ocular 400 (59.9%), [including irritation pain 397 (59.4%), red eye 159 (23.8%), lacrimation 89 (13.3%), blurred vision 9 (1.3%), burns 2 (0.3%)], dermal 94 (14.1%) [including irritation 66 (9.9%), erythema flushed 27 (4%), edema 15 (2.2%), and rash 11 (1.6%)], and gastrointestinal 82 (12.3%) [oral irritation 65 (9.7%), throat irritation 20 (3%), abdominal pain 3 (0.4%), and one oral burn (0.1%)].
Discussion: The majority of patients involved in *E. tirucalli* exposures reported to the poison centers were adults and male. Most exposures were unintentional and occurred at the patient's residence. The most common routes of exposure were ocular, ingestion, and dermal contact. The majority of patients were known or expected to have no more than minor effects and successfully managed outside of healthcare facilities. The most frequently reported specific adverse clinical effects were ocular, dermal, and gastrointestinal. Such information may prove useful for targeting education and prevention activities relating to *E. tirucalli* exposures.
Conclusion: *E. tirucalli* exposures were mainly unintentional and resulted in mostly ocular, gastrointestinal, and dermal effects.

KEYWORDS Euphorbia tirucalli; pencil cactus; plant toxicity

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56. *Salmonella* contaminated Kratom ingestion associated with fulminant hepatic failure requiring liver transplantation

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Case report: A previously healthy 27-year-old man started ingesting Kratom powder (*Mitragyna speciosa*), purchased online, as a supplement for his workout regimen by adding the powder to a shake. Several weeks after using this product multiple times weekly, he developed nausea, vomiting and diarrhea. On day 3 of his symptoms he presented to the emergency department with persistent vomiting, diarrhea, and abdominal pain. Initial laboratory results showed an acetaminophen level of 174 umol/l (2.6 mg/dl) (consistent with reported consumption of 4 g/day for 72 h for symptomatic relief), AST 1431 U/l, ALT 330 U/l, ALP, 109 U/l, and total bilirubin 16.8 umol/l (0.98 mg/dl). Over the next 48 h his liver enzymes peaked: AST >14000 U/l, ALT 6969 U/l, ALP 162 U/l, GGT 186 U/l, with a rise in total bilirubin to 192 umol/l (11.2 mg/dl), an INR 8.8 and PTT 60 s. Comprehensive urine toxicology screen was negative, except for acetaminophen and caffeine. Blood cultures were positive for *Salmonella Javiana*. Extensive work-up for other causes of liver failure was negative. This patient went on to receive a liver transplant due to lack of hepatic function recovery on day 5 of his hospital admission. Core biopsies of his native liver prior to transplant showed extensive hepatocellular necrosis involving 70% of the liver, with extracellular cholestasis. Analysis of two of the bags of Kratom powder purchased online detected Mitragynine, paynantheine, and speciogynine (an isomer of mitragynine), all known plant alkaloid components of Kratom. No other product adulterants were detected by gas chromatography/mass spectrometry analysis. There may have been an additional bag of Kratom powder ingested that was not available for analysis. Confirmation of Salmonella contamination and serotype of the Kratom product was arranged through the local Public Health Unit.
Case Discussion: Kratom (*Mitragyna speciosa*) is a tree native to Southeast Asia. The leaves have been used as a traditional medicinal plant and more recently as a drug of abuse due to its stimulant and opioid receptor agonist properties. It has also been considered as an alternative treatment for opioid dependence management. Despite variable legal status around the world, the product is easily obtainable from online product sites with the disclaimer that the product is "Not for Human Consumption". Just days prior to this case presentation, the FDA issued a mandatory recall of a number of Kratom products found to contain Salmonella after a multistate outbreak of salmonellosis in the United States. To the authors' knowledge, this was the first reported case of suspected Salmonella contamination of a Kratom product purchased from a Canadian distributor. Despite likely widespread use of Kratom around the world, there is little published information available about complications from use and safety of the product. There are some reports of transient hepatotoxicity, predominantly cholestatic type, reported in the literature and a less severe case identified in our Poison Centre database in 2016.
Conclusion: To our knowledge, this is the first reported case of fulminant hepatic failure requiring liver transplantation presumed secondary to Salmonella contaminated Kratom ingestion.

KEYWORDS Kratom; hepatotoxicity; salmonella

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57. Systemic loxoscelism. Effective therapy with F(ab')2 antibodies: report of two cases.

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Introduction: Loxosceles spider venom contains several toxins; conformed by three molecular families: the phospholipases D, astacin-like metalloproteases and Inhibitor Cystine Knot (ICK) peptides. The toxins have proinflammatory, cytotoxic, hemolytic, vasculitic, direct nephrotoxic, and procoagulant properties and are found in all the species of Loxosceles American spiders with a homology between them; although there is variability according to the region; in Mexico the spider Loxosceles laeta predominates. Because of all these biochemical properties, the clinical manifestations of loxoscelism are diverse and vary in intensity.
Case presentations: A 7-year-old female with pain intensity 8/10 in her left leg, and unquantified fever of 6 h of evolution. The mother observed a vesicle surrounded by erythema in the inner malleolus and edema of the left foot in addition to erythematous macules without pruritus over the ipsilateral lymphatic chain with progressive evolution of the size of the lesion.
Exam: There was a dark point excavated of 3 mm surrounded by a white halo of 1.5 centimeters surrounded by an erythematous area of 14 × 7 cm in diameter. She developed leukocytosis, elevated transaminases, hyperfibrinogenemia, epistaxis, and respiratory failure. The patient received one dose of antivenom with F(ab')2 antibodies ("Reclusmyn ®") however, she developed cytotoxic reactivation 22 h after the first dose; thereafter, she received a second dose of antivenom; she had clinical improvement and left the hospital 4 d after. A 82-year-old woman, while who was in his backyard gathering grass, referred to felt a discomfort located unspecifically in her right arm. She arrived at the hospital 5 d after the event.
Exam: Dermonecrosis in the right arm and forearm. She develops acute renal failure, leukocytosis, and systemic inflammatory response syndrome. The patient received two doses of antivenom with F(ab')2 antibodies ("Reclusmyn®") in the first dose. The patient was admitted to the intensive care unit for support management of complications. She was monitored until the clinical resolution 5 d after.
Discussion: The systemic loxoscelism occurs in a minority of cases but may be severe and occasionally fatal. "Reclusmyn®" polyvalent antivenom with F(ab')2 antibodies is constituted by F (ab') 2 fragments of the antiloxosceles immunoglobulin G hyperimmune obtained of horses. The horses are hyperimmunized with phospholipase D; the recombinant toxin of the Loxosceles spider: reclusa, laeta and bonetti species. F (ab') 2 Antibodies are useful for all types of loxoscelism, however, they are not available to the public access. The biology of the spiders loxosceles, fisiopathology of envenomation and the immunogenicity of Loxosceles venom are complicated, as are the clinical features, diagnosis and clinic treatment but the various current therapies are not effective and can be even damaging.
Conclusion: The antivenom with F(ab')2 antibodies is the only specific treatment that neutralizing the venom of spiders from Loxosceles genus, in order to prevent the necrotic lesions and systemic manifestations including intravascular hemolysis, disseminated intravascular coagulation and acute renal failure. According to the improvement observed in these cases, the F (ab')2 Antibodies are an effective therapy for systemic loxoscelism.

KEYWORDS Systemic loxoscelism; therapy with F(ab')2 antibodies; loxosceles spider venom

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58. A case of bradycardia, nausea, vomiting, and diarrhea after *Echinops kebericho* ingestion

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Background: *Echinops kebericho* is one of over 120 species in the Echinops genus. It is a plant found in the Ethiopian highlands. Traditionally, it is used for the treatment of various ailments including fever, diarrhea, and abdominal pain and to promote overall health. Additionally, it has been reported to have antimalarial and antihelminthic effects.
Case report: A 54-year-old Ethiopian woman with a history of hypertension presented to a local emergency department with nausea, vomiting and diarrhea approximately 1 h after ingesting slurry containing *E. kebericho* that she obtained from a health care provider in Ethiopia for "overall health". Vital signs at presentation were: BP:138/62, Pulse: 43, and Respiratory Rate: 20, Temperature 36.6 °C, SpO_2 99%. EKG revealed junctional bradycardia at a rate of 43 with diffuse *T*-wave abnormalities. Labs including CBC, chemistry and troponin ×3 were within normal limits. CT abdomen and pelvis did not reveal any acute process. Given the EKG findings, and persistence of bradycardia, 0.5 mg of atropine was administered intravenously. The patient's heart rate rose into the normal range, and the remainder of her vital signs were within normal limits. Her GI symptoms were addressed supportively and resolved after administration of intravenous fluids and antiemetics. She was observed in the emergency department for 4 h, and upon re-evaluation, she reported feeling back to baseline. Repeat EKG demonstrated resolution of the junctional bradycardia. The repeat study revealed sinus rhythm at a rate of 9 with a left bundle branch block of unknown chronicity that did not meet Sgarbossa's criteria. The patient was subsequently discharged home with strict return precautions in stable condition.
Case discussion: We present a case of a patient who ingested *E. kebericho* who then developed with gastrointestinal symptoms and a persistent junctional bradycardia that was responsive to a single dose of atropine and supportive care.
Conclusions: *E. kebericho* is a plant used for medicinal purposes in Ethiopia. There are few reports in the literature that characterize the potential adverse effects associated with its use. Bradycardia and GI illness may be associated with *E. kebericho* ingestion. More cases documenting the effects of this plant when ingested are needed.

KEYWORDS Echinops kebericho; herbal; plant

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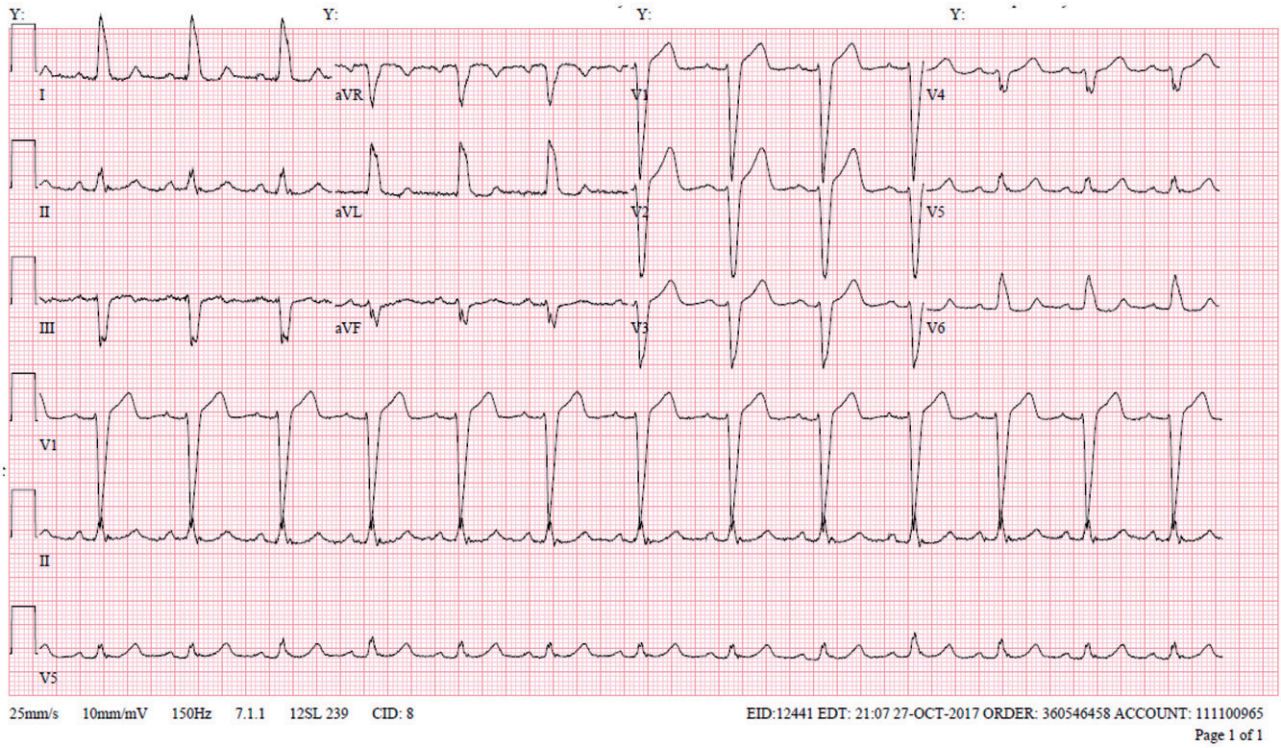

Figure 1. ECG after atropine showing a sinus rhythm and left bundle branch block.

59. Type E botulism: a case series from Northern Canada

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Background: Botulism is a rare, potentially life-threatening syndrome caused by a neurotoxin produced by *Clostridium botulinum*, a gram-positive, spore-forming obligate anaerobe, ubiquitous in soil and marine environments. Types of botulism include infant botulism, foodborne botulism, and rarer presentations such as wound-associated botulism, inhalational and iatrogenic botulism. We describe a cluster of five cases of type-E foodborne botulism.
Cases: A group of individuals from a Northern Canadian community ingested a meal of fermented seal and became symptomatic. Two patients were managed in the community.
Case 1: A middle aged female presented to a community nursing station 2 d after ingestion with nausea, vomiting, dry mouth, and sore throat. Her vital signs were normal. She received dimenhydrinate and was sent home. She returned the next day with worsening symptoms, fever, hypotension, and hypoxia. She developed respiratory failure and was transferred to our centre. She had fixed dilated pupils, ptosis, and symmetrical proximal muscle weakness with preserved deep tendon reflexes, an ileus, and urinary retention. She developed respiratory failure requiring intubation and ventilation. Serum testing for botulism toxin was negative. Botulism antitoxin was administered 4 d after ingestion and 2 d after onset of symptoms. She was extubated after 5 d and discharged home 3 d later.
Case 2: A school-aged child ate one bite of the meat. Three days later she developed a dry, sore throat and gastrointestinal symptoms. She was transferred to our centre for observation. Her stool tested positive for *C. botulinum* type-E, which was the only laboratory confirmed case in our series. The other diagnoses were made based on the CDC definition of being clinically compatible and epidemiologically linked.
Case 3: It was an elderly female who presented 2 d after ingestion with dysphonia and dysphagia and required intubation and ventilation for respiratory failure.
Cases 4 and 5: An elderly and young female respectively had mild symptoms and were managed conservatively.
Discussion and Conclusions: Botulism antitoxin is not approved for sale in Canada and is available only through Health Canada's Special Access Program. A supply is stored in major centres and is released upon the approval of a designated clinician. Type-E botulism cases are predominantly due to the ingestion of fermented arctic foods like fish, seal, or whale. Our patients presented with classic manifestations of botulism, including acute-onset of bilateral cranial neuropathies, fixed dilated pupils, and symmetric descending weakness. Gastrointestinal symptoms are more common in type-E. Botulism is a clinical diagnosis requiring a high index of suspicion with confirmation by serum toxin assay or detecting the toxin stool. Isolating the toxin from contaminated foods aids in diagnosis. Laboratory confirmation in case two supports the diagnosis in the cohort. Management includes monitoring for respiratory failure and early administration of botulism antitoxin. Administration has been shown to decrease mortality and symptom duration if given within 24 h. Antibiotics are indicated for wound botulism only. This is the largest case series to date describing an outbreak of type-E foodborne botulism.

KEYWORDS Botulism; antitoxin; toxin

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60. Bidirectional ventricular tachycardia and hyperkalemia after *Nerium oleander* ingestion that responded to high-dose of digoxin-immune fragments

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Background: Nerium oleander is a shrub originating from the Mediterranean region and is now found in different parts of the world. Ingestion of parts of this plant carries a risk of cardiac glycoside toxicity believed to be due to the toxin oleandrin.
Case report: This is a single patient chart review. A 40-year-old diabetic man presented to emergency room with nausea, vomiting and confusion after ingesting an unknown amount of *N. oleander* leaves to treat his diabetes (based on the advice of a friend). His heart rate was 45 bpm and his blood pressure was 97/55 mmHg at presention. He was lethargic and disoriented. The rest of his exam was normal. EKG showed atrial fibrillation with AV-block for which he was given 0.5 mg of Atropine without response. Thirty minutes later, he developed bidirectional ventricular tachycardia which was resistant to transcutaneous pacing and amiodarone (150 mg IV). His initial potassium was 5.04 meq/l. Twenty vials of Digibind® were infused IV. Repeat EKG showed atrial fibrillation with a ventricular rate of 45 bpm and repeat potassium was 6.50 meq/l. Another 10 vials were then administered with noticeable improvement in his blood pressure (105/64 mm Hg) and the EKG which showed a sinus rhythm at a rate of 65 bpm. Repeat potassium was 3.80 meq/l.The patient was admitted to the hospital, the serum digoxin level was 12.9 ng/ml. He was discharged home after 4 d without complications.
Discussion: Bidirectional ventricular tachycardia is a rare but specific finding in cardiac glycoside or aconitine toxicity. This case is unique because it is the first case report describing this findings in such plant. The patient developed this rare finding from a confirmed oleander poisoning and at the same time the arrhythmia and hyperkalemia responded to a high dose of digoxin-immune fragments. This study is limited because it is a single case report and plus the amount of toxin ingested is uncertain.
Conclusion: Oleander toxicity can cause bidirectional ventricular tachycardia. It can respond to high doses of digoxin-immune fragments.

KEYWORDS Nerium oleander; bidirectional ventricular tachycardia; oleandrin

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61. Gastric perforation after ingestion of baking soda to beat a drug test

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Background: Sodium bicarbonate has long been touted among alternative remedy aficionados as an effective agent for general cleansing and detoxification of the body, skin, and hair. This reputation propelled it into another customer base for home-remedy detox – the drug user facing a urine drug screen. Internet suggestions for sodium bicarbonate dose to beat a drug test range from 1 teaspoonful to as much as 3–5 tablespoonsful taken in water, followed by a gallon of water 1–3 h before the test. Although the internet sources warn of diarrhea as an adverse effect, none seem to warn about anything more serious. We report a case of baking soda ingestion prior to an occupational drug screen that resulted in gastric perforation.
Case report: A 50-year-old man (weight: 100 kg) presented to the ED with severe abdominal pain and vomiting. He gave a history of ingesting five tablespoons of baking soda earlier that day to clear his system of marijuana for a drug test at work. Initial electrolytes were unremarkable; notably serum sodium was 137 mEq/l. Abdominal CT revealed free air and he was taken directly to surgery. He aspirated during intubation. Perforation of the stomach was found during laparotomy, as well as peritonitis. Black enteric contents (2.5 l) were suctioned from the peritoneal cavity and the stomach was repaired. Piperacillin/tazobactam, famotidine, and hydrocortisone sodium succinate were started. On day 2, he was afebrile, hypotensive (BP 104/59, HR 128), and over breathing the ventilator. Lab results included serum Na 147, Cl 113, and K 5.3 mEq/l; and Mg 1.6 and Ca 6.9 mg/dl. The hospital course was complicated with sepsis and ARDS. By day 19, the patient was alert, ventilator independent and breathing through his tracheostomy.
Case discussion: Gastric rupture is a rarely reported consequence of oral sodium bicarbonate. It occurs after pressurized accumulation of excessive volumes of carbon dioxide released by reaction with hydrochloric acid in a stomach already distended with food, liquid, and swallowed air. An *in vitro* model that simulated the stomach environment previously characterized the variables that contribute to the rapidity and quantity of CO_2 gas release. These include the acidity, fluid/solid volume, and air volume of the stomach, any external release through eructation, and the weight and dilution-volume of sodium bicarbonate taken. For this patient, most of these variables are unknown except that five tablespoonsful of sodium bicarbonate, roughly 70 g, is clearly an excessive dose.
Conclusion: Gastric rupture following baking soda ingestion has only been rarely reported in the literature. Although recommended dosing for indigestion on the package is almost certainly safe, the doses suggested in the wild environment of the internet are not. Because of the consumer interest in holistic-health, general detox cleansing, and drug test manipulation, poison centers should be alert to the life-threatening complication of gastric perforation.

KEYWORDS Baking soda; ingestion; gastric perforation

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62. Nicotiana glauca toxicity in California: a case series

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Background: *Nicotiana glauca*, the tree tobacco plant native to South America, contains high levels of anabasine, a structural

analog of nicotine that acts agonistically at the nicotinic-type acetylcholine receptors. It is a successful invasive of semi-arid disturbed areas worldwide. While it was introduced in to the United States' west coast approximately 100 years ago, reports of anabasine toxicity in California are rare. We present three cases of anabasine toxicity with laboratory confirmation related to inadvertent *N. glauca* ingestion that occurred in California.
Case reports: Case 1: A 57-year-old woman presented to the emergency department with 7 h of progressively worsening generalized weakness, extremity numbness and tingling, dizziness, nausea, vomiting, and diarrhea that began within 1 h after ingesting a stir fry containing five to six "hand-sized leaves" picked from her garden. Her vital signs were normal. She had persistent nausea, tremors, dysmetria, and ataxia, and was otherwise neurologically intact. A complete blood count, chemistry panel, and urinalysis were normal. An MRI of her brain was unremarkable. Treatment included ondansetron, lorazepam, benztropine and acetaminophen. Her symptoms improved and she was discharged home nine h after arrival. Qualitative analyses of the patient's urine and of a plant sample were positive for anabasine.
Case 2 and Case 3: A 74-year-old man and his 97-year-old mother ate a breakfast consisting of bacon, eggs, and a green leafy vegetable harvested from their yard. Thirty minutes after ingestion, both patients developed dizziness, lightheadedness, muscle weakness, nausea, and vomited several times. On arrival to the emergency department, both had vital signs notable for mild hypertension and unremarkable physical examinations. A complete blood count, chemistry panel, and urinalysis were normal for both patients. An electrocardiogram for the 74-year-old man was normal, while the electrocardiogram for the 97-year-old patient showed a stable right bundle branch block. Symptoms resolved after treatment with ondansetron and intravenous fluids. Both patients were admitted for overnight observation and discharged without symptoms on hospital day 1. Qualitative analysis of both patients' urine was positive for anabasine. Discussion: Anabasine binds to the nicotinic acetylcholine receptor at the neuromuscular junction, autonomic ganglia and brain, and is also a weak inhibitor of acetylcholinesterase. Clinical toxicity is primarily due to its neuromuscular blockade effects. *N. glauca* is not a new invasive to California, though there exists only four other published cases of toxicity in the state in the past 60 years. Notably, our cases and prior cases of *N. glauca* toxicity occur after periods of drought and during the state's wettest seasons, suggesting increased accessibility and potential for human consumption during these times. In addition, this characteristic emphasizes the plant's ability to persist in extreme conditions.
Conclusion: This case series highlights the potential danger of inadvertent ingestion of a highly toxic plant *N. glauca*, and suggests that climate change may have contributed to California's cases of anabasine toxicity.

KEYWORDS Nicotiana glauca; anabasine; plant

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63. Pharmacokinetics of acetaminophen and metabolites after accidental acute overdose in a neonate

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Background: There are few reports of acetaminophen overdoses in neonates. Neonates have a lower capacity to metabolise therapeutic doses of acetaminophen, which reaches 90% of adult capacity by one year. Reduced capacity for glucuronidation might increase the proportion that undergoes oxidative metabolism to the toxic metabolite (NAPQI). Existing guidelines for neonatal overdose are based on adult acetaminophen ingestion guidelines, rather than neonatal data. We present a case of acute accidental acetaminophen overdose in a neonate and report the concentrations of acetaminophen and its metabolites.
Case reports: A healthy 2-week-old full term (3 kg) male was accidentally administered 600 mg (200 mg/kg) of acetaminophen liquid. According to national consensus guidelines, plasma acetaminophen concentration was measured at 2 and 4 h post-ingestion (154 mg/l and 144 mg/l, respectively). The Poisons Information Centre was consulted and as the 4 h concentration was below the nomogram treatment line (150 mg/l at 4 h) no acetylcysteine was commenced and the child was discharged. Later, discussion of the case with a clinical toxicologist prompted a recommendation for treatment because the acetaminophen concentration had not fallen substantially over 2 h despite being a liquid formulation and because neonates are known to have altered acetaminophen metabolism. The child was well 10 h post-ingestion and repeat acetaminophen concentration was 90 mg/l (above the nomogram treatment line) and ALT was normal (18 U/l). A standard 21 h course of intravenous acetylcysteine was commenced and at 32 h post-ingestion the acetaminophen concentration was undetectable and ALT remained normal (17 U/l). Acetaminophen and metabolites were measured by LC/MS/MS, including nontoxic glucuronide (APAP-Glu) and sulphate (APAP-Sul) conjugates. The metabolites of NAPQI, APAP-cysteine (APAP-Cys) and APAP-mercapturate (APAP-Mer), were also measured (Figure 1). The apparent acetaminophen half-life was initially 9 h and then later 3 h. The clearance estimate from Dose/AUC was 0.25 l/h. At 2 and 4 h post-ingestion the major metabolite present was APAP-Sul (43 and 47 mg/l) which exceeded APAP-Glu (17 and 36 mg/l). At 8 h post-ingestion APAP-Gluc concentration increased to 88 mg/l while APAP-Sul remained unchanged. The AUC was compared for all metabolites, with APAP-Glu and APAP-Sul accounting for 61% and 34% of total metabolite AUCs, and APAP-Cys and APAP-Mer combined accounting for the other 5%.

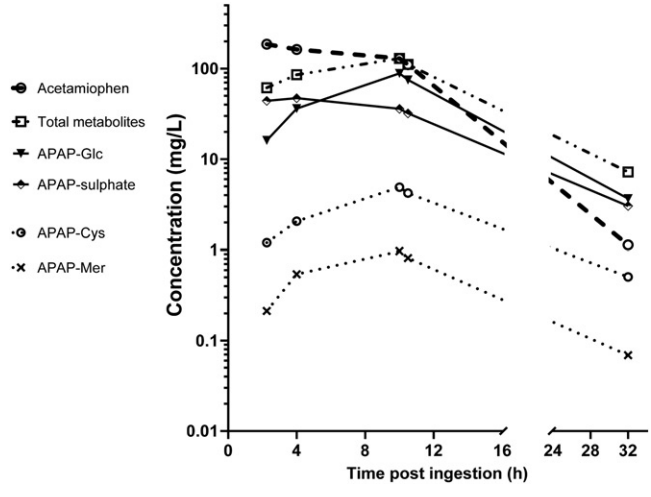

Figure 1.

Discussion: Little is known about the toxicokinetics of acetaminophen in neonates. Isbister (2001) reported a neonatal acetaminophen ingestion of 136 mg/kg with 4 and 8 h acetaminophen concentrations of 121 mg/l and 84 mg/l. Their reported apparent half-life and clearance of acetaminophen was 5.7 h and 0.22 L/h. In adults, the half-life in therapeutic doses is approximately 2 h and clearance 20 L/h. Neither neonatal case developed liver injury, so the prolonged half-life likely represents slower metabolism which is normal for neonates. In adults on therapeutic acetaminophen, sulphate conjugation becomes saturated and accounts for 30–44% of metabolism, glucuronidation 52–57% and CYP 5%. These ratios are like those observed in our case. If the ratios of metabolites are consistently in line with adult doses, then this may indicate that standard algorithms are also suitable for neonates.

KEYWORDS Acetaminophen; neonate; metabolites

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64. Validating a scoring system for a poison center's quality improvements in coding clinical effects, treatments and medical outcomes

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Background: Poison centers use electronic data collection software such as Toxicall® to encode clinical effect(s) (CE), treatment(s) (TX) and medical outcome (MO) categories (minor, moderate or major). This study proposes an objective scoring system using coded CE and TX that supports the appropriate case MO.
Method: Toxicall® was queried for human, ingestion-only exposures, for the year 2008, and for a MO of minor, moderate or major. Each MO category had 100 cases randomly selected and exported to an Excel® spreadsheet. A scoring system was devised for CE and TX in 7 Organ Systems (OS) (Table 1). For each case ($n = 300$), a coded CE (related/unknown if related) or coded TX (performed) were assigned value of 1, otherwise given a value of 0. The CE(Value) or TX(Value) of "0" or "1" were then multiplied by a 10-fold severity scoring system, producing a CE or TX(ScoreValue) = 10 n (for $n = 1$–3, range 10, 100, 1000). Only OS-specific TX were included in scoring as specified. Excel(R) formulas calculated CE and TX composites scores for each OS, namely OSCE(CompScore) and OSTX(CompScore), all replicable with the mathematical expressions shown at the bottom of Table 1. Lastly, the 7 OS CE/TX composite scores were totaled for a final composite case score. Three reviewers were randomly assigned cases in each MO category for "coding correction" using NPDS version 3.2. The corrected cases were evaluated and tested for MO score distinctness using a post hoc Tukey test.
Results: Reviewers changed the MO in 55 out of 300 cases (18.3%) including minor to moderate (12), minor to major/major to minor (1 each), moderate to major (16), moderate to minor (10), major to moderate (13). Two minor cases without MO were excluded, as were 4 non-ingestion cases, leaving 294 for comparison. A CE and/or TX net gain was seen in 126 cases, net loss in 33 and no net change in 135. Table 2 summarizes the scoring changes. After re-coding, the mean CE + TX(CompScores) ±standard deviation in each MO category were: Minor 43(±72),

Table 1. System for Defining and Calculating Clinical Effect (CE) and Treatment (TX) Composite Scores in 7 Organ Systems (OS).

CE/TX(value) Total CE(#): 104	CE(ScoreValue,10^n) for n = 1-3 Any CE not shown has a CE(ScoreValue) = 10 (See NPDS manual for complete CE list)	TX(ScoreValue, 10^n) for n = 1-3. Only the treatments shown were used to calculate TX(ScoreValues) and OSTX(CompScore)
Cardiovascular CE(#) =11 TX(#)=14	100 = Asystole, Ventricular(tachycardia/Fibrillation) 1000 = Cardiac arrest CE(ScoreValue) = 0-1280 — ^{1}OSCE(CompScore) = 0-2040	10 = Alkalinization, Atropine, Calcium, pacemaker, glucagon, vasopressor , Anti–Arrhythmic/Hypertensive, methylene blue 100 = Cardioversion, CPR, DigiFab, Insulin 1000 = ECMO TX(ScoreValue) = 0 -1490 — ^{2}OSTX(CompScore) = 0-3410
Gastrointestinal CE(#)=20 TX(#)=7	100 =Esophageal injury, gastric/oral burns 1000 = Esophageal Stricture CE(ScoreValue) = 0 -1460 — ^{1}OSCE(CompScore) = 0-4460	10 = SOI, AC (x1), AC (Multi),lavage, cathartic, WBI, antiemetic TX(ScoreValue) = 0 - 70 — ^{2}OSTX (CompScore) = 0-490
Heme/Hepatic CE(#)=9 TX(#)=4	100 = AST,ALT>1000, Cytopenia, hemolysis, ↑PT 1000 = DIC CE(ScoreValue) = 0 -1440 — ^{1}OSCE(CompScore) = 0-2760	10 = IV /PO NAC, Phytonadione 1000 = Transplantation TX(ScoreValue) = 0 -1030 — ^{2}OSTX (CompScore) = 0-1090
Neuro CE(#)=24 TX(#)=11	100 = Coma, Paralysis, Seizures (any type, 1 coded) 1000 = Intracranial hemorrhage, CVA (stroke) CE(ScoreValue) =0 -2470 — ^{1}OSCE(CompScore) = 0-7790	10 = Antihistamine, benzodiazepine, ethanol, flumazenil, fomepizole, pyridoxine, naloxone, sedation, physostigmine, anticonvulsant 100 = ventilator TX(ScoreValue) = 0 - 210 — ^{2}OSTX (CompScore) = 0-1310
Renal CE(#)=10 TX(#)= 4	100 = Oliguria/anuria 1000 = Renal failure CE(ScoreValue) = 0-1180 — ^{1}OSCE(CompScore) = 0-1740	10 = ethanol, fomipezole 100 = hemo-dialysis/perfusion TX(ScoreValue) = 0 -220 — ^{2}OSTX (CompScore) = 0-440
Respiratory CE(#)=10 TX(#)= 6	100 = Cyanosis, pulmonary edema, respiratory depression 1000 = Respiratory arrest CE(ScoreValue) = 0 -1360 — ^{1}OSCE(CompScore) = 0-2260	10 = bronchodilator, methylene blue, O_2 100 = Hyperbaric oxygen, ventilator 1000 = ECMO TX(ScoreValue) = 0 -1230 — ^{2}OSTX (CompScore) = 0-1490
Miscellaneous CE(#)=20 TX(#)= 7	100 = Rhabdomyolysis 1000 = Fetal death CE(ScoreValue) = 0 -1280 — ^{1}OSCE(CompScore) = 0-4340	10 = Food, Alkalinization, IV fluids, glucagon, glucose>5%, octreotide 100 = insulin TX(ScoreValue) = 0 - 160 — ^{2}OSTX (CompScore) = 0-460
Composite Formulas for OSCE and OSTX	^{1}Organ System CE Composite Score = OSCE(CompScore) = $\sum_{n=1}^{3}\left(\sum_{CE=1}^{OSCE(\#)}[CE(ScoreValue, 10^n)] * \sum_{CE=1}^{OSCE(\#)}[CE(\#, 10^n)]\right)$	^{2}Organ System TX Composite Score = OSTX(CompScore) = $\sum_{n=1}^{3}\left(\sum_{TX=1}^{OSTX(\#)}[TX(ScoreValue, 10^n)] * \sum_{TX=1}^{OSTX(\#)}[TX(\#, 10^n)]\right)$

ABBREVIATIONS: PT = Prothrombin Time DIC = Disseminated Intravascular Coagulation ECMO = Extracorporeal Membrane Oxygenation Σ = serial sum
CE/TX(#, 10^n) = # of Clinical Effect/Treatments for n =1, 2, 3
CE/TX(ScoreValue, 10^n) = Clinical Effect/Treatment scores for n =1, 2,3
OSCE/OSTX(CompScore) = Organ system Clinical Effect/Treatment Composite Score

Table 2. Net Scoring Changes (n = 294)

	M1 = MINOR			M2 = MODERATE			M3 = MAJOR		
	Before (n = 96)		After (n = 94)	Before (n = 98)		After (n = 97)	Before (n = 100)		After (n = 103)
	Total ∑CE#	a Total ∑OSCE (CompScore)	b Total ∑OSCE+∑OSTX (CompScore)	Total ∑CE#	a Total ∑OSCE (CompScore)	b Total ∑OSCE+∑OSTX (CompScore)	Total ∑CE#	a Total ∑OSCE (CompScore)	b Total ∑OSCE+∑OSTX (CompScore)
Before Parameter, Average (SD)[1]	1.7 (0.9)	23.1 (22.8)	39.5 (46.4)	3.2 (1.8)	95 (135.8)	144.9 (165.6)	5 (3.2)	337.1 (376.1)	496.5 (433.9)
After Parameter, Average (SD)[2]	1.8 (1.1)	27.1 (31.4)	43.0 (71.9)	3.8 (2.0)	100.4 (96.1)	155.8 (134.4)	6.1 (3.8)	449.5 (456.6)	617.5 (485.2)

Score comparisons M1, M2 and M3. NS (not significant) p<0.05 (significant)	[1]Tukey test (Before)			[2]Tukey test (After)		
	M1a vs M2a (NS)	M1a vs M3a (p<0.01)	M2a vs M3a (p<0.01)	M1a vs M2a (NS)	M1a vs M3a (p<0.01)	M2a vs M3a (p<0.01)
	M1b vs M2b p<0.05)	M1b vs M3b (p<0.01)	M2b vs M3b (p<0.01)	M1b vs M2b (p<0.05)	M1b vs M3b (p<0.01)	M2b vs M3b (p<0.01)

Moderate 156(±134) and Major 618(±485). These MO scores were statistically distinct (at least $p < .05$ with Tukey test). However, the minor and moderate groups often had similar scores as can be seen by sequentially plotting the individual cases.

Discussion and limitations: Net score changes primarily reflected the reviewer's CE coding changes and resulted in increased average scores overall. However, the scores differences for minor versus moderate cases only achieved statistical significance when OS-specific TX scores were added. Yet, individual scores did not always predict reviewer-designated MO or reveal the reasons for reviewers changing MO. A larger sample should be attempted, as the 300 cases did not fully elaborate the potential MO score spectrum.

Conclusion: A PC scoring system may assist with quality improvement and provide objective evidence to guide clinical impression of case severity. With further refinements, a scoring system could supplement clinical impressions and provide objective benchmarks for future NPDS improvements.

KEYWORDS Qualitative improvement; scoring system; medical outcomes

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65. Ingestion of denture cleansing tablets resulting in severe airway edema and fatal respiratory arrest

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Background: Denture cleansing tablets commonly contain oxidizing agents, surfactants, and pH buffering agents. Ingestion of these products has previously been reported to cause localized corrosive effects, including upper gastrointestinal (GI) ulcerations, esophageal stricture, and perforated gastric ulcer. Additionally, the FDA released a consumer alert warning of the potential for allergies and anaphylaxis in susceptible individuals due to persulfates, a commonly used oxidizing agent in these products. We report a case of denture tablet ingestion leading to rapid airway compromise and death.

Case report: A 74-year-old female nursing home resident with a history of anorexia nervosa, admitted to nursing home staff that she had ingested two Dynarex brand denture cleansing tablets. Empty wrappers for eight tablets were found in the garbage can. The patient initially had a blister on her lip and dysphonia. She was given diphenhydramine and transferred to the emergency department (ED) for evaluation. Upon arrival to the ED, approximately 2 h post-ingestion, the patient was noted to have multiple blisters of her oral mucosa and a swollen tongue. Her oxygen saturations remained in the 90%'s. Approximately 1 h later (3 h post-ingestion) the patient became dyspneic and intubation was attempted. Due to profound laryngeal edema the patient was unable to be endotracheally intubated and emergency cricothyroidotomy was unsuccessfully attempted. Despite these efforts, the patient died of respiratory failure.

Case Discussion: Toxicity from denture cleansers has been reported to cause localized caustic injury to the oropharynx, esophagus, and stomach, occasionally resulting in ulceration or stricture. This is the first reported case resulted in injury to the respiratory tract and was one of only a few attributable deaths. The components of denture cleanser tablets vary by manufacturer, but in this case, the most significant toxins were potassium monopersulfate (Oxone) and sodium percarbonate, both of which are oxidants which generate hydrogen peroxide upon contact with water (Table 1). Caustic injury from denture tablets has been reported to be more severe when solid, rather than dissolved tablets, are ingested, and could have occurred due to acid-base or free-radical mediated cellular injury. The development of airway edema would imply that a penetration or aspiration event occurred, although this would not be unexpected given the patient's glossal edema and likely impaired swallowing function. A plausible alternative mechanism to cause airway compromise and respiratory arrest would be a hypersensitivity reaction to potassium monopersulfate, a known allergen, for which the FDA released a consumer alert in 2008 after receiving 73 reports of adverse events including at least one death. However, the presence of mucosal injury and lack of other reported signs of allergic reaction make that mechanism less likely.

Conclusions: We report a novel case of death due to airway edema and respiratory failure from ingestion of denture tablets. This case highlights the need for close airway monitoring with early

Chemical Name	CAS No.	Weight-%
Oxone	70693-62-8	10 - 30%
Citric acid	77-92-9	10 - 30%
Sodium carbonate	497-19-8	10 - 20%
Sodium percarbonate	15630-89-4	5 - 10%
Sodium sulfate	7757-82-6	3 - 7%
Sodium Lauryl Sulfoacetate	1847-58-1	0.1 - 1%

intervention due to the potential for rapid decompensation in patients presenting after ingestion of caustic denture cleansing tablets.

KEYWORDS Caustic injury; potassium monopersulfate; denture cleaning tablets

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66. Treatment of pediatric black widow spider envenomation: a national poison center's experience

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Background: Black widow species (Latrodectus species) envenomation can produce a syndrome characterized by painful muscle rigidity and autonomic disturbances. Symptoms tend to be more severe in young children and adults. We describe black widow spider exposures and treatment in the pediatric age group, and investigate reasons for not using antivenom in severe cases.
Methods: All black widow exposures reported to the Rocky Mountain Poison Center between January 1, 2012, and December 31, 2015, were reviewed. Demographic data were recorded. Patients were divided into two groups. Group 1: contact through families from their place of residence, public schools and/or cases where patients were not referred to healthcare facilities. Group 2: patient contact through healthcare facilities.
Results: Ninety-three patients were included. Forty (43%) calls were in Group 1 and 53 (57%) in Group 2. Symptoms were evident in all victims; 43 (46.2%) were grade 1, 16 (17.2%) grade 2 and 34 (36.5%) grade 3, but only 14 patients (41.1%) of this group received antivenom. Antivenom use was associated with improvement of symptoms within minutes, and all treated patients were discharged within hours, without an analgesic requirement or any complications. Reasons for not receiving antivenom included: skin test positive (2/20), strong history of asthma or allergies (2/20), physician preference (2/20), non-availability of the antivenom at the health care facility (14/20).
Conclusion: In our study, most symptomatic black widow envenomations were minor. Relatively few patients received antivenom, but antivenom use was associated with shorter symptom duration among moderate and major outcome groups.

KEYWORDS Spider; envenomation; antivenom

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67. Characteristics of poisoned patients requiring inter-facility transfer

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Background: Given the increasing regionalization and specialization of healthcare, inter-facility transfers are becoming more common. Little is known about how inter-facility transfers affect the management of poisoned patients. This study aims to describe the characteristics of poisoned patients requiring transfer of care.
Methods: This was a retrospective study of consecutive cases reported to a regional poison center from June 1, 2017 to December 31, 2017. Included were cases that involved inter-facility transfer for any reason; excluded were cases without complete outcome data. Data were abstracted by two trained and monitored investigators. Age, gender, day of week, and time of arrival to the first healthcare facility (HCF), reasons for transfer, and time to transfer were analyzed using descriptive statistics.
Results: A total of 14,355 cases were reviewed, of which 604 cases (4.2%) met inclusion criteria. Kappa inter-rater reliability for data abstraction was 0.95. Average age was 24 years (range 6 months–85 years) with a median age of 16 years. Majority were female (61.8%: 373 females, 231 males). Transfer was done more commonly for patients who presented on Monday compared to other days: 108 on Monday, 91 Tuesday, 80 Wednesday, 79 Thursday, 63 Friday, 86 Saturday, and 95 Sunday. Transfer was done more commonly for patients who first arrived after 5 pm: $n = 333$ between 5 pm to 5 am, $n = 136$ from 5 am to 12 pm, $n = 131$ from 12 pm to 5 pm. In 43 (7%) cases patients were initially treated at a freestanding ED. The most common reasons for transfer were to a HCF with an intensive care unit ($n = 413$) or for pediatric inpatient service ($n = 343$). Other reasons for transfer included evaluation by other specialty services ($n = 51$), transplant evaluation ($n = 21$) for acetaminophen hepatotoxicity, hyperbaric oxygen ($n = 16$), hemodialysis ($n = 12$), insurance reasons ($n = 4$), patient preference ($n = 4$), antidotal or other medication not available at initial HCF ($n = 4$), and not specified ($n = 58$). In 58 cases multiple reasons for transfer were noted. The estimated time from initial HCF presentation to transfer to the 2nd HCF averaged 6 h.
Conclusions: Inter-facility transfer of poisoned patients is common, especially to a HCF with an intensive care unit or pediatric services most commonly on Monday night. The need for other specialized treatments was also common. Since patients often choose where to go first, the number needing transfer from free standing EDs will likely increase. Since poisoned patients often require inter-facility transfer, further studies are needed to understand its impact on regional and national resource allocation.

KEYWORDS Inter-facility transfer; transfer of care; poisoning management

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68. Supratherapeutic acetaminophen ingestions managed at a regional poison center

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Background: There is extensive literature on acute acetaminophen (APAP) overdose; fewer publications address management of repeated supratherapeutic ingestion (RSTI). Previous studies have suggested that a normal alanine aminotransferase (ALT) at presentation is predictive of a good outcome. The purpose of this study was to review RSTI cases followed at a regional poison center (RPC) to determine if a subset of patients might be appropriate for abbreviated treatment.

Methods: The RPC database was searched from January 2000 to February 2018 for adult patients (defined as age ≥19 years) admitted to a hospital, treated with N-acetylcysteine (NAC), who had at least two ALT determinations. Cases of acute APAP overdose or unknown timing of ingestion were excluded. Those with undetectable APAP were eligible for inclusion so long as a history of RSTI (>4 g APAP/24 h) was documented. The following information was recorded: age, gender, acuity, patient intent, APAP products involved, dosing scenario, initial serum APAP, initial and peak ALT, international normalized ratio, NAC route and duration, development of hepatotoxicity (ALT >1000 IU/l) or hepatic injury (ALT >100 IU/l), and medical outcome (recovery, death, transplant, or undetermined).
Results: The initial search yielded 358 patients. After further review, exclusion of duplicates and non-RSTI cases, 265 patients were included for analysis. Age range was 19–90 years (median 43.0). One hundred and sixty-nine (63.8%) were female. All were treated with NAC (72.4% IV, 20.4% PO, 7.2% IV + PO). Sixty-seven of the two hundred and sixty-five patients (25.3%) developed hepatotoxicity, of whom 74.6% had ALT >1000 at presentation. In cases where the initial ALT was <100 ($n = 119$) only 3 (2.5%) subsequently developed hepatotoxicity (1 fatality, initial ALT 69; 1 transferred to a transplant center, initial ALT 72; 1 recovery, initial ALT 83). Of note, all three presented with detectable serum APAP (217, 149, and 14 mcg/ml, respectively). One hundred and eleven of the two hundred and sixty-five (41.9%) patients presented with a normal ALT and did not develop hepatic injury. Regarding medical outcome, 245/265 (92.5%) either improved or ALT remained normal, 10 (3.8%) died, 6 (2.3%) were transplanted or transferred out of state to a transplant center, and in 4 (1.5%) cases the outcome was unknown.
Discussion: RSTI presumably increases the risk of APAP toxicity through glutathione depletion, though other factors such as timing/duration of APAP misuse and nutritional status likely also play a role. This retrospective review has several limitations. During the study period the RPC catchment area included two states without transplant centers, sometimes resulting in patients' follow up being transferred to a different PC. Although all patients had repeat labs and received NAC, timing of blood draws and duration of treatment were not always documented. The RPC recommended standard 21 h IV NAC treatment, but hospital providers sometimes discharged patients earlier.
Conclusions: In this review, the outcome of APAP RSTI patients followed a bimodal pattern. About 25% presented with or developed hepatotoxicity, while over 40% did not develop even mild liver injury. RSTI patients treated with NAC who have undetectable APAP and maintain flat ALT may be appropriate for abbreviated treatment, but prospective studies are needed to determine the optimal timing.

KEYWORDS Acetaminophen; repeated supratherapeutic ingestion; hepatotoxicity

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69. Do internet search query trends relate to intentional gabapentin exposures reported to U.S. poison centers?

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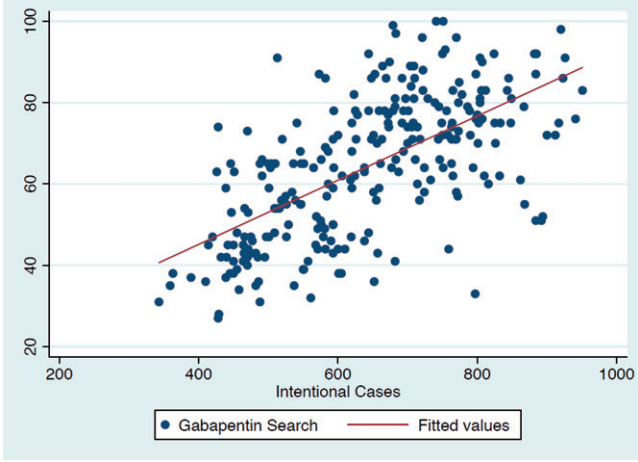
Background/objectives: Internet search queries have been used to peripherally monitor various health-associated events, including infectious disease outbreaks and reports of medication-related adverse effects. As more Internet users turn to the web for medical advice, users' search terms may help signal real-time health concerns. Google Trends assesses a search term's popularity by assigning an "interest over time" (IOT) score. The higher the score, the more popular the specified search term was over a defined time period. A score of 100 means that the search term was at the height of its popularity, while a score of 50 means that it was 50% as popular. The score allows researchers to evaluate relative popularity of a search term over time. Gabapentin, a relatively new antiepileptic medication, has seen a significant rise in cases reported to U.S. Poison Centers from 2012 to 2015. To the authors' knowledge, no study has utilized the Internet search data approach with poison center case information. The purpose of this study was to determine if internet search queries correlated with changes in intentional exposures over time for this emerging drug of abuse.
Methods: Google Trends "interest over time" (IOT) data was collected for "gabapentin high" searches from January 6, 2013 to December 30, 2017. This search term was selected as other similar terms suggested by either the authors or Google Trends did not have enough results for full analysis (i.e., "gabapentin abuse," "gabapentin exposure," or "gabapentin misuse"). Intentional gabapentin exposures reported to the National Poison Data System (NPDS) were analyzed for the study period, which included the state in which the exposure occurred. Pearson's correlation test was calculated to assess correlation, and location information was analyzed using descriptive statistics.
Results: The average IOT score over the time period studied was 64.5 (range: 0–100). A total of 167,292 intentional gabapentin exposures were included. The observed correlation between IOT scores and intentional reported gabapentin exposures was +0.6313. Four of the five states with the highest number of cases per million per year reported higher than average IOT scores (Kentucky, Minnesota, New Mexico), one was below average (West Virginia), and one did not have enough data to compute a score (South Dakota). There was not enough data for Google Trends to report an IOT score for a total of 11 states and the District of Columbia.
Conclusions: Overall, IOT scores positively correlated with intentional gabapentin exposures reported to U.S. Poison Centers. More data is needed to analyze results by individual states. Additional studies should be done to find associations with other user-driven Internet queries and content, such as social media sites. These approaches may help identify emerging drugs of abuse, potentially serving as a real-time early warning system.



Graph 1. Correlation between Intentional Gabapentin Exposures Reported to U.S. Poison Centers and Google Trends Intensity Over Time (IOT) Score.

KEYWORDS Surveillance; internet search trends; gabapentin
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70. Toxicology education in emergency medicine: a formal assessment and pilot study

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Background: Accreditation Council for Graduate Medical Education (ACGME)-accredited emergency medicine programs have no formal requirements regarding training and education in medical toxicology. From review of previously published survey data less than two-thirds of emergency medicine residencies had formalized access to teaching with toxicologists.
Objectives: To evaluate capacity for toxicology education at ACGME-accredited emergency medicine residency programs, assessment of satisfaction in toxicology education and receptiveness to tele-education modalities. Secondarily to determine feasibility of a pilot web education toxicology program.
Methods: A survey was conducted in 2015 to evaluate toxicology education capacity, satisfaction with current toxicology education, and technological capabilities of emergency medicine residencies ($n = 167$). Non-responding residency programs were reviewed online to determine access to toxicology education. Questions in the survey elicited affiliations of residency programs with toxicology fellowships, poison centers, and board-certified toxicologists, the way these resources are utilized, and program directors' perceived satisfaction in toxicology education at their institutions. The survey also elicited interest, capability, and availability to participate in the pilot program. Subsequently, a curriculum was piloted at one emergency medicine residency program that demonstrated the need and desire for improved access to toxicology expertise and education based on survey results. The four-session curriculum developed by the investigators of the study included "Toxidromes", "Synthetic Drugs of Abuse", and a two-part session on "Antidotes" and was taught by board-certified medical toxicologists and medical toxicology fellows-in-training. The curriculum was implemented over 1 month using a live, internet-based video-conferencing platform. Feedback on each session was solicited through a post-session survey. The post-session survey elicited ratings on format of the didactics, interest and utility of the session topic, and suggestions for modifications. Response options included 1 (very poor), 2 (poor), 3 (fair), 4 (good), 5 (very good), as well as free text response fields.
Results: Of programs that completed the survey ($n = 35$, 21%), 77% offered a toxicology rotation for trainees with 66% of the rotations at a poison center and 60% had an American Board of Emergency Medicine (ABEM)-certified Toxicologist on staff. Programs dissatisfied with toxicology education were not associated with a toxicology fellowship or an ABEM-certified toxicologist. Additional web research on programs not participating in the survey found that 14% had a toxicology fellowship at their institution, 50% had an ABEM certified toxicologist on faculty, 61% offered a toxicology rotation, and 34% listed an association with a poison center. Pilot education program post-session survey results using a Likert scale (1 (very poor) to 5 (very good)) indicated that participants found the usefulness of the technology, effectiveness of the lecture, value of the subject topic and overall education value to be "good".
Conclusions: Access to toxicology education through a clinical rotation or medical toxicologist is not consistently available among emergency medicine residency programs, which may indicate dissatisfaction with toxicology education. Successful components of the pilot educational program could be disseminated, however technology difficulties with sound and communication was a limitation to an effective discussion during the sessions.

KEYWORDS Toxicology education; emergency medicine; survey
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71. Fatal hypermagnesemia secondary to chronic epsom salt ingestion

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Background: Epsom salt – hydrous magnesium sulfate – ingestion is a rare cause of hypermagnesemia and resultant cardiotoxicity, especially in the setting of normal renal function. High-flux hemodialysis is an effective treatment for hypermagnesemia secondary to Epsom salt ingestion and should be used even in cases where renal function remains normal. Prior documented cases of Epsom salt ingestion leading to cardiotoxicity have involved acute massive ingestions. We describe a unique case of chronic Epsom salt ingestion leading to severe hypermagnesemia and death.
Case report: A 40-year-old woman presented to an outside hospital after ingesting an unknown amount of epsom salt. Per family, the patient had been taking epsom salts chronically in order to attempt weight loss. Over time she became weak and syncopized. An ambulance was called and she was found in cardiac arrest. Cardiopulmonary resuscitation was initiated with a return of spontaneous circulation after 35 min. She was intubated in the field and on arrival to the emergency department was started on a norepinephrine infusion for hypotension and bradycardia and admitted to the intensive care unit. Her initial magnesium level was 25.2 mEq/ml and improved to 16 mEq/ml after crystalloid resuscitation and calcium gluconate. Her creatinine was reportedly "normal." High-flux hemodialysis was recommended due to significant cardiotoxicity and encephalopathy. On hospital day 2, the patient underwent hemodialysis with improvement of her serum magnesium to 2.9 mEq/ml, and her hemodynamic status improved. She continued to have profound central nervous system abnormalities including seizures. Additional testing included an electroencephalogram demonstrating severe cortical injury and magnetic resonance imaging was significant for hypoxic ischemic injury. The patient was declared clinically brain dead.
Case Discussion: There have been several case reports of Epsom salt ingestion leading to cardiotoxicity, and levels as significantly elevated as in this case often lead to death. Although this patient had normal renal function, the severity of hypermagnesemia was enough to cause fatal cardiotoxicity. Hemodialysis was initiated on day 2 with hemodynamic improvement, but the patient was ultimately declared clinically brain dead despite this intervention. This case is unique in that it was reportedly the result of an acute on chronic ingestion and rather than a single acute ingestion, which has not been described.
Conclusion: High-flux hemodialysis should be considered early on in the course of hypermagnesemia that is associated with cardiotoxicity and hemodynamic instability even if renal function is normal. Clinicians should be aware that fatal hypermagnesemia can develop secondary to chronic ingestions and in patients with normal renal function.

KEYWORDS Magnesium; epsom salt; hemodialysis
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72. Lance-Adams syndrome resulting from an unintentional heroin overdose

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Background: Lance-Adams Syndrome (LAS), or chronic post-hypoxic action myoclonus, is a rare neurological condition following anoxic brain injury involving dysfunction in neural circuits rather than structural pathology. LAS is exceedingly rare with less than 200 documented cases. Only one case of LAS has been documented following heroin overdose, although it was after subsequent cardiac arrest. We present a case of LAS following recreational heroin overdose without cardiac arrest.
Case report: A 25-year-old man with opioid use disorder was found unresponsive in a hotel room after using heroin. When EMS arrived, the patient had a respiratory rate of 2 breaths per min. He was given 8 mg of intravenous naloxone without improvement and subsequently intubated. He was transferred to a tertiary care facility. His urine enzyme multiplied immunoassay technique (EMIT) screen was positive only for opiates, and urine gas chromatography/mass spectrometry (GC/MS) showed morphine and iatrogenic propofol and levetiracetam. On hospital day (HD) 2 he was noted to have myoclonus despite sedation with propofol. Myoclonic status epilepticus (MSE) was excluded via continuous electroencephalogram (EEG) and magnetic resonance imaging of the brain showed no structural abnormalities. His mental status improved, he was extubated on HD 3, and transferred out of the ICU with persistent intention myoclonus and ataxia. He was diagnosed with LAS and started on clonazepam and levetiracetam with slow improvement of myoclonic movements. He was discharged from the hospital to physical rehabilitation facility on day 5 in improved condition with preserved intellect, and had neurologic recovery prior to discharge home on day 26.
Case discussion: LAS is a rare condition, which may be under recognized in overdose patients. It is important to recognize this rare hypoxic complication amidst the current epidemic of opioid overdoses. While the pathology of LAS is not fully understood, it is known to disrupt neuronal circuits without necessarily demonstrating structural pathology. Current evidence suggests disinhibition of the GABA-A signaling pathways as the primary mechanism responsible for this presentation. Current standard treatment for LAS is low-dose benzodiazepines and antiepileptic medications. The diagnosis of LAS is based on a specific constellation of symptoms, including action myoclonus, postural imbalance and ataxia, and mild to absent cognitive deficit following an anoxic event. Imaging and EEG are not diagnostic. LAS is differentiated from posthypoxic myoclonus (PHM) because LAS patients have intact consciousness, whereas PHM patients remain comatose. Additionally, MSE developing within 24 h of anoxic event is a marker of poor outcome, while LAS is associated with preserved intellect. LAS symptoms can resolve or remain chronic. Our patient's symptoms improved with pharmacologic therapy but did not resolve prior to discharge.
Conclusions: After an unintentional heroin overdose, our patient developed LAS. Despite evidence of hypoxia, our patient had full neurologic recovery. LAS is a rarely-diagnosed condition occurring after anoxic brain injury. Delineation of LAS from MSE early on is important due to the widely different prognosis, and the diagnosis of LAS is important for establishing long term treatment.

KEYWORDS Lance-adams syndrome; heroin; myoclonus

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73. Massively elevated plasma titanium levels without systemic toxicity

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Background: Titanium is frequently used in medical and surgical implements – particularly in orthopedic hardware, prostheses and implants – because it has a high strength-to-density ratio and corrosion resistance. Reports of toxicity from titanium implants are exceedingly rare in the literature, and little is known about the correlation between serum titanium levels and toxicity. There are no reported cases of massive systemic titanium exposures with extremely elevated plasma titanium levels.
Case report: An 87-year-old woman was admitted to the hospital for weakness in the setting of recurrent UTIs, however, after treatment she continued to experience extreme difficulty with ambulation and right hip pain. She had a remote history of total right hip replacement 38 years prior to admission. The hip implant was manufactured by Stryker and had previously been recalled, but the patient had not sought any revised surgeries. The patient's Stryker implant contains their proprietary titanium alloy which is composed of titanium, molybdenum, zirconium and iron. Due to this, levels of titanium, chromium and cobalt were checked as a means to monitor the integrity of her hip implant. Repeated plasma samples tested by Inductively Coupled Plasma Mass Spectrometry (ICP/MS) confirmed massively elevated titanium levels, at 250 mcg/l, with other metal ion ranges within normal values, including cobalt level of 0.7 mcg/l (normal range $<$1.8 mcg/l) and chromium level of 1.2 mcg/l (normal range $<$1.4 mcg/l). In healthy patients, the normal range for titanium is less than 5 mcg/l, while a level up to 10 mcg/l can be considered normal in patients with titanium-based implants. Titanium concentrations greater than 10 mcg/l are often indicative of wear or hardware failure. Radiographs of the implant confirmed breakdown and hardware failure. After evaluation by orthopedic surgery she was deemed a poor surgical candidate for removal or replacement.
Case discussion: Titanium itself is known as a mucosal and pulmonary irritant, however, little is known about the effect from massive systemic titanium exposures. Reports have associated elevated titanium levels with anemia, however, the mechanism is unknown and causation has not been proven. This patient was not anemic, with Hemoglobin of 12.6 gm/dl, and had no other laboratory evidence of end organ dysfunction, specifically normal blood cell counts and morphology, normal renal function with creatinine 0.6 mg/dl, normal hepatic function and a normal neurologic exam. Overall, she displayed no observed toxicity from her massively elevated titanium levels. The elevated levels in this patient most certainly indicated the degree of prosthesis breakdown and failure.
Conclusions: Titanium is commonly used in implanted medical hardware, which represents a potential source for systemic titanium exposure. We describe a case of extreme elevation in plasma titanium levels secondary to hardware failure, without evidence of end organ dysfunction or other toxicity.

KEYWORDS Titanium; implant; metal

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74. Toxic leukoencephalopathy following intravenous exposure to nonpharmaceutical fentanyl and fentanyl derivatives

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Background: Toxic leukoencephalopathy (TLE) is a type of neurologic injury specific to white matter of the brain that can occur following exposure to various agents, commonly drugs of abuse, with opioids being the most common. The mechanism of injury in TLE is largely unknown, but the presentation consists of acute to subacute onset of cerebellar, pyramidal, and extrapyramidal symptoms with associated neurobehavioral changes such as confusion, apathy, and akinetic mutism. There is limited information regarding the development of TLE following exposure to fentanyl and its derivatives.
Case report: A 19-year-old man with history of polysubstance abuse was found unresponsive by his girlfriend after injecting illicit opioids. EMS was called and found the patient unresponsive with frothy oral secretions and myoclonic jerking. The patient was given 4 mg intramuscular naloxone with mild improvement in respiratory drive, and but was intubated due to ongoing seizure activity at the scene. Urine drug screen was positive only for THC and cocaine. Urine GC/MS was positive for fentanyl, benzylfentanyl, N-allynorfentanyl, cocaine, and cocaine metabolites. MRI imaging revealed extensive bilateral restricted diffusion of cerebral and cerebellar white matter in a distribution most consistent with TLE. The patient had concomitant hypoxic brain injury and had an extensive hospital stay in the ICU, and, subsequently inpatient rehab, with course complicated by paroxysmal sympathetic hyperactivity, rhabdomyolysis, and opioid withdrawal. The patient was discharged home 3 months later with deficits in executive functioning and ongoing motor deficits due to muscle spasticity.
Case discussion: TLE has been well-documented following opioid use, particularly heroin insufflation, however it is also a known complication of other opioids and other routes of ingestion. TLE has been seen following transdermal exposure to pharmaceutical fentanyl patch in a pediatric patient. This patient reportedly injected intravenously. The derivatives found in the patient's urine are conclusive of non-pharmaceutical, illicit fentanyl exposure, which is an increasing phenomenon in the current opioid epidemic. There are no documented cases of TLE following exposure to fentanyl analogues without evidence of other opioid exposure, as in this patient. The patient's concomitant cocaine use presents a potential confounder, however, TLE related to cocaine ingestion is rarer, and the diffusion restriction seen on MRI has a different pattern with greater predilection for the frontal lobes, absent in this patient. Treatment for TLE is mostly supportive. Empiric antioxidant therapy with coenzyme Q, vitamin C, and vitamin E is recommended, and was given in this patient, however its effect was indeterminate given the patient's hypoxic brain injury.
Conclusions: We document a case of toxic leukoencephalopathy occurring after exposure to illicit fentanyl, as evidenced by the presence of fentanyl and non-pharmaceutical fentanyl analogues on urine GC/MS. This is the first documented case of toxic encephalopathy resulting from exposure to nonpharmaceutical fentanyl and fentanyl derivatives. As illicit fentanyl use becomes more widespread, physicians should be aware of this potential complication.

KEYWORDS Toxic leukoencephalopathy; fentanyl; opioid
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75. Surreptitiously administered ethylene glycol resulting in murder

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Background: Ethylene glycol (EG) poisoning cases are commonly encountered in the practice of clinical toxicology. In the United States there were 7089 cases reported to poison centers in 2016. However, cases of surreptitiously administered EG with the intent to commit murder are rare. We report a case of early EG toxicity presenting to a health system following surreptitious administration. The death resulted in conviction of the murder with numerous lessons learned by the health care team managing the patient and the prosecuting team pursuing justice.
Case report: A 76-year-old female with past history of stroke, nephrolithiasis, hypertension, and colostomy suffered a fall. She had slurred speech, confusion and was unable to walk or sit-up on her own when emergency services arrived (19:49). She presented to the emergency department (ED) with slurred speech and pulse 89 bpm, respiratory rate 20 breaths per min, and blood pressure 207/110 mmHg (20:16). The patient was unable to give any history with physical examination significant for incomprehensible dysarthria. Presenting laboratory values (20:50) were significant for: serum bicarbonate 14 mEq/l, anion gap 17, creatinine 1.06 mg/dl, total calcium 9.1 mg/dl. She was admitted to the critical care unit (CCU) for potential sepsis and stroke. She developed gradual and progressive tachycardia, tachypnea, and declining GCS. At 0415, her arterial blood gas revealed: pH 6.83, pCO_2 22 mmHg, pO_2 210 mmHg, and lactate 7.6 mmol/l. At 04:30, she was intubated and received sodium bicarbonate. The poison center was contacted and the patient was subsequently treated with fomepizole and dialysis. A review of her 01:30 urine analysis revealed "amorphous crystals" with "occasional" calcium oxalate crystals and the testing of previous blood from 20:50 reveled an EG level of 487 mg/dl. Despite aggressive therapy, the patient was later declared brain dead. Autopsy revealed acute tubular necrosis with severe calcium oxalate crystal deposition and hypoxic-ischemic encephalopathy with oxalate crystal deposition in basal ganglia.
Discussion: EG poisoning can mimic many other disease processes. According to ATSDR toxicological profile and other available literature, EG is rapidly absorbed (1–3 h) causing acute intoxication. Metabolism of EG to acidic metabolites occurs rapidly (elimination half-life 1–8 h with glycolic acid peak within 5 h) and accounted for her early and progressive anion gap metabolic acidosis. Due to the treating team's lack of knowledge of her early EG toxicity, in transition from the ED to the CCU, the patient continued to metabolize, resulting in her declining GCS, tachycardia, and hyperventilation. Her subsequent laboratory testing revealed a marked metabolic acidosis, hypocalcemia, elevated creatinine, and oxalate crystals in the urine. (Expected crystals detection in urine is 4–8 h post-ingestion).
Conclusions: Surreptitiously administered ethylene glycol is rare and difficult for clinicians to diagnose. Early in the course of management, EG toxicity can resemble numerous other medical conditions. A characteristic clinical course of declining mental status, worsening acidosis despite quality supportive care, elevating creatinine with decreased urine output, hypocalcemia and

calcium oxalate crystaluria should clue the clinical teams to the presence of ethylene glycol as the cause.

KEYWORDS Ethylene glycol; poisoning; homicide

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76. Multi-center analysis of marijuana use in sexual assault patients stratified by state marijuana legalization status

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Background: Marijuana is more accessible to citizens pending upon state legalization status. In these analyses, we evaluated whether adult women presenting after sexual assault (SA) were more likely to report marijuana use prior to assault in states with more permissive marijuana legislation.
Methods: We performed a nested cross-sectional analysis using data collected as part of a prospective NIH-funded prospective longitudinal observational study of adult women SA survivors. Data were collected between June, 2015 and March, 2018 from adult women SA survivors presenting to 13 emergency department and clinical-based sexual assault programs across the United States (11 states and the District of Columbia). 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. Data regarding marijuana use prior to sexual assault (excluding surreptitious administration) were obtained as part of clinical and forensic history collection. Data are reported in frequencies and percentages.
Results: Eleven states and the District of Columbia were included in the data analysis. States were stratified by marijuana legalization status: (1) medical broadly legalized (2) marijuana legalized for recreational use and broad medical use (3) no broad laws legalizing marijuana. Five states in our study represented medical marijuana broad legalization, one state and the District of Columbia had laws legalizing marijuana for medical and recreational use, and five states had no broad laws legalizing marijuana. In states with broad legalization of medical marijuana 11/292 (4%) of sexual assault patients self-reported marijuana use, 16/179 (9%) patients from states with medical and recreational marijuana self-reported use and 26/265 (10%) of patients in states without broad legalization reported use.
Conclusion: This data suggests sexual assault patients from states with medical and/or recreational marijuana laws do not self-report marijuana at time of sexual assault at higher rates than patients from states with no broad laws legalizing marijuana. Limitations include small sample size, self-reporting, lack of validation of agents by conformational screening, and exclusion of non-English speaking patients.
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KEYWORDS Marijuana; sexual assault; legalization

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77. Drug of abuse testing: a retrospective analysis of test utilization and detection characteristics

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Background: Substance Use Disorders (SUD) and particularly Opioid Use Disorder (OUD) have reached epidemic proportions over the past 15 years and continue to grow unabated. Previous studies have demonstrated that SUD significantly increases the probability of using an Emergency Department (ED) for medical and psychiatric services. Accordingly, drug of abuse (DOA) testing by enzyme immunoassay and gas chromatography-mass spectrometry (GCMS) are routinely ordered in the ED. However, there is limited literature describing DOA test utilization and detection patterns, specifically among adult ED visits. To this end, we present a 16 month retrospective review detailing ordering and detection characteristics, turn-around-time (TAT), analytic performance metrics, and incidence of analyte co-detection for ED patients.
Methods: We performed a retrospective review of all urine DOA orders at a single tertiary, level I trauma center. Specimen order, collection, accession, and final verify dates were reviewed for calculation of TAT. DOA screen assays and results were correlated with associated confirmatory testing to allow for calculation of true and false positive rates and co-detection patterns for confirmatory testing was reviewed.
Results: Between January 2017 and March 2018, 24,114 urine specimens were screened for DOA. Ten thousand seven hundred and sixty-one were ordered for ED patients, of which 38% were negative ($n = 4094$), 33% were positive for a single analyte ($n = 3589$), and 29% were positive for multiple analytes ($n = 3078$). Benzodiazepines and cannabinoids were the two most commonly detected analytes, with detection rates of 30% and 25% of positive specimens respectively. High incidence co-detection patterns included combinations of benzodiazepines, cannabinoids, cocaine, or opiates. Reflex confirmatory testing was available for cocaine, methadone, opiates, and oxycodone, and was ordered on 28% of DOA screens. Subgroup analysis on positive DOA screens which underwent reflex testing by GCMS demonstrated a positive predictive value (PPV) of 97.2%. Lastly, the median TAT from the time of collection to final result verify was 62 min for DOA screening and 8 days 16 h for confirmatory testing.
Conclusions: In this study, we presented test utilization data, TAT, analytic performance metrics, and detection patterns for DOA testing on patients in the ED. Our data indicate that DOA testing is common at a tertiary level I trauma center, with an average of 22 DOA screens ordered per day. Benzodiazepines, cannabinoids, cocaine, and opiates demonstrated a high

incidence of detection, which was similarly reflected in the total distribution of co-detection patterns, suggesting that polysubstance use patterns may be related to isolated illicit substance use. In addition, the analytic performance of screening assays demonstrates high PPV for analytes with confirmatory reflex testing. Lastly, DOA testing continues to have a long TAT, particularly for confirmatory testing, as treatment decisions are likely made prior to final verification of results.

KEYWORDS Toxicology; emergency medicine; retrospective

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78. Suicide by injection of different Snake venoms

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Background: Snake bites have always been a common cause of death mainly in tropical countries, most of these are accidents occurring during work in the fields. Suicide attempts by snake bites or injection of venom from one species are reported in recent publications. We describe a case, where a person injected himself with a mixture of poisonouś snake venoms into his cubital vein area.
Case report: A 32-year-old man called his ex-girlfriend in the evening and announced his suicide. Four months prior he was hospitalized due to a suicide attempt. Shortly before midnight his sister found him lying on the balcony and gasping. At arrival the emergency physician could only determine the death. At this moment the causative agent was not clear. When the police arrived they found the apartment of the person devastated and it was obvious that he had a hard death struggle. He had kept many different snakes, which were identified by a snake expert. The snakes were: *Protobothrops mucrosquamatus*, *Bothrops venezuelensis, Porthidium nasutum, Naja haje legionis, Naja siamensis, Naja nigricollis,Crotalus atrox, Crotalus horridus, Trimeresurus gumprechti, Trimeresurus trigonocephalus,* and *Vipera ammodytes*. The post mortem examination showed dried blood droplets in the left elbow, also a swelling of the skin with deep dark blue colouration and subdermal a thick layer of loosely clotted, and partly still liquid blood. On the upper arm circumference a thin pallor strip was found, which was induced by a shoe lace that had been used as a tourniquet prior to the injection. In different parts of the body (head, the knees, and the back of the feet) slight dried excoriations were found. Petechiae were found in the conjunctivae, the brainstem, both heart ventricles, the pulmonary pleura and in subserosal tissue of the gut. In both heart ventricles plenty of liquid blood was found. Body liquids and tissue samples were taken for analysis. The autopsy showed no third party fault. The urine immunoassay drug screen was negative for opioids, benzodiazepines, amphetamines, cannabis, buprenorphine, cocaine, and methadone. In Gas Chromatography-Mass Spectrometry a subtherapeutic level of lidocaine was found (0.1 µg/kg). The analysis for snake venoms was not possible in the laboratory.
Case discussion: In our case a snake keeper had milked venoms from different poisonous snake- species, most of them cause local tissue-necrosis and coagulopathy, and some are neurotoxic. He injected himself an unknown amount of the pooled venoms in the cubital vein area leading to a hard death struggle.
Conclusion: As far as we know this is the first publication of an unusual method of suicide committed with self-injection of various snake venoms.

KEYWORDS Suicide; snake venom; coagulopathy

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79. Carfentanil-associated mortality in Wayne county 2015–2017

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Background: Over the past 25 years, the United States has experienced sporadic epidemics of accidental overdose and death from heroin substitution or adulteration with fentanyl/fentanyl analogues. A spike in mortality was noted in Wayne County Michigan, July 2016–February 2017 shortly after carfentanil was first detected in Michigan. Carfentanil is an especially potent mu opioid agonist fentanyl analogue previously used as a veterinary tranquilizing agent. It is reportedly 100 times more potent than fentanyl and 10,000 times more potent than morphine. We hypothesized carfentanil was the cause of the mortality spike and determined that certain areas of Wayne County have higher mortality rates than others.
Methods: We partnered with the Wayne County Medical Examiners and obtained records of those who died of accidental non-pharmaceutical opioid overdoses from July 2015 to July 2017. We recorded basic demographics, locations of death, and all opioid toxicology results and excluded those who died in hospitals. We utilized geolocation software to identify areas with the highest mortality.
Results: We identified a total of 645 people who died of non-pharmaceutical opioid overdoses. Of those, carfentanil was detected in 129 (20% of cases). During the mortality spike from July 2015 to February 2017, we noted carfentanil was detected in 114 of 419 cases (average 27%; range 6.4–45.2%). Majority of decedents were male (65%) and white (63%) with an average age of 43. We found the substances most frequently detected with carfentanil included morphine (57%), 6-monoacetylmorphine (6-MAM) (38%), fentanyl (43%), norfentanyl (33%), THC (34%), and cocaine (29%). Furthermore, we located two areas of the county with highest mortality rates and created a heat map with the results.
Conclusions: Carfentanil was highly associated with excess mortality noted during the period from July 2016 to February 2017

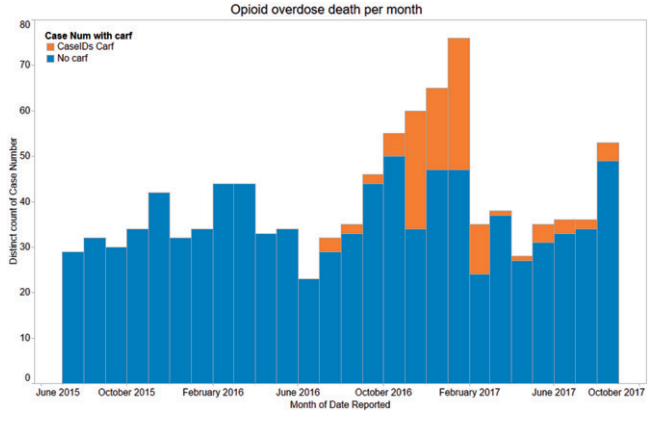

Figure 1. Accidental non-pharmaceutical opioid overdose deaths by month with and without carfentanil June 2015–October 2017.

in Wayne County, Michigan. In mid-February, China's National Narcotics Control Commission announced a ban on a number of fentanyl analogues, including carfentanil. This announcement paralleled the end of the mortality spike and suggests source control via origin country regulation efforts is effective. Finally, geographical analysis of medical examiner data can identify high risk areas that can be targeted for interventions by health departments, EMS, and law enforcement.

KEYWORDS Carfentanil; overdose; epidemiology

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80. Fentanyl- and fentanyl analog-related deaths across five counties in central New York between 2013 and 2017

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Background: Across the United States, a fivefold increase in synthetic opioid-related deaths occurred between 2013 and 2016. Illegal manufacturing of fentanyl has largely been identified as the source of the surge in overdose deaths. In New York State, opioid-related deaths have similarly increased. Between 2015 and 2016, a 35% increase in opioid-related deaths was reported with an increase in fentanyl-related deaths by 160% state-wide. The emergence of newly identified fentanyl analogs has been increasing. The objective of this study is to report the incidence of deaths involving fentanyl and fentanyl analogs across five counties in Central New York between January 1, 2013 and June 30, 2017.
Methods: Demographic data of all deaths determined to have a cause of "unintentional drug-related" across five counties in Central New York between January 1, 2013 and June 30, 2017 from the Medical Examiner's Office were included in this study. Deaths attributed to fentanyl and fentanyl analogs were isolated with all other drug-related causes excluded. Demographic data was collected including; age, gender, ethnicity, and specific identified fentanyl analogs.
Results: There were 213 total cases. All of the cases were male with a mean age of 38 years; 89% were Caucasian and 11% African American. The number of cases involving fentanyl- and fentanyl analog-related deaths increased from 2013 to 2016. There were 5 cases in 2013, 13 cases in 2014, 35 cases in 2015, 107 cases in 2016, and 53 cases up to June 30, 2017 (Figure 1). Despropionyl fentanyl and furanyl fentanyl were the fentanyl analogs most frequently identified (Table 1). Fentanyl and fentanyl analogs were present in 35% of total drug-related deaths across the five counties.
Discussion: Overdose deaths in which fentanyl and fentanyl analogs were identified increased from 5 cases to 107 cases across the five counties assessed in Central New York. Our data demonstrate that mortalities in which specific fentanyl analogs are found are increasing with 50 cases identified in 2017. An emergence in the number of newly identified fentanyl analogs occurred specifically in 2016, with despropionyl fentanyl and furanyl fentanyl being identified most frequently with increases of 60% and 57%, respectively between 2016 and 2017.
Conclusion: Opioid-related deaths continue to climb at an unprecedented rate. Fentanyl and newly identified fentanyl analogs are playing an increasing role in contributing to overdose deaths. We describe an exponential increase in fentanyl- and fentanyl analog-related deaths and significant increases in newly identified fentanyl analogs including despropionyl fentanyl and furanyl fentanyl.

KEYWORDS Fentanyl; analog; deaths

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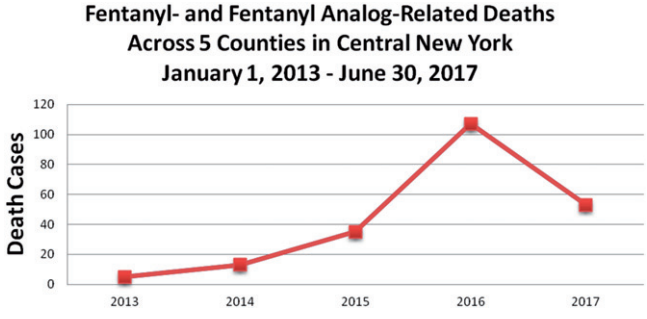

Figure 1. Graphical representation of trend in fentanyl- and fentanyl analog-related deaths occurring in 5 counties of Upstate New York between January 1, 2013 to June 30, 2017.

Table 1. Specific fentanyl analogs identified in post-mortem analysis of death cases across five counties in Central New York between January 1, 2013 and June 30, 2017.

	2013	2014	2015	2016	2017
Acetylfentanyl	0	0	2	1	3
Fluoro-Butyrylfentanyl	0	0	0	3	1
Despropionyl fentanyl	0	0	0	15	24
Furanyl fentanyl	0	0	0	14	22

81. Characterization of chemical, biological, radiological, nuclear (CBRN) incidents worldwide from 1970 to 2016 as reported by the global terrorism database (GTD)

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Background: The Global Terrorism Database (GTD) is an open-source, unclassified database that has cataloged over 17,000 terrorism events worldwide from 1970 to 2016. It is maintained by the National Consortium for the Study of Terrorism and Responses to Terrorism, a Department of Homeland Security Center of Excellence, in an effort to enhance understanding of terrorism and facilitate its defeat. It is the most extensive unclassified database on terrorism events worldwide and contains information on the date and location of each incident, the weapons used, the nature of the target, the number of casualties, and the group or individual responsible.
Methods: We analyzed all Chemical, Biological, Radiological, and Nuclear (CBRN) terrorism incidents reported by the GTD. Data analysis was performed to determine incidence over time, mortality, morbidity, and geographical distribution for each weapon

type. We included all CBRN incidents reported by the GTD and excluded other non-CRBN incidents.
Results: There were a total of 170,350 reported terrorism attacks between 1970 and 2016 in the database, of which 398 (0.23%) used CBRN weapons. There were 349 chemical (87.7%), 30 biological (9.1%), 13 radiological (3.3%), and 0 nuclear attacks. There was a 538% increase in the annual incidence in chemical attacks after 2011. Throughout the study period, chemical weapons resulted in a mean fatality of 6.6 deaths per incident (range 0–1300, median 1) and mean morbidity of 51.8 injuries per incident (range 0–5500, median 1). Biological weapons had a mean fatality of 0.3 deaths per incident (range 0–2, median 0) and mean morbidity of 26.0 injuries per incident (range 0–751, median 0). There were no fatalities or injuries associated with radiological attacks. The majority of events occurred in South Asia ($n = 101$, 25.4%), the Middle East and North Africa ($n = 69$, 17.3%), Western Europe ($n = 55$, 13.8%), and North America ($n = 54$, 13.6%).
Conclusions: This data analysis is our attempt to characterize trends in CBRN terrorism attacks worldwide using the GBD, an open-access, unclassified database of terrorist events from 1970 to 2016. Chemicals were found to be the most commonly reported weapons in these events. There was a five-fold increase in chemical attacks in the last 5 years of the study period, implicating the need for adequate chemical terrorism education and disaster preparedness among first responders and healthcare providers. Particularly in regions with the highest incidence of CBRN attacks, efforts to both prevent further attacks and prepare to respond to attacks should take a priority in the global fight against terrorism.

KEYWORDS Terrorism; chemical; biological

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82. Trends in buprenorphine film product toxicities

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Background: Treatment of opioid use disorder with buprenorphine has expanded significantly, with 58% opioid treatment programs now offering buprenorphine. Additionally, 2.1 million ambulatory visits reported uptake of buprenorphine in 2013. Buprenorphine films, released for use in October 2010, with a single dose foil packaging are considered child-resistant and abuse deterrent. The objective of this study is to evaluate the trends, and characteristics of exposures to buprenorphine film formulations.
Methods: We retrospectively queried the National Poison Data System (NPDS) for all confirmed exposures to buprenorphine films from January 1, 2012 to December 31, 2016 as specified by the American Association of Poison Control Center Code (AAPCC) generic code and product name. 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. Frequencies and rates of buprenorphine film exposures (per 100,000 human exposures) were evaluated using Poisson regression methods, with the percent changes and corresponding 95% Confidence Intervals (95% CI) reported.
Results: Overall, there were 6205 reports of exposures to buprenorphine sublingual films to the PCs during the study period. The reports of buprenorphine film exposures increased from 852 to 1425 during the study period. Children under 6 years of age represented 26.0% of the sample, while adults between 20 and 39 years of age accounted for 42.1% of the cases. The most common reason for exposure was unintentional (35.8%), with intentional abuse (21.4%) and suspected suicides being common (15.1%). Single substance exposures accounted for 61.6% of the cases and ingestion was the most common route of exposure. In 57.6% of cases, the patient was enroute to a healthcare facility. The case fatality rate for such exposures was 0.3%, with 4.2% cases demonstrating major effects. Among children under 6 years of age, majority were single substance (96%), and unintentional exposures (98%), with resulting minor clinical effects (36.4%). Overall, multiple substance exposures resulted in a higher number of deaths (16 versus 2 cases) and major clinical effects (193 versus 65 cases). Similarly, the proportion of major effects was highest among suspected suicides (11.4%) and abuse (5.3%) in comparison to cases of other exposure reasons such as unintentional. New Mexico (32.8) demonstrated the highest rate of buprenorphine film exposures (per 100,000 population). Naloxone therapy was reported for 18.4% cases. The frequency of buprenorphine film exposures increased by 67.2% (95% CI: 42.3%, 81.7%; $p < .001$) over the study period, and the rate of such exposures increased by 75.9% (95% CI: 59.8%, 93.4%; $p < .0001$).
Conclusions: Analysis of national data from the NPDS exhibited a significantly increasing trend in the exposures to buprenorphine film products, with such exposures being frequent among children under 5 years of age. Considering the complexity of film packaging, it is imperative to explore in greater detail, the reasons for the observed rise in these exposures. There were fewer major outcomes in unintentional overdoses, compared to cases of suicidal ingestion and abuse, especially when used with other substances.

KEYWORDS Buprenorphine films; NPDS; epidemiology

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83. National trends in the opioid exposures reported to the U.S. poison centers, 2013–2017

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Background: Opioid-related deaths are one of the leading causes of accidental deaths in the U.S., with the mortality rates having tripled in the last two decades. According to the Healthcare Cost and Utilization Project (HCUP), opioid-related emergency department (ED) visits increased by 99.4% from 2005 to 2014. This study aims to examine recent national trends in opioid exposures reported to U.S. poison centers (PCs).
Methods: The National Poison Data System (NPDS) was queried for all closed, human exposures to opioids from January 1, 2013 to December 31, 17 using the American Association of Poison Control Center (AAPCC) generic code identifiers for substances. We identified and descriptively assessed the relevant demographic and clinical characteristics. Opioid reports from acute care hospitals and EDs were evaluated. Trends in opioid frequencies and rates (per 100,000 human exposures) were analyzed using Poisson regression methods. Percent changes from the first

year of the study (2013) were reported with the corresponding 95% confidence intervals (95% CI).

Results: There were a total of 408,482 opioid exposure calls made to the PCs from 2013 to 2017, with the number of calls decreasing from 86,439 to 76,292 during the study period. Among the overall opioid calls, the proportion of calls from acute care hospitals and EDs increased from 52.1% to 60.3% from 2013 to 2017. Multiple substance exposures accounted for 48.2% of the overall opioid calls and 60.4% of the opioid calls from acute care hospitals and EDs. Approximately one-fifth of patients reporting opioid exposure were admitted to critical care. Residence was the most common site of exposure (90.8%) and 62.5% cases were enroute to the hospital when the PC was notified. The most frequent age groups were 20–39 years (35.2%) and 40–59 years (24.9%); 56.4% were female. Suspected suicides (37.5%), and intentional abuse (13.1%) were commonly observed reasons for exposure, with these proportions being higher in cases reported by acute care hospitals and EDs (56% and 16%, respectively). Major effects were seen in 6.6% cases and the case fatality rate for opioids was 0.8%, with 3476 deaths reported within the sample. The most frequent opioids associated with the cases were hydrocodone (26.2%) and oxycodone (20.4%), while the most common co-ingestant was benzodiazepines (16%). Drowsiness and tachycardia were the most frequent clinical effects. Naloxone was a reported therapy for 17.9% cases. During the study period, the frequency of opioid exposures decreased by 11.8% (95% CI: −12.6%, −10.9%; $p < .001$), and the rate of opioid exposures decreased by 8.1% (95% CI: −12.5%, −4.4%; $p < .001$).

Conclusions: Analysis of calls to U.S. PCs from 2013 to 2017 indicated an overall decreasing trend of opioid exposures. However, the proportion of calls from the acute-care hospitals and EDs increased. Opioid calls demonstrated a high proportion of intentional reasons for exposures and occurred in older age groups. Poison centers can play a critical role in the U.S. opioid crisis in regards to appropriate management and case capture for public health engagement as one viewpoint of the current crisis in real time.

KEYWORDS Opioids; NPDS; epidemiology

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84. Understanding a Pesky poisoning: bromadiolone toxicokinetics

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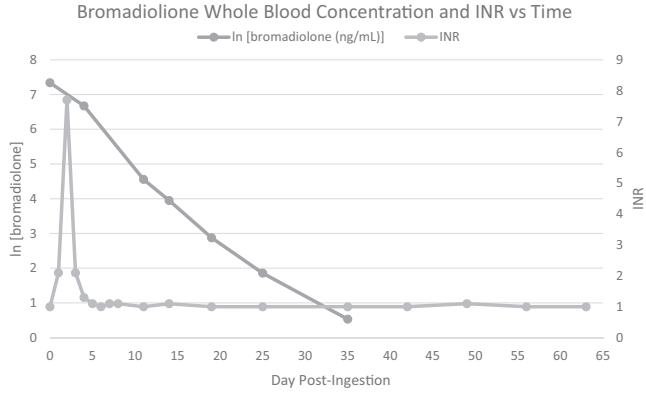
Background: Long-acting anticoagulant rodenticide (LAAR) poisoning can lead to a severe and prolonged coagulopathy. The ability to obtain LAAR concentrations and understand the toxicokinetics of LAARs could lead to individualized treatment plans and potentially decrease the intensive and prolonged treatment course following LAAR poisoning. We describe a single overdose case of the LAAR bromadiolone with serial blood concentrations and provide bromadiolone toxicokinetics.

Case report: A 32-year-old woman presented to the emergency department (ED) after an acute ingestion of an unknown amount of 0.5% bromadiolone. Her husband called EMS immediately following the ingestion. On arrival to the ED, her vital signs were: BP, 120/80 mmHg; HR, 87/min; RR, RR 14/min; SpO_2 97%; T 36.9 °C. She was initially awake and tearful, but then became obtunded with tonic posturing. There was concern for seizure activity, so she was intubated for airway protection. A nasogastric tube was placed and bright pink tablet-like substance was removed in the gastric contents. The patient then received activated charcoal and was given 5 mg of intravenous vitamin K1. Her initial coagulation studies were: INR, 1.0; PT, 12.0 s; PTT, 32.9 s. The day after admission, her mental status improved and she was extubated. A repeat laboratory analysis showed a rising INR on hospital day 1, at which point she was initiated on Vitamin K1 25 mg by mouth every 6 h. Her INR peaked at 7.7 on hospital day 2, at which point her Vitamin K1 dose was increased to 50 mg every 6 h. Her INR normalized by hospital day 5 on this dosing regimen. During her inpatient stay, the patient disclosed that her husband had coerced her into drinking the bromadiolone and other unknown substances. After discharge, the patient was monitored with weekly coagulation studies and slow tapering of her Vitamin K1 therapy. She took Vitamin K1 for a total of 8.5 weeks without recrudescence of a coagulopathy (Table 1). Serial bromadiolone concentrations were obtained from a laboratory outside of the United States after the patient completed treatment. Due to hemolysis of the samples, EDTA-tube specimens were analyzed using a new assay with a whole-blood-based standard curve. Her initial whole blood bromadiolone concentration on arrival to the hospital was 1540 ng/ml.

Table 1.

Day Post-ingestion	INR	Whole Blood Bromadiolone Concentration (ng/ml)	Daily Vitamin K (mg)
0	1.0	1540	
1	2.1		100
2	7.7		100
3	2.1		200
4	1.3	790	300
5	1.1		200
6	1.0		200
7	1.1		200
8	1.1		200
11	1.0	95.2	200
14	1.1	51.9	160
19	1.0	17.7	160
25	1.0	6.4	120
35	1.0	<2	80
42	1.0	<2	40
49	1.1	<2	20
56	1.0	<2	5
63	1.0	<2	0



Graph 1.

Case discussion: While most patients who ingest LAARs present to medical care already with a severe coagulopathy, our patient presented early following ingestion allowing us to obtain serial bromadiolone concentrations throughout her hospital stay and post-discharge. Our preliminary analysis suggests that bromadiolone toxicokinetics are consistent with a one-compartment model with first order kinetics and half-life of 76 h (Graph 1). Additionally, our patient's bromadiolone concentration was less than 2 (lower than the assay's detectable limit) by 35 d post-ingestion, but because these concentrations cannot be readily obtained, she continued Vitamin K1 therapy for an additional 24 d.
Conclusion: Although bromadiolone concentrations are not currently available in the United States, real time bromadiolone concentrations may assist in determining improved therapeutic endpoints for Vitamin K1 therapy in patients with bromadiolone ingestions.

KEYWORDS Long-acting anticoagulant rodenticide; bromadiolone; toxicokinetics
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85. Increased reporting of indirect fatalities: collaboration between a poison center and county health department

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Background: The American Association of Poison Control Centers (AAPCC) owns and maintains the National Poison Data System (NPDS), which collects both direct and indirect fatalities submitted by 55 regional Poison Control Centers (PCCs), to analyze and report on poison-related deaths. Despite continued efforts, most poison-related deaths are not currently captured by NPDS due to lack of reporting to regional PCCs. While comparing our PCC and County Health Department (CHD) data sets for poison-related deaths, a significant gap was identified. We report efforts to improve PCC notification about poison-related deaths within our region.
Method: Our PCC has conducted biannual onsite review of our region's Office of the Medical Examiner (OME) toxicology data for poison-related deaths directly reported to our PCC. Attempts to receive data concerning other poison-related deaths, investigated by the OME but not reported to our PCC, were unsuccessful until we became aware of an existing process where the OME provides these as quarterly reports to the CHD. The reports included: decedent name and residence, case number, date of birth, date and location of death, cause and manner of death, and substance(s) involved. We used existing relationships with the CHD to receive electronic copies of the OME report. Trained PCC staff documented these indirect deaths into our electronic medical record (EMR) system, which automatically uploaded to NPDS. We entered the following data into the EMR: decedent's name, date of birth, medical history, date/time the report was received from the OME, date/time/location/manner of death, substances (up to three), and autopsy findings.
Results: In the first year of reporting an increase from zero to over one thousand indirect fatalities were recorded.
Conclusions: PCC collaboration with the CHD and OME resulted in improved data reporting regarding poison-related deaths. The ability to report more of these cases will enhance the power and marketability of NPDS data, as well as provide regional poison centers valuable information on poison-related deaths in their community. Our experience may be useful for similar endeavors at PCCs.

KEYWORDS Fatalities; reporting; collaboration
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86. Longitudinal, temporal, and geospatial trends of adolescent suicide attempts reported to a state poison control center, 2006–2016

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Background: In the United States, adolescent suicide attempts/completions are increasing. Indiana has the highest rate of adolescent suicidal ideation in the U.S. Using the National Poison Data System (NPDS), we sought to characterize Indiana's increase in suicide attempts by poisoning.
Methods: Utilizing NPDS and Toxicall data repositories, we selected 10–19 year-old intentional poisoning cases categorized as suicide from 2006 to 2016. Cases without an Indiana ZIP code or categorized as anything other than "confirmed exposure" were excluded. Cases were filtered by number of substances to eliminate duplicate records. The distribution of age, sex, and case volume by weekday and month were assessed. Changepoint analysis was used to indicate the point of inflection within time series. Average case volumes by day and month were compared using Kruskal-Wallis, and Nemenyi tests. For geospatial analysis we used the proportion of adolescent suicide to all adolescent cases reported by county. To determine the association between known social determinants of health and adolescent suicide attempts, we used county-wide statistics from the County Health Rankings and Roadmaps dataset from 2010 to 2016 and the proportion of teen suicide calls by county. Correlations between factors and adolescent suicide cases were determined by calculating Spearman's correlation coefficients. All calculations and graphs were done in R version 3.4.3.
Results: Over the eleven years, adolescent suicide cases significantly increased starting in 2012 (p-value $< .001$) with each successive year exceeding the prior. The majority of cases (73.7%) involved females with an average age of 15.96 ± 0.27 years. The mean age of females decreased over the time period. Monday had the highest rate of cases, Friday and Saturday had the lowest. June and July were the months with the lowest case rates. Geospatial analysis shows the highest adolescent suicide case proportions in urban centers. County statistics (length of life, physical inactivity, sexually transmitted infections, excessive alcohol, high school graduation, children in poverty, single parent households, violent crime, low birth weight, HIV cases, drug overdoses, unemployment, and household median income by county) were not statistically associated with the 11-year proportion of adolescent suicide cases for the majority of Indiana counties.
Conclusion: Our results are consistent with literature showing that suicide attempts by adolescent females are significantly

increasing. As we used Poison Center data, our results cannot be generalized to all types of suicide attempts. We also show that rates correlate with the school schedule with summer months and weekends having a lower frequency of cases. We did not find associations between county wide social determinants of care and cases involving adolescent suicide attempts. Further studies are being conducted to assess similar trends for national poison center data, as well as to establish factors that might significantly correlate with adolescent suicide by poisoning.

KEYWORDS Suicide; adolescent; Poison Control Center

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87. Heavy methamphetamine use and elevated blood lead levels: NHANES 2003–2014

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Background: Lead acetate may be, but is not always, used in the clandestine manufacturing of methamphetamine. Acute lead poisoning has been reported in clusters of patients following use of lead acetate contaminated with methamphetamine. The effect of chronic methamphetamine use on blood lead levels (BLL) is unknown but it is not routinely considered a risk for potential lead exposure. We hypothesized that frequent methamphetamine users were the most probable population to encounter lead acetate contaminated methamphetamine and they may have an increased total lead body burden secondary to repeated low lead level exposures. Our objective was to examine the National Health and Nutrition Examination Survey (NHANES) to determine if frequent, repetitive methamphetamine use was associated with elevated BLL's among U.S. residents.
Methods: We analyzed the NHANES 2003–2014. Inclusion criteria included persons 16 years of age or older with a documented BLL. The drug use questionnaire was reviewed for information regarding a person's lifetime methamphetamine use. We defined "heavy" methamphetamine use as a person who reported using methamphetamine over 20 times. "Intermediate" methamphetamine use was defined as person who used methamphetamine 6–19 times. "Light" methamphetamine use was defined as a person who used methamphetamine 1–6 times. A total of 26,963 people were included in this analysis. BLL's were positively skewed and log-transformed to normalize distribution. Differences in demographic distributions were assessed using Pearson chi square and Mann-Whitney test. Independent t-test was utilized to compare BLL means among type of methamphetamine users (heavy versus intermediate versus light) and non-users. Multiple linear regression was used to determine effects of heavy methamphetamine use on BLL with age, gender, and race/ethnicity as covariates. People with the highest BLL's (top quartile and BLL >10 mcg/dl) were reviewed to see if they were more likely to be methamphetamine users.
Results: Heavy methamphetamine users were younger (41 versus 45, <0.00) than non-users and more likely to be male (64% versus 48%, <0.00). Independent t-test demonstrated a statistically higher BLL among "heavy" methamphetamine users compared to non-users (1.72 mcg/dl versus 1.61 mcg/dl, <0.016). This remained true when accounting for age, gender, and race ($p < .00$). There was no difference in mean blood lead level between intermediate or light methamphetamine users and non-users. People with blood lead levels in the highest quartile were more likely to be methamphetamine users than those in the lowest quartile (<0.00). One hundred and sixty-seven people had a BLL >10 mcg/dl however only 3% were methamphetamine users.
Conclusions: Heavy methamphetamine users have elevated blood lead levels compared to non-users. However, whether or not this carries any clinical significance is unclear. A limitation of the data is it is difficult to determine the timing of when a person's methamphetamine uses actually occurred, which may be an important covariate when analyzing their BLL's. A small percentage of methamphetamine users had a BLL >10 mcg/dl. We identify a history of repeated methamphetamine use as a potential source of lead exposure among US residents.

KEYWORDS Methamphetamine; lead; NHANES

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88. Urinary concentrations of endocrine disrupting chemicals found in personal care products and infertility: NHANES 2013–2014

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Objective: Infertility effects approximately 15% of the US population. There is increasing concern regarding environmental toxicants contributing to infertility through disruption of the endocrine system, although their exact role on reproductive health has yet to be defined. Our objective was to determine whether exposure to endocrine disruptor chemicals found in common personal care products (PCPs), including parabens, phenols, and phthalates, is associated with infertility among female US residents.
Methods: We analyzed the National Health and Nutrition Examination Survey (NHANES) 2013–2014. Inclusion criteria included females ages 18–37 with measurements of PCP urine chemical concentrations. Females over the age of 37 were excluded to confound for female age-related infertility decline. Infertility was defined by answering yes to one of the following questions: "have you ever attempted to become pregnant over a period of at least a year without becoming pregnant?" and "have you/has your spouse ever been to a doctor or medical provider because you have been unable to become pregnant?" Differences in demographic distributions were assessed using Pearson chi square and Mann Whitney test. Logistic regression was performed to assess for an association between infertility and PCP chemical urine concentrations. Covariates included age, current tobacco use, and previous diagnosis of pelvic inflammatory disease. A sensitivity analysis was then performed to account for body mass index. Independent samples t-test was used to assess if urine PCP chemical concentrations were higher among infertile respondents compared to the general population.
Results: A total of 25 chemicals were analyzed (Table 1). Elevated urinary concentrations of mono-isononyl phthalate were associated with infertility (OR 1.62, $p = .046$). After controlling for body mass index, an increased urine triclosan concentration was

Table 1.

Personal care product chemicals and metabolites
Benzophenone-3
Bisphenol A
Bisphenol F
Bisphenol S
Triclocarban
Triclosan
Butyl paraben
Ethyl paraben
Methyl paraben
Propyl paraben
2,5-dichlorophenol
2,4-dichlorophenol
Mono(carboxynonyl) phthalate
Mono(carboxyoctyl) phthalate
Mono-2-ethyl-5-carboxypentyl phthalate
Mono-n-buyl phthalate
Mono(3-carboxypropyl) phthalate
Mono-ethyl phthalate
Mono-(2-ethyl-5-hydroxyhexyl) phthalate
Cyclohexane 1,2-dicarboxylic acid monohydroxy isononyl ester
Mono-(2-ethyl)-hexyl phthalate
Mono-isobutyl phthalate
Mono-isononyl phthalate
Mono-(2-ethyl-5-oxohexyl) phthalate
Mono-benzyl phthalate

associated with infertility (OR 1.2, $p = .046$). There was no statistical difference when comparing the means of PCP chemical urine concentrations among infertile and fertile female survey respondents.

Conclusions: An association between female reported infertility and urine triclosan and mono-isobutyl phthalate concentrations was identified. Approximately 30%–40% of couples are classified as having unexplained infertility after initial diagnostics fail to identify an abnormality with either partner. Hormone imbalances secondary to endocrine disruptors are a possible cause of unexplained infertility. A limitation of this study was the NHANES data set does not contain any information regarding male participant's reproductive history.

KEYWORDS Infertility; parabens; pthalates

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89. Pain relief in the emergency department: an assessment of patient's perspectives and expectations as a risk reduction strategy

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Background: As emergency medicine (EM) providers increasingly treat patients for chronic pain, the lack of patient information regarding history of pain, medication use, or quality of life is an ongoing concern. Additionally, providers are often unaware of pain relief expectations, resulting in inadequate pain relief upon discharge. To address these gaps, we sought to initiate a dialog with patients at point-of-care in the Emergency Department (ED) regarding these and other factors related to risk of long-term pain medication use or risk of a medication-related injury.

Methods: Our target population were patients over 18 years of age being treated for nontrauma/noncancer pain in an urban ED. Using a convenience sampling approach, trained research assistants conducted bedside assessments utilizing validated questions and answer choices from the NIH-funded Patient-Reported Outcomes Measurement Information System (PROMIS). Questions included history of relevant health-seeking behavior, medication use, pain relief expectations, and impact of pain on quality of life. We used Chi square analyses to detect differences in overall response trends, and logistic regression for gender-specific trends. Significance was determined at $p < .05$.

Results: Within our cohort ($n = 174$), mean age was 43.8 years, 53% were females, 62% reported over 7 d of pain prior to arriving at the ED, and females were more likely to report previous ED treatment for pain ($p = .02$). We also detected gender-specific anatomical variability in pain: arm pain was more frequent among males ($p = .004$), while head/face pain ($p < .001$) and abdominal pain ($p = .01$) were more frequent among females. With respect to mean pain level upon ED arrival, a higher proportion of females reported severe pain (e.g., 7–10 on the Numerical Rating Scale, $p = .01$). When asked about pain relief expectations in the ED, 58% expected to be at a pain level 4 or less upon discharge, and over 50% believed they would leave the ED with a pain medication prescription. Eighty percent reported taking prescribed pain medications for more than 30 d, and the Primary Care Provider was the leading prescriber. The quality of life assessment found that pain had a daily impact on the ability to pay attention (78%), conduct daily activities (90%), and sleep (94%). Interestingly, 80% of patients believed their pain needs would be addressed in the ED, and 80% expressed strong interest in discussing short- and long-term expectations of pain relief and non-medication strategies before discharge.

Conclusions: Patients seeking pain treatment in the ED were more likely to have been in pain for over 30 d and were currently being managed with pain medication – each which confers the risk of long-term pain medication use or accidental overdose. We also found gender-specific anatomical differences in pain, and females were more likely to present with severe pain. Most wanted to discuss short- and long-term expectations of pain relief and non-medication strategies upon discharge. We believe our findings could support the need for ED discharge planning processes specific to the pain patient.

KEYWORDS Emergency department pain management; patient expectations for pain relief; opioid risk reduction strategy

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90. Epidemiology of methemoglobinemia: a National Poison Data System observational study

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Background: Oxidation of hemoglobin can occur from a diverse range of drugs and chemicals. Lists of agents are typically provided in textbooks, however there is little data in the medical literature distinguishing common from rare causes. The aim of this investigation was to identify etiologic agents most commonly implicated in methemoglobinemia using data from the National Poison Data System.

Table 1. Number of cases for each drug or chemical category.

Substance	Number of cases (%)	Cumulative %
Local anesthetics	310 (25)	25
Phenazopyridine	194 (16)	41
Dapsone	192 (16)	56
Nitrates & Nitrites	191 (15)	72
Unknown	185 (15)	87
Aniline & Dyes	38 (3)	90
Other: pharmaceutical	35 (3)	93
Other: non-pharmaceutical	31 (3)	95
Antimalarial	26 (2)	97
Sulfonamides	11 (1)	98
Petroleum products	8 (1)	99
Methylene blue	6 (0.5)	99
Chlorates	5 (0.4)	100
Naphthalene	2 (0.2)	100
Phenol/menthol	2 (0.2)	100

Methods: This was a retrospective cross-sectional chart review using electronic data from the National Poison Data System (NPDS). The NPDS database was queried to identify cases from July 1, 2007 to June 30, 2017 that were coded as methylene blue recommended and/or performed. Methemoglobin is not a coded clinical effect, therefore methylene blue administration was our surrogate for clinically significant methemoglobinemia. Cases were excluded if the substance(s) were not known to cause methemoglobinemia or the substances suggested methylene blue was used adjunctively for refractory shock (e.g., calcium channel or beta blocker) rather than to treat methemoglobinemia. Multiple substance exposures were reviewed and substances not known to cause MetHb were excluded. The primary endpoint was to summarize the most frequent etiologic agents associated with the administration of methylene blue for presumed methemoglobinemia.
Results: There were 2563 products reported in 1209 cases. The average age was 36 (SD 21) years and 50% were female. Age categories were as follows: > 5 years, 13%; 6–12 years, 3%; 13–18 years, 7%; < 18 years, 77%. After excluding co-ingestants and cases clearly not associated with methemoglobinemia, there were 1237 substances. The top five substance categories were: local anesthetics, phenazopyridine, dapsone, nitrates/nitrites and unknown (Table 1). "Other pharmaceuticals" represented 35 cases (3%). Within this group, rasburicase represented 9 cases (26%) and metoclopramide and ifosamide were each coded in six cases (17% each).
Conclusion: There are no comprehensive reviews reporting prevalence of various etiologic agents associated with methemoglobinemia. This study reveals the relative contribution of various drugs and chemicals associated with methylene blue administration. Nearly three quarters of all cases were associated with local anesthetics, phenazopyridine, dapsone and nitrates/nitrites.

KEYWORDS Methemoglobin; epidemiology; adverse drug reaction

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91. Brodifacoum poisoning with severe coagulopathy from synthetic cannabinoid use

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Background: Cases of unexplained coagulopathy were identified in US synthetic cannabinoid users in March of 2018. Synthetic cannabinoids (SC) have not previously been shown to cause coagulopathy. We report two cases of severe coagulopathy and bleeding complications in regular users of SC. Their laboratory testing show that they had exposure to brodifacoum and SC. Furthermore, product testing confirmed that the SC was the source of the brodifacoum exposure.
Case reports: Patient 1: A 45-years-old woman presented to the ED with episodes of hematuria, abnormal vaginal bleeding, epistaxis and hemoptysis. She admitted to using SC 20–25 times a day. Her presenting INR was >12 (exceeding the upper limits of detection) with Hgb 18.4, though she was not actively bleeding. She denied ingestion of rat poison or anticoagulants and had no suicidal ideation. She was treated with FFP and IV Vitamin K and transitioned to oral Vitamin K the next day. She was also treated with dronabinol due to concerns of cannabis withdrawal given her chronic heavy use. She was discharged on oral vitamin K when her INR was <2.0. She provided six samples of SC she had been using for forensic testing. The patient's blood anticoagulant panel returned positive for brodifacoum, difenacoum and bromadiolone. In addition, her urine was positive for 5F-AMB 3-methyl-butanoic acid, 5F-ADB 3.3-dimehtyl-butanoic acid, and FUB-AMB 3-methyl-butanoic acid (metabolites of synthetic cannabinoids 5F-AMB, 5F-ADB, and FUB-AMB). All of the SC samples tested contained brodifacoum at concentrations of 0.7–1.5% by weight. Patient 2: A 36-years-old woman presented to the ED twice with complaints of hematuria. She was a daily user of synthetic cannabinoids and friends with Patient 1. On initial visit Hgb was 16. She represented the following day with continued hematuria, new abdominal pain and swelling, chest pain and dyspnea. She denied ingestion of rat poison or anticoagulant and had no suicidal ideation. Her abdominal CT showed free abdominal fluid and pericardial fluid. Her INR was >12 and her Hgb dropped to 10.2. She was treated with FFP and IV vitamin K. She was started on dronabinol for cannabis withdrawal. She was transitioned to oral vitamin K and discharged when her INR was <2.0. The patient's blood anticoagulant panel returned positive for brodifacoum, difenacoum and bromadiolone. In addition, her urine was positive for FUB-AMB 3-methyl-butanoic acid, which is a metabolite for the synthetic cannabinoid FUB-AMB. Both patients are being treated with oral vitamin K and have weekly INR monitoring.
Case discussion: Patients with unexplained coagulopathy should be asked about SC use. Those patients with coagulopathy should be suspected of having brodifacoum poisoning and treated with FFP and vitamin K as needed. The common SC detected in both these cases was FUB-AMB. The brodifacoum concentrations detected are far higher than those found in residential rodenticides suggesting that the addition of brodifacoum was likely not accidental.
Conclusion: In patients with SC use, INR should be obtained to screen for brodifacoum poisoning

KEYWORDS Brodifacoum; synthetic cannabinoid; coagulopathy

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92. The risk of seizure after naloxone administration in tramadol exposures

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Background: Tramadol is a synthetic opioid that can cause seizures in therapeutic and overdose situations. Naloxone is an opioid receptor antagonist that can reverse the respiratory depression caused by tramadol. The literature contains a number of studies evaluating the relationship between naloxone administration and the occurrence of seizures, the results of which are conflicting. We attempt to study this relationship using a national database of single-agent tramadol exposures in adults and children.
Methods: This is a retrospective chart review of tramadol exposures reported to the National Poison Data System (NPDS) from January 2004 to December 2013. Charts of cases for which naloxone was given and seizures occurred were requested from the individual poison centers to ascertain the temporal relationship between the administration of naloxone and the occurrence of a seizure. Both naloxone and seizures were dichotomized and analyzed as binary variables. Generalized estimating equations were used to estimate the effect of naloxone on the occurrence of a seizure.
Results: During the 10-year period of this study, 48,028 cases were reported. The median age was 27 years (IQR 16–44 years); males represented 42.26% of the cases. The median dose ingested was 4.7 mg/kg (IQR 1.6–14.8 mg/kg). 76.8% presented as acute exposure, 18.21% as acute on chronic and 4.98% as chronic exposure. 2.91% of cases received naloxone; seizures were recorded in 9.6% of cases. In the unadjusted model, naloxone was associated with an 80% increase in the odds of a seizure (OR =1.80, 95% CI: 1.37–2.37, $p < .001$). However, when this model was adjusted for age, sex, dosage of tramadol, chronicity, level of health care facility, intubation, and the presence of other neurologic symptoms, the administration of naloxone was no longer associated with the occurrence of seizures (OR =1.12, 95% CI: 0.82–1.52, $p = .47$).
Discussion: Our study reveals that naloxone is associated with an 80% increase in the unadjusted risk of seizure in tramadol exposures. However, the association disappears after adjustment for other confounders.
Conclusion: Naloxone administration in tramadol exposures was not associated with the occurrence of seizures after adjustment for confounding variables, as reported to NPDS during a 10-year period.

KEYWORDS Tramadol; naloxone; seizure

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93. National Poison Data System fatalities involving loperamide, 2012–2015

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Background: Loperamide is an over-the-counter antidiarrheal medication increasingly being abused and misused for its mu-opioid agonist activity in order to manage opioid withdrawal syndrome or achieve euphoric effects. In contrast to most opioids, which cause mortality secondary to respiratory depression, deaths due to loperamide abuse and misuse may be due to its cardiotoxic effects. Methods The National Poison Data System (NPDS) was searched for exposures involving loperamide-containing products that were reported between 2012 and 2015. Fatality abstracts for all deaths were obtained, reviewed, and summarized. Extracted data included patient demographics, medical history, coingestions, circumstances of presentation, loperamide dose, presenting cardiac rhythm, presenting vital signs, laboratory evaluation results, and autopsy findings. Results A total of 4856 exposures to loperamide-containing products were reported, of which 12 (0.2%) were fatalities. The fatalities involved intentional abuse ($n = 4$), intentional unknown ($n = 2$), intentional suspected suicide ($n = 1$), and unknown ($n = 5$) reasons for exposure. Patients had a mean age of 30.7 years with a median age of 27.0 years (range 21–54 years), with 1 patient whose age was not reported. There were six females and six males. Eight of the 12 cases involved polysubstance ingestion, with the most common coingestants being opioids ($n = 5$), anticholinergics ($n = 4$), and benzodiazepines ($n = 4$). Self-reported quantity was only available in three cases with the reported range of 30–200 tablets per day. Two patients were declared deceased in the field by emergency medical personnel. Of the ten patients who were brought to healthcare facilities, nine had cardiac arrests and one had refractory hypotension necessitating extracorporeal membrane oxygenation. Return of spontaneous circulation was achieved in seven of the cardiac arrest patients, although all eventually died. One patient had persistent seizure activity with cerebral ischemia. The relative contribution to fatality of loperamide was considered "undoubtedly responsible" in three cases, "probably responsible" in three cases, "contributory" in two cases, "probably not responsible" in two cases, and "unknown" in two cases.
Conclusion: Loperamide was associated with 12 fatalities reported to the NPDS between 2012 and 2015. As opioid-dependent patients seek alternative methods of managing substance use disorders, loperamide may emerge as a significant cause of poisoning. The contribution of loperamide-induced cardiotoxicity to the fatalities in this series was difficult to determine as ECG intervals and presenting rhythms were not reported in most cases. In addition, it was difficult to evaluate the relative contribution of loperamide to mortality in polysubstance ingestions. This report highlights the need for further evaluation of deaths involving loperamide ingestion to establish the relationship between loperamide dose, cardiotoxicity, and outcomes.

KEYWORDS Loperamide; fatalities; NPDS

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94. National Poison Data System (NPDS) summary of intentional abuse and intentional misuse exposures to loperamide (2012–2015)

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Background: Massive overdoses involving misuse and abuse of loperamide resulting in serious cardiovascular (CV) clinical effects have been reported in the medical literature and from US poison centers. To promote the safe use of over-the-counter loperamide, the US Food and Drug Administration is working with manufacturers to reduce the number of doses in a package and implement blister packs or other single dose packaging. The purpose of this analysis is to describe trends as well as outcomes and factors associated with severe CV-related clinical effects with

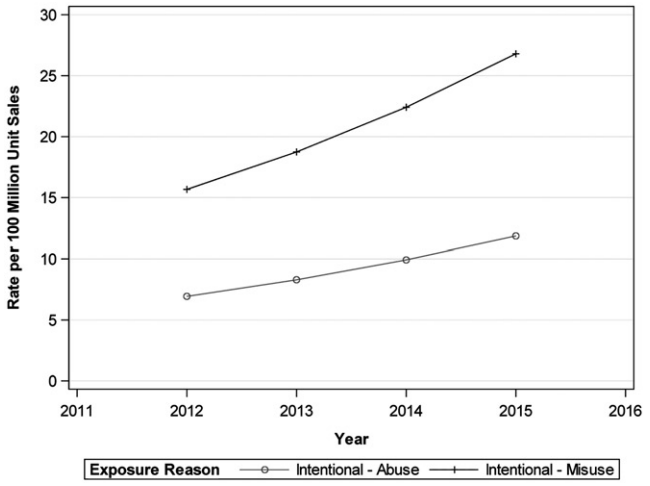

Figure 1. Sales-adjusted rates of intentional abuse and intentional misuse of Loperamide reported to the National Poison Data System (2011–2015).

Table. Frequency of outcomes and quantity associated with loperamide exposures.

	All exposures	Intentional abuse	Intentional misuse
Admission to a Healthcare Facility	16.8%	56.2%	17.9%
Severe Medical Outcome (major effect or death)	2.6%	19.5%	2.9%
Severe CV-Related Clinical Effect	6.8%	30.3%	9.8%
Median quantity reported (acute exposures only)	4.0 mg	120 mg	24 mg
IQR	2, 13.5	40, 240	14, 50

intentional abuse and misuse exposures to loperamide as reported to the National Poison Data System (NPDS).

Methods: Loperamide exposures (including all loperamide-containing products) were obtained from the NPDS for 2012 to 2015 and stratified by exposure reason. Sales-adjusted rates were calculated per one million units (i.e., tablets, gelcaps, liquid equivalents) sold to evaluate trends over time. Level of care, medical outcome, and the frequency of severe CV-related clinical effects were described. A severe CV-related clinical effect was defined as one or more CV clinical effect with a medical outcome of major effect or death. Quantity was calculated for acute exposures to loperamide and evaluated by exposure reason and by the report of severe CV-related clinical effects.

Results: Four thousand eight hundred and fifty-six loperamide exposures were reported between 2012 and 2015, with 12.4% ($n = 603$) involving intentional abuse (3.8%; $n = 185$) or misuse (8.6%; $n = 418$). Sales-adjusted rates of intentional abuse and misuse of loperamide increased from 2012 to 2015 (Figure 1). Intentional abuse was more likely to involve admission to a healthcare facility and a severe medical outcome (major effect or death) than intentional misuse exposures or all exposures (Table). The median quantity ingested among all exposures was 4 mg (IQR 2.0, 13.5) compared to 120 mg (IQR 40, 240) for intentional abuse and 24 mg (IQR 14, 50) for intentional misuse exposures. Severe CV-related clinical effects were reported in 6.8% percent of all loperamide exposures, with 30.3% of intentional abuse and 9.8% of intentional misuse exposures resulting in a severe CV-related clinical effect (Table). Severe CV-related clinical effects were more common with exposure to loperamide plus another substance (20.0%) than with loperamide only (2.3%). The median amount of loperamide among exposures with a severe CV-related clinical effect was 192 mg (IQR 40, 544), whereas 4 mg (IQR 2, 12) was the median amount of loperamide among exposures without a severe CV-related clinical effect.

Conclusions: Intentional abuse and misuse of loperamide was reported infrequently to the NPDS but increased from 2012 to 2015. Intentional abuse of loperamide was associated with an increased quantity, severity of medical outcome, and frequency of severe CV-related clinical effects. Polypharmacy may be another factor associated with increased risk and should be further explored in the context of loperamide abuse. NPDS data can be used to describe real-world use of loperamide and inform industry and regulators on appropriate interventions to promote the safe use of non-prescription products like loperamide.

KEYWORDS Loperamide; misuse and abuse; NPDS

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95. Synthetic cannabinoid-related coagulopathy: the tip of K2

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Background: There are isolated case reports of inhalational exposure to coumarin rodenticides through smoking of cannabis and crack cocaine. In early 2018 a regional poison center and inpatient toxicology service became aware of an outbreak of bleeding symptoms associated with synthetic cannabinoid (SC) use. We present a case that is illustrative of the 12 patients managed at the bedside by our service. Written informed consent for publication was obtained for all cases.

Case report: During an outbreak of SC-related coagulopathy in our region, a previously healthy 32-year-old male presented to the emergency department (ED) with 5 d of left flank pain, hematuria, and intermittent hematochezia. On the day of ED presentation, he developed epistaxis. We suspected SC use; direct questioning revealed SC use multiple times daily "for years" and he used SCs primarily to avoid urine drug testing. The specific product was labeled "Releaf." After obtaining detailed medical, social, and occupational history we could not identify an alternative source of coagulopathy. Initial vital signs: HR 110, BP 135/88, RR 16, SpO_2 100% on room air. Physical examination was remarkable for left anterior naris epistaxis requiring topical tranexamic acid and Merocel® packing to achieve hemostasis, melena, and frank hematuria. Laboratory testing revealed a coagulopathy (PT >120 s, INR >20), anemia (initial hemoglobin 14.2 g/dl, nadir 9.7 g/dl), thrombocytopenia ($113 \times 103/mm^3$), and acute kidney injury (BUN 25 mg/dl, Cr 1.89 mg/dl) which corrected during hospitalization. Qualitative urine and serum SC testing was positive for the AMB-FUBINACA. Qualitative anticoagulant testing on serum was positive for brodifacoum. Because of gastrointestinal bleeding, the patient was given ten units of IV Vitamin K1, 20 ml of cryoprecipitate, and four units of fresh frozen plasma (FFP). The INR decreased to 4.3 after cryoprecipitate and to 1.9 after the FFP. An additional two units of FFP were required on hospital day three for ongoing GI bleeding. The patient was started on 50 mg of oral vitamin K1 three times daily on hospital day three, then titrated down to 50 mg daily at discharge on hospital day ten. Working with our hospital pharmacy network, we were able to secure an adequate supply of oral vitamin K1. The patient has been compliant with ongoing outpatient follow-up of INR, hemoglobin, and adjustment of oral vitamin K1 dosing.

Case Discussion: This is an illustrative hospital course of unexpected bleeding from SC use managed at the beginning of this

outbreak. As with most of our subsequent bedside consultations, both SC exposure and the presence of brodifacoum were confirmed. Management challenges included stabilization of bleeding, titration of vitamin K1 dose, and procurement of adequate supplies of vitamin K1 at a reasonable cost.
Conclusions: We present a case of synthetic cannabinoid-related coagulopathy that illustrates the presentation and hospital course typical of cases managed by our medical toxicology service.

KEYWORDS Synthetic cannabinoid; brodifacoum; rodenticide

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96. Characterizing tianeptine exposures reported to the National Poison Data System – United States, 2000–2017

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Background: Tianeptine is an atypical tricyclic drug that is used as an antidepressant in Europe, Asia, and Latin America. Although it is not approved for medical use by the U.S. Food and Drug Administration (FDA), tianeptine is available for purchase online. Animal and human studies showed that tianeptine is an opioid receptor agonist. Several published cases of tianeptine poisoning describe various adverse effects from recreational abuse. Our study objective is to characterize calls about tianeptine exposures reported to the National Poison Data System (NPDS) between 2000 and 2017.
Methods: We reviewed all calls reporting tianeptine exposure in NPDS during January 2000–December 2017. Call counts were analyzed by year, region (U.S. census regions), demographics, exposure reason, exposure route, and co-exposures. We analyzed single tianeptine exposure calls (excluding withdrawal-associated calls) to characterize clinical effects, therapies, medical outcome, and level of care. We calculated frequencies of categorical variables and means of continuous variables using SAS 9.3. The SAS procedure, GENMOD, was used to test for trend significance in exposure calls from 2014 to 2017. We used Fisher's exact test to test for associations between outcome severity and multiple versus single exposures, age groups, and gender. Statistical significance was defined as <0.05.
Results: During the study period, NPDS received 218 tianeptine exposure-related calls. Of those, 114 (52%) were single substance exposures to tianeptine, excluding withdrawal-associated calls ($n = 29$). The increasing yearly trend was statistically significant ($p < .0001$) for all exposure calls and for calls related to "intentional abuse" or "misuse". The majority of calls were from the South, followed by the West. The majority were males ($n = 177$, 82%), with a mean age of 35 years (range 1–80 years). An intentional exposure (abuse, misuse, suicide, other) was reported in 119 (55%) of calls. The primary route of exposure was ingestion ($n = 183$, 84%), followed by parenteral ($n = 15$, 7%). Among the 83 (38%) calls with at least one co-exposure, Phenibut ($n = 26$, 31%), ethanol ($n = 13$, 16%), benzodiazepines ($n = 10$, 12%), and opioids ($n = 10$, 12%) were the most commonly reported. Among the 114 single substance exposures to tianeptine, the most common clinical effects included neurological, cardiovascular, and gastrointestinal effects. Therapies included fluids, benzodiazepines, naloxone, alkalinization, and intubation. Among single exposures with a known medical outcome ($n = 93$), 50 (54%) resulted in moderate outcomes. Among the 105 exposure calls with a known level of care reported, 46 (44%) were treated, evaluated, and released from the emergency department; there were 25 (24%) critical care admissions. Among all exposure calls with a known outcome ($n = 183$), significant associations were found between outcome severity and multiple versus single exposures ($p = .01$), and between outcome severity and gender ($p = .02$). No differences between outcome severity and age groups were found ($p = .93$).
Conclusion: There was a significant increase in all tianeptine exposure calls and in those calls related to intentional abuse/misuse across the U.S. from 2014 to 2017. Health care providers and public health officials need to be vigilant for potential tianeptine exposures and report adverse effects to their local poison center and FDA's voluntary MedWatch reporting system.

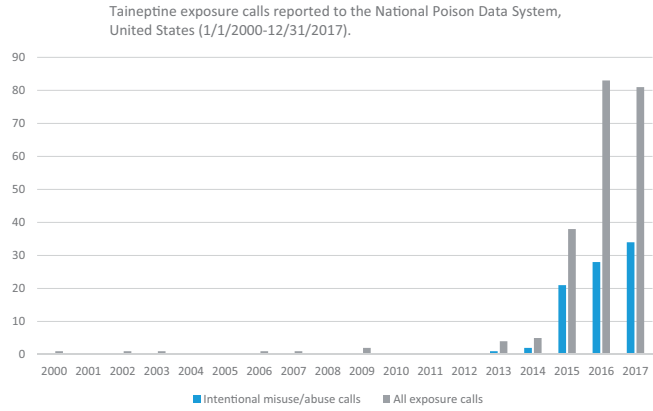

Figure 1. Tianeptine exposure calls reported to the National Poison Data System by year, January 1, 2000–December 31, 2017, United States.

Table 1. Most common reported clinical effects per body systems and performed treatments in single tianeptine exposures excluding withdrawals ($N = 114$).

Most common clinical effects by body systems, *n* (%)			
Cardiovascular (CVS)		***Respiratory (Resp)***	
≥1 CVS effect	**37 (32.5)**	**≥1 Resp effect**	**8 (7)**
Tachycardia	29 (25.4)	Respiratory depression	6 (5.3)
High blood pressure	13 (11.4)	Dyspnea	3 (2.6)
Conduction delays	5 (4.4)	Tachypnea	1 (0.9)
Nervous System (NS)		***Ocular***	
≥1 NS effect	**55 (48.3)**	**≥1 ocular effect**	**6 (5.3)**
Agitation	25 (21.9)	Mydriasis	4 (3.5)
Drowsiness	19 (16.7)	Miosis	2 (1.8)
Confusion	15 (13.2)		
Gastrointestinal (GI)		***Renal***	
≥1 GI effect	**12 (10.5)**	**≥1 Renal effect**	**5 (4.4)**
Nausea	9 (7.9)	Urinary retention	3 (2.6)
Vomiting	5 (4.4)	Creatinine abnormality	2 (1.8)
Diarrhea	3 (2.6)	Kidney failure	1 (0.9)
Dermal		***Metabolic***	
≥1 dermal effect	**10 (8.8)**	**≥1 metabolic effect**	**5 (4.4)**
Pallor	3 (2.6)	Electrolyte disturbances	3 (2.6)
Pain	3 (2.6)	Acidosis	2 (1.8)
Cellulitis	2 (1.8)		
Constitutional (Const)		***Musculoskeletal (MSK)***	
≥1 Const effect	**10 (8.8)**	**≥1 MSK effect**	**5 (4.4)**
Diaphoresis	8 (7)	Muscle weakness	2 (1.8)
Fever	3 (2.6)	Rigidity	1 (0.9)
Pain	1 (0.9)	***Psychiatric***	
		≥Psychiatric effect	**2 (1.8)**
		Delusions	2 (1.8)
Treatments, *n* (%)			
Fluids	**40 (35.1)**	Anti-emetics	**7 (6.1)**
Benzodiazepines	**31 (27.2)**	Alkalinization	**6 (5.3)**
Oxygen	**12 (10.5)**	Intubation	**5 (4.4)**
Naloxone	**11 (9.7)**	Ventilator support	**5 (4.4)**
Antibiotics	**11 (9.7)**	Antihistamine	**3 (2.6)**
Sedation	**9 (7.9)**		

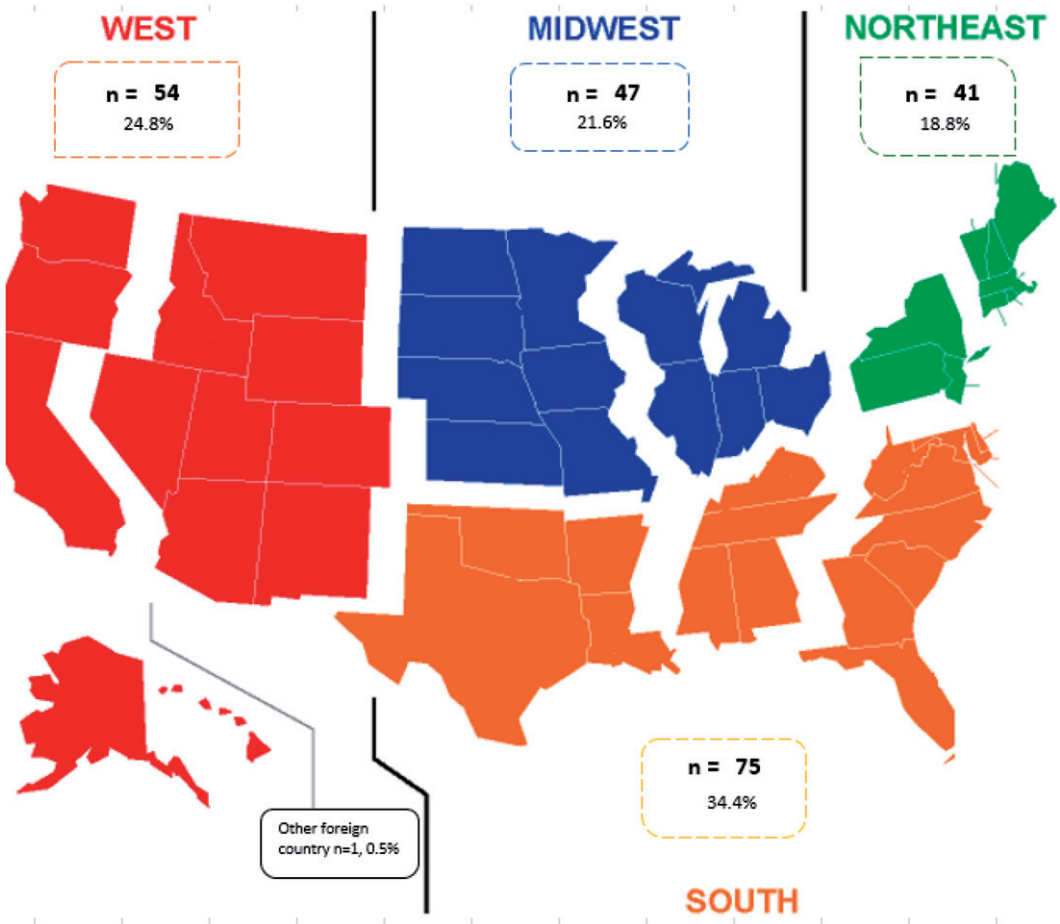

Figure 2. Distribution of all tianeptine exposure calls ($n = 218$) reported to the National Poison Data System by United States census region, January 1, 2000–December 31, 2017.

KEYWORDS Tianeptine; drug; abuse
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97. Anterograde amnesia associated with cocaine and despropionyl fentanyl exposure

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Background: There are increasing reports of a syndrome of anterograde amnesia in patients with opioid use. Bilateral hippocampal changes were noted on MRI in these cases. Causative agent(s) have not been clearly established, but some have hypothesized that this syndrome may be related to fentanyl or fentanyl analogues, particularly in combination with cocaine.
Case reports: We report two patients that presented to an urban emergency department with acute onset of anterograde amnesia following reported use of cocaine.
Case 1: A 54-year-old man with unknown medical history presented with pinpoint pupils and respiratory depression that responded to naloxone in the field. Witnesses reported that the patient had insufflated cocaine only. Initial vital signs were: BP 136/92, HR 94/min, RR 16/min, O_2 sat 96% on room air, temperature 98.8 °F. The patient was responsive to noxious stimuli only. Pulmonary exam demonstrated rales. A naloxone drip was started to treat recurrent respiratory depression, and the patient was subsequently intubated due to worsening hypoxia despite improved respiratory drive. After extubation, he was noted to have anterograde amnesia but was otherwise neurologically intact. Chest XR demonstrated hazy opacities at the bases consistent with aspiration pneumonia. CT head was unremarkable. MRI demonstrated areas of areas of T2 hyperintensity in bilateral hippocampi, as well as bilateral cerebellar hemispheres, globus pallidi, caudate nuclei, and lentiform nuclei. Initial toxicology testing was positive for cocaine. Send-out designer opioid testing was positive for despropionyl fentanyl. The patient was discharged 5 d later with persistent memory deficits. At outpatient follow up 4 months later, he reported persistent memory deficits compared to previous baseline, although symptoms were improving.
Case 2: A 59-year-old woman with history of type II diabetes mellitus and hypertension presented with altered mental status 2 d after insufflating cocaine. Initial vital signs were: BP 193/83, HR 108/min, RR 16/min, O_2 sat 100% on room air, temperature 97.7 °F. Neurological exam demonstrated anterograde amnesia, subtle weakness of her left hand, and difficulty with left arm finger-to-nose and finger tapping. CT scan revealed multiple areas of low density involving both cerebellar hemispheres and a large are in the right parietal lobe. Subsequent MRI showed large areas of subacute infarction in the bilateral cerebellar hemispheres, right parietal lobe and orbitofrontal lobe, as well as T2 hyperintensity of the bilateral hippocampi. Initial toxicology testing was positive for cocaine. Send-out designer opioid testing was positive for despropionyl fentanyl. The patient was discharged 8 d

later with resolution of her motor deficits but only minimal improvement of her amnesia. At outpatient follow up 3 months, she reported mild persistence of memory deficits compared to previous baseline.
Case discussion: We report two cases of anterograde amnesia, MRI demonstrating T2 hyperintensity in bilateral hippocampi after exposure to cocaine and despropionyl fentanyl. Fentanyl contaminated cocaine is a growing problem. Clinicians should consider MRI and toxicology testing for cocaine and designer opioids in patients with new onset of anterograde amnesia.
Conclusions: Combined use of cocaine and fentanyl or fentanyl analogues may contribute to the development of a syndrome of anterograde amnesia.

KEYWORDS Cocaine; despropionyl fentanyl; anterograde amnesia

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98. Acute psycosis after repeated use of N-ethyl pentylone (Ephylone) sold as cocaine

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Background: Novel psychoactive substances (NPS) have become popular for recreational use. Among NPS, synthetic cathinones are frequently used for their psychoactive and euphoric properties . N-ethyl pentylone (ephylone) was synthetized for the first time in 1969 but only recently found in drug seizures in the USA and Europe in 2016. It has probably become a cheap substitute for stimulants as methamphetamine and cocaine. To date there are very few published reports involving this synthetic cathinone. Ephylone blood levels were detected in specimens collected for death investigation cases and for drugged driving cases in a recent study. Two other lethal cases were recently published in 2017. We describe a laboratory confirmed case where acute psycosis developed after ephylone repeated sniffing, bought as cocaine.
Case-report: A 29-year-old health worker with past history of depression, during his night shift in hospital became agitated with visual hallucinations, delirium, mydriasis and nausea. At the emergency room (ER) admission tachycardia 100 pulse/min with normal arterial pressure 130/80 mmHg and O_2 saturation 99% on room air were registered. On the electrocardiogram non-specific ST alteration was observed without troponin increase. Laboratory evaluation showed neutrophil leukocytosis (9.53 10○9/l) and mild rhabdomyolysis (CPK 1069 U/l) with positive ecstasy in urinary drug of abuse first level essay. The patient was initially treated with lorazepam 4 mg im and, after 45 min, sedated with midazolam 5 mg iv. Four hours later the patient was again agitated and needed lorazepam 5 mg po, delorazepam 5 mg iv and lastly midazolam 5 mg iv with an improvement of the clinical picture. He was admitted in the psychiatric unit and discharged after 4 d asymptomatic with normal electrocardiogram and routine laboratory exams. He declared he has bought 2 g of the substance sold as cocaine and sniffed that for the 3 d prior ER admission. Mild paranoid symptoms were present the day before the acute psycosis. Laboratory analysis performed by GC-MS at second level on urine sampled at ER admission revealed the presence of ephylone and did not confirm the presence of ecstasy and any other drugs. Ephylone was found also in the urine sampled 4 d after the ER admission.
Case discussion: N-Ethyl Pentylone is a substituted cathinone with psycostimulant effects. Its identification was first reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in January 2016 by Slovenia in a forensic case. As other cathinones, psychiatric and neurotoxic effects are reported after ephylone use but due to its novelty very little is known regarding its toxicological effects on human users, making management and clinical prognosis difficult. Ephylone was quantitatively confirmed in oral fluid specimens collected from dance music festival attendees after ingestion of "Molly", in conjuction with other subtsances of abuse.
Conclusions: Our case report underlines the acute neurological and psychiatric effects after repeated use of ephylone alone, sold as cocaine, and the false-positive urine first level essay for ecstasy.

KEYWORDS New psychoactive substances (NPS); synthetic cathinones; N-ethyl pentylone (ephylone) poisoning

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99. Alprazolam misuse among young people in the United Kingdom

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Background: There is growing concern in the United Kingdom (UK) about the misuse of alprazolam (Xanax) among young people following numerous media reports of hospitalisations and addiction, even though it is not readily available on prescription in the UK. It is believed that its use has been glamorised by celebrities and through social media. A UK Parliament debate noted there is limited research available on UK misuse of alprazolam.
Methods: Data from the UK Survey of Non-Medical Use of Prescription Drugs (NMURx) Program collected from 2015Q4 to 2017Q3 were analysed. This online survey collects data on the prevalence, reasons, routes of administration, and method of drug acquisition for non-medical use (NMU) of prescription drugs. From those who reported NMU of alprazolam and/or diazepam, the nationally-estimated prevalence of lifetime and last 90 d NMU and reasons for NMU were calculated and compared.
Results: The 2017Q3 NMURx sample included 10,019 respondents and was weighted by age, gender, and region to represent 52,927,659 adults in the UK: mean ± SD age 46.7 ± 0.2 years; 13.6% 16–24 years; 16.8% 25–34 years; 67.6% 35+ years. The estimated national prevalence of lifetime NMU of alprazolam was 0.32% (95% CI: 0.19, 0.46), and 1.3% (95% CI: 1.1, 1.5) for diazepam. The most common reason for lifetime NMU for both substances was to treat a medical condition (alprazolam: 0.18%; diazepam: 0.93%). The second most common reason for lifetime NMU was to get high (alprazolam: 0.13%; diazepam: 0.44%). As shown in Table 1, the prevalence of NMU in the last 90 d was significantly different when split by age category for alprazolam ($p < .001$), but not for diazepam ($p = .262$). The prevalence estimates in NMU in the last 90 d in 2016Q3 compared to 2017Q3

Table 1. Recent non-medical use of alprazolam and diazepam by age category.

	Last 90 d non-medical use (95% CI)	*p*-Value
ALPRAZOLAM		
All Ages	0.08 (0.01,0.15)	N/A
16–24 years	0.37 (0.01,0.81)	
25–34 years	0.14 (0.01,0.34)	<.001
35+ years	0.01 (0.01,0.03)	
DIAZEPAM		
All Ages	0.21 (0.12,0.31)	N/A
16–24 years	0.17 (0.01,0.41)	
25–34 years	0.39 (0.07,0.72)	.262
35+ years	0.18 (0.08,0.27)	

were not significantly different for either substance (alprazolam: $p = .416$; diazepam: $p = .190$).

Conclusion: Whilst the national prevalence of NMU of alprazolam is lower than diazepam, prevalence of NMU is significantly higher among younger age categories than older categories; a similar difference was not observed for diazepam. The most common reasons for use were the same between the two substances, but the relative prevalence of the reasons between substances differed. The national prevalence estimate of NMU to treat a medical condition was similar to the estimate of NMU to get high for alprazolam. However, for diazepam, the prevalence of NMU to treat a medical condition was twice the prevalence of NMU to get high. Further research is needed to fully understand the motivations of alprazolam misuse and to monitor whether the popularity of alprazolam will rise.

KEYWORDS Alprazolam; xanax; misuse

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100. Association of ingested dose of diphenhydramine and QRS widening in acute overdose

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Background: Diphenhydramine (DPH) is frequently misused and ingested recreationally for its sedative-hypnotic effects. This widely available and frequently used over-the-counter antihistamine is commonly involved in fatal poisonings, either in isolation or in combination with other xenobiotics. There is little existing literature regarding the dose-dependent toxicity of DPH, especially with regard to DPH-associated cardiotoxicity, manifesting as dysrhythmias and conduction abnormalities.

Objectives: The purpose of this study was to determine the dose-dependent toxicity of diphenhydramine in overdose. Our primary objective was to compare the rate and severity of ECG disturbances (QRS widening, QTc prolongation) with reports of ingested DPH dose. We also wanted to compare other serious clinical effects (seizures, hallucinations, agitation) with ECG disturbances and estimated ingested dose.

Methods: This was a 10-year retrospective observational case series of adult and pediatric diphenhydramine mono-

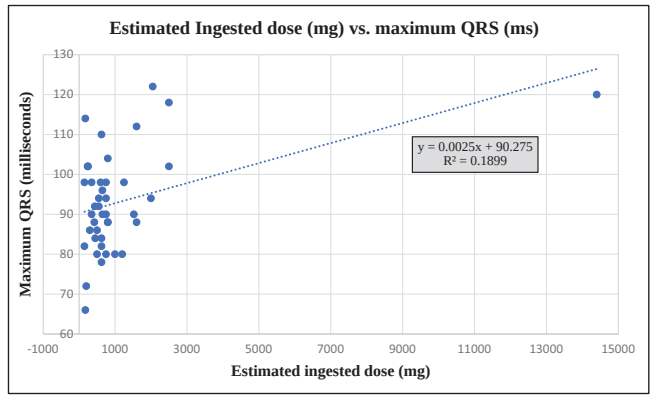

Figure 1. Estimated ingested dose vs maximum QRS

intoxications treated at one academic medical institution. A single poison center database was queried using the search terms and product substance codes "diphenhydramine" and "Benadryl." Exclusion criteria: History of co-ingestants, lack of a recorded ingested dose, and those not evaluated at the aforementioned medical institution. Detailed medical records were then obtained for each case. Data extracted included demographics, dose, clinical effects, including ECG disturbances, and patient outcome.

Results: Forty-two cases of single-substance diphenhydramine exposures including 20 (47%) women and 22 (52%) men whose ages ranged from 23 months to 54 years. Ingested doses were between 175 mg and 14,400 mg (median: 625 mg). The most frequently reported symptoms included tachycardia (64.2%, $n = 27$), dry skin/mucous membranes (33.3%, $n = 14$), confusion (23.8%, $n = 10$), somnolence (21.1%, $n = 9$), flushing (19%, $n = 8$), and agitation (11.9%, $n = 5$). Although symptoms developed over the whole range of reported doses, moderate and severe symptoms (agitation, confusion, hallucinations) did not occur with ingestions less than 175 mg and seizures did not occur with ingestions less than 750 mg. The median ingested dose in cases with a maximum QRS <100 ms ($n = 32$) and >100 ms ($n = 10$) was 625 mg and 1200 mg respectively. The median ingested dose in cases with a maximum QTc <460 ms ($n = 23$) and >460 ms ($n = 19$) was 550 mg and 750 mg respectively. Only one patient, who ingested 14 g, developed a QTc >500 ms. The median ingested dose in cases with a maximum heart rate <120 bpm ($n = 27$) and >120 bpm ($n = 25$) was 625 mg and 750 mg respectively. There was a linear relationship between ingested dose and QRS widening (Figure 1). Patients who ingested greater than 1500 mg had increased cardiotoxicity versus those that ingested <1500 mg: rate of QRS >100 ms =63% ($n = 5/8$) versus 15% ($n = 5/34$); QRS >120 ms =40% (2/5) versus 0%. No patient that ingested less than 2000 mg developed QRS >120 ms. Sodium bicarbonate was administered in 5 cases, either as a bolus dose or infusion. There was no clear temporal relationship between sodium bicarbonate administration and QRS narrowing. All patients made a full recovery and there were no fatalities.

Discussion: These data demonstrate a dose-dependent relationship between QRS widening and frequency of severe symptoms in DPH overdose.

Conclusion: This data may aid in decision making and prognostication regarding severity of symptoms, including conduction disturbances, based on patients reported ingested DPH dose.

KEYWORDS Diphenhydramine; toxicity; dose-response

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101. Opioid toxicity from a potent novel fentanyl analog, Beta-hydroxyfentanyl

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Background: Clandestinely produced synthetic fentanyl analogs continue to emerge and re-emerge as drugs of abuse. sz-hydroxyfentanyl is a designer synthetic fentanyl analogue that was scheduled by the DEA in the 1980s. To our knowledge, there are no prior incidents of sz-hydroxyfentanyl toxicity with confirmatory laboratory analysis reported in the literature. We report a case of unintended sz-hydroxyfentanyl toxicity in a patient self-treating her migraine.
Case report: A 22-year-old opioid-naïve woman was told by a co-worker to take "fentanyl" to treat her migraine headache. The co-worker provided her with a white powder and she subsequently ingested a small quantity by touching the tip of her tongue to the powder. Within minutes the patient became unresponsive and apneic. Paramedics were called and administered 2 mg intramuscular naloxone on their arrival. The patient awoke and had complete resolution of her apnea. She remained asymptomatic and was later discharged from the Emergency Department. The patient's serum was sent for confirmatory analysis which detected the presence of sz-hydroxyfentanyl as well as alprazolam. A sample of the "white powder" was also sent for laboratory analysis and was confirmed to be sz-hydroxyfentanyl.
Case discussion: Fentanyl derivatives continue to be introduced into the illicit drug market and are increasingly being abused by the public. The potency of these designer fentanyl analogs make them extremely dangerous to those who abuse them, as demonstrated by our patient developing apnea after a small exposure. This is especially true in individuals who are naïve to the effects of opioids.
Conclusion: This case of sz-hydroxyfentanyl toxicity highlights this drug's potency as well as the utility of non-targeting testing in the detection of emerging synthetic fentanyl analogs.

KEYWORDS Fentanyl analog; opioid; toxicity

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102. Gabapentinoid abuse among EUROPAD subjects

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Background: Prescribing of gabapentinoid drugs (gabapentin and pregabalin) has increased over the past decade. These drugs are commonly used to treat seizure disorders, anxiety disorders, and neuropathic pain. However, these drugs also carry a potential for misuse, and reports of such have increased as well. We describe gabapentinoid abuse among subjects seeking opioid treatment in the European Opiate Addiction Treatment Association (EUROPAD) Program.
Methods: EUROPAD is a multi-center observational study comprised of 11 participating European opioid treatment programs in 6 countries (France, United Kingdom, Italy, Germany, Spain, and Norway). EUROPAD surveys the abuse of substances among patients entering drug dependence treatment programs. Data from fourth quarter 2014 to first quarter 2017 were analyzed. Descriptive statistics on demographic and co-endorsement variables for respondents endorsing abuse of gabapentinoids and for respondents who did not are presented.
Results: From fourth quarter 2014 to first quarter 2017 inclusive, EUROPAD enrolled 1865 respondents. One hundred and twenty-five (6.7%) endorsed gabapentinoid abuse within the past 90 d. Respondents endorsing gabapentinoids were more likely to be female (36.0% versus 24.7%, $p = .005$), endorse heroin as their primary drug of abuse (70.4% versus 46.3%, $p < .001$), and endorse abuse of a greater number of Active Pharmaceutical Ingredients (5.50 versus 2.06, $p < .001$) than respondents who did not endorse gabapentinoids. Of those who endorsed gabapentinoids, 26.4% also endorsed tramadol, compared to only 6.15% of other respondents.
Conclusions: Among EUROPAD subjects, respondents who endorse gabapentinoid abuse are more likely to be female, use heroin as their primary substance of abuse, and endorse polysubstance abuse than those who do not abuse gabapentenoids. Tramadol abuse is more common among respondents who endorse gabapentenoid abuse than those who do not.

KEYWORDS Gabapentin; pregabalin; substance abuse

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103. Hemodynamic effects associated with synthetic cannabinoid use

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Background: The use of synthetic cannabinoid receptor agonists (SC) is increasing worldwide. These products are marketed in attractive packaging and are readily available from the Internet, head shops and sometimes even in convenient stores. SCs are typically not detected on commercially available cannabinoid immunoassays. The endocannabinoid system, in which the SCs are active, has a variety of effects on the cardiovascular system and exhibits varying effects on sympathetic and parasympathetic tone. Clinical experience and published cases of patients purportedly SC intoxicated have reported both parasympathetic (bradycardia and hypotension) as well as sympathetic effects (tachycardia and hypertension). We strove to determine if a consistent hemodynamic effect could be attributed to a specific SC intoxication.
Methods: The study was a retrospective study of 19 patients from an ongoing clinical data/tissue repository of patients reported to be SC intoxicated. The repository collected data from March 2017 to March 2018 and is ongoing. Each clinical chart is abstracted into REDCap database and serum analysis for known SC is performed using High-Performance Chromatography/Tandem Mass Spectrometry (LC-MS/MS). Of the 19 patients entered into the repository, only 11 individuals had confirmed SCs detected in their blood. These patients were further analyzed with descriptive statistics to develop a hypothesis about the cardiovascular effects of specific SCs.

Results: The mean age of the population analyzed was 33 years (range 22–47 year) with the majority being African–American (72%) male (90%) population. All of these individuals had at least 2 serial vital signs entered into their record. The most commonly detected SC in the serum was ADB-FUBINACA (53.8%) twice in combination with another SC, followed by FUBAMB (23%), AB-FUBINACA (15.3%) and 5F-ADB (7.6%). Mean HR was 76/min (range 54–180) and mean mean-arterial pressure (M-MAP) was 85 mm Hg. Bradycardia at any time was observed in four individuals, half of whom tested positive for ADB-FUBINACA. Interestingly, both the lowest M-MAP (66 mm Hg) and the highest M-MAP (107 mm Hg) were observed in ADB-FUBINACA positive patients. Hypotension at any time was observed in 21% individuals; 66.7% of which tested positive for ADB-FUBINACA.
Conclusions: To our knowledge, this is the first study to report hemodynamic vital sign derangements among SC users. In this small early sample, the type of SC abused did not consistently predict a sympathetic or parasympathetic effect on the cardiovascular system. However, pronounced cardiovascular effects were often observed in ADB-FUBINACA group and therefore a testable hypothesis is emerging. Enrollment in the clinical repository and data analysis is ongoing.

KEYWORDS K2; synthetic cannabinoid; spice

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104. Graft failure rates of opioid overdose donors compared to other drug overdose donors

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Introduction: Each year the number of individuals awaiting organ transplantation outnumbers the sum of available organs and donors. At the same time opioids and other drug-related deaths are on the rise. Victims of opioid overdose may be a potential reservoir of organ procurement in the era of the growing transplantation need. This study aims to evaluate the graft failure rates of organs procured from patients who died specifically of opioid overdose and compare them to patients who died of other illicit drugs.
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 organization that is a one of 58 organizations that make up the US organ procurement system. This particular regional registry provides services to Illinois and northwest Indiana. Registry data of organ transplants from September 2015 to March 2017 was queried for organs procured from presumed opioid related deaths and all other illicit drug-related deaths. Graft failure rates were followed on a short-term (<15 months) basis. Of note donors who co-ingested benzodiazepines in addition to opioids were included in the opioid-related death group given that benzodiazepines rarely directly cause death alone. Deaths involving multiple other drugs were not included in the opioid group given the difficulty discerning the exact cause of death. Donors lost to follow up were also excluded.
Results: A total of 81 donors who died of drug-related causes were identified. Of these donors, 30 died primarily of presumed opioid-related causes compared to 51 who died of other illicit drugs. Categories of other illicit drugs included polypharmacy, alcohol including toxic alcohols, cocaine, psychedelic mushrooms, and unknown. Donors who died of opioid overdose were on average 32.6 years, and had a total of 101 organs procured (12 hearts, 11 lungs, 48 kidneys, 5 pancreases, 25 livers) or an average of 3.4 organs/donor procured. Of these 1/101 (1%) resulted in graft failure on short-term follow up. Donors who died of other illicit drug overdoses were on average 34.3 years, and had a total of 163 organs procured (25 hearts, 11 lungs, 84 kidneys, 7 pancreases, 36 livers) or an average of 3.2 organs/donor procured. Of these 2/163 (1.2%) resulted in graft failure on short-term follow up.
Conclusion: Organs procured from donors who died of opioid overdose when compared to donors who died of other drug-related deaths appeared to have similar rates of graft failure on short-term follow up. Opioid overdose does not appear to be a contraindication for organ procurement.

KEYWORDS Opioid; organ transplant; graft failure

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105. I get high with a little help from my … venlafaxine?

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Background/Objectives: Venlafaxine is a serotonin and norepinephrine reuptake inhibitor used primarily for major depressive disorder and generalized anxiety. While there are several published cases of venlafaxine abuse to produce an amphetamine-like high, information about venlafaxine abuse is sparse.
Methods: This was a retrospective review of venlafaxine abuse exposures reported to the National Poison Data System (NPDS) from January 1, 2000 to December 31, 2016. Inclusion criteria were: age 12 years and older, reason for ingestion coded as intentional – abuse, and either (1) single substance exposure to venlafaxine or (2) venlafaxine coded as the first substance. The primary outcome was the incidence of venlafaxine abuse reported to the NPDS. Secondary outcomes were to characterize the demographic information, geographic distribution, clinical effects, and outcomes. All cases were included in analysis of incidence, demographic information, route, and geographic distribution. Characterization of clinical effects, final management sites, treatment, and coded medical outcomes was limited single-substance cases followed to a known medical outcome. Summary statistics were performed with Microsoft Excel (Microsoft, Renton, WA).
Results: A total of 85,621 venlafaxine cases were reported for patients age 12 and older. Abuse exposures accounted for 752 cases, for an incidence of 87.8 per 10,000 cases (range, 59.3 to 117.64 per 10,000 cases) over the 17-year period. The rate of abuse exposures reported to NPDS decreased from 107 per 10,000 cases in 2000 to 59.3 per 10,000 cases in 2016. Using US Census data, rates were highest in the West, followed by the Northeast, then South, and then Midwest. States with highest rates were New York, California, and Colorado. Patients abusing venlafaxine were 50% male with a mean age of 27.5 years. Primary route of use was ingestion (90.8%) with 4.7% using venlafaxine via inhalation/intranasal routes; 3.7% were both ingestion and inhalation/nasal. Of 227 single-substance venlafaxine abuse cases, most were treated/released from the emergency department (54%) while 20% were admitted to the hospital for medical management, 9% were admitted to a psychiatric facility and the remaining 17% were managed at home. Known medical outcomes for single-substance venlafaxine cases were: no effect (24%), minor effect (39%), moderate effect (33%), and major

effect (4%); no deaths occurred. Only 46% of venlafaxine only cases required treatment; in those cases, therapies included IV fluids (47%), single dose activated charcoal (36%) and benzodiazepines (17%). At least one related effect occurred in 73% of cases. The most frequent effects in these patients were tachycardia (46%), drowsiness (28%) and agitation (16%). Of those with known durations of effect, most lasted 2 to 24 h (66%).
Conclusion: The incidence of venlafaxine abuse reported to poison centers has decreased from 2000 to 2016. Venlafaxine abuse occurs most frequently in young adults. Medical outcomes were primarily minor and moderate effects with less than 50% receiving specific therapies. Clinicians should be aware of the abuse potential for venlafaxine when making prescribing decisions.

KEYWORDS Venlafaxine; abuse; serotonin norepinephrine reuptake inhibitor (SNRI)
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106. Comparison of second substances used in patients abusing or misusing LSD and psilocybin containing mushrooms

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Background/Objectives: Lysergic acid diethylamide (LSD) and psilocybin containing mushrooms (PCM) are hallucinogenic substances commonly used for abuse purposes. LSD and PCM produce different euphoric effects and the types of users and social activities of users is likely different. The objective of this study was to compare additional substances used by patients who are abusing and misusing LSD plus one agent (LSD +1) or PCM plus one agent (PCM +1). Secondary objectives include comparing the rates of moderate and severe effects and highest level of medical care with LSD/PCM/LSD +1/PCM +1.
Methods: This was a retrospective study of LSD and PCM exposures reported to the NPDS from January 1, 2000 to December 31, 2016. Inclusion criteria for the primary outcome were patients >9 years of age, use of LSD or PCM coded as intentional – abuse or intentional – misuse and were either single substance or 2 substance (LSD +1, PCM +1) exposures. For the secondary outcome, patients followed to a known medical outcome were included and findings were compared to LSD only and PCM only. Drugs that are not known to be abused were combined as "other drugs," any opioid-containing product was coded as an opioid, and antipsychotics were coded as "other sedative." Data were analyzed by chi-square or Fisher's exact test for categorical variables
Results: For the primary outcome, there were 1335 PCM +1 patients and 1392 LSD +1 patients. An additional 57 patients were using both. Mean age was 20.2 years and 78.9% male. The most frequent additional substances used for both groups were marijuana, ethanol, and hallucinogenic amphetamines. Patients using PCM were significantly more likely to be also using marijuana (38.7% PCM versus 24.7% LSD, $p < .0001$) or ethanol (22.8% PCM versus 14.1% LSD, $p < .0001$), while patients using LSD were more likely to be abusing hallucinogenic amphetamines (7.3% LSD versus 18.0% PCM, $p < .0001$) or any type of stimulant (8.0% LSD versus 4.2% PCM, $p < .0001$). For 4784 PCM, 2909 LSD, 1116 PCM +1 and 1166 LSD +1 patients followed to a known outcome, the rate of admission to critical care unit was lowest with PCM alone (7.4%) and was significantly higher for LSD alone (18.0%), LSD +1 (25.6%), and PCM +1 (13.8%); $p < .0001$ for each. The rate of moderate effect was similar for each group at 65.7% for PCM, 64.8% for LSD, 65.7% for LSD +1, and 65.5% for PCM +1; $p > .05$ for each. Rates of major effect were 2.2% for PCM, 6.5% for LSD, 9% for LSD +1 and 4% for PSM +1. Compared with PCM, rates of major effect were significantly higher for each other group; $p < .001$ for each.
Conclusion: Abuse or misuse of LSD was more commonly associated with concurrent use of stimulant agents whereas use of PCM was more commonly associated with depressants. Compared with psilocybin alone, addition of second substances was associated with more severe medical outcomes and need for higher levels of care. The two substances are pharmacologically different, and use may be associated with different social groups. This may be reflected in the additional substances used.

KEYWORDS Mushroom; LSD; stimulant
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107. Loperamide adverse events reported to the FDA Medwatch system from 2008 to 2017

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Background: Serious cardiac conduction disturbances and deaths are described with loperamide abuse, though the incidence remains unknown. Medwatch, the Food and Drug Administration's (FDA) safety and adverse event reporting program, allows healthcare professionals, consumers, patients, and industry to report adverse events. Recently, the FDA issued safety alerts regarding loperamide toxicity based on reports of severe adverse events. We conducted a retrospective review of loperamide related adverse events reported to Medwatch from 2008 to 2017.
Methods: Adverse events reported to Medwatch containing the term "loperamide" from January 1, 2008 to October 31, 2017 were obtained via a Freedom of Information Act request. All cases containing the term bradycardia, decreased heart rate, torsades de pointes, arrhythmia, ventricular tachycardia, QT prolongation, syncope, loss of consciousness, cardiac arrest, ventricular fibrillation, QRS prolongation, pulse absent, pulseless electrical activity, or death were extracted. Cases involving loperamide with or without a proton pump inhibitor or cimetidine as the suspected agent(s) were included. Cases without a reported gender, age, that occurred outside the United States, that reported anaphylaxis, or that listed a medication other than loperamide, cimetidine, or a proton pump inhibitor as a suspect agent were excluded. All cases were reviewed twice for inclusion by a member of the team (WE, MH, JM, AY, SS, and MN). If two reviewers did not agree, a three reviewer panel (MH, WE, JM) reviewed the case and determined consensus opinion. Demographics, cardiac events, and reported dose were collected.
Results: A total of 9499 adverse events involving loperamide were identified. Two hundred and sixty-nine cases met both inclusion and exclusion criteria. The population was 68% male, had a median age of 29 years, included 193 cases of single drug exposure, and 76 cases

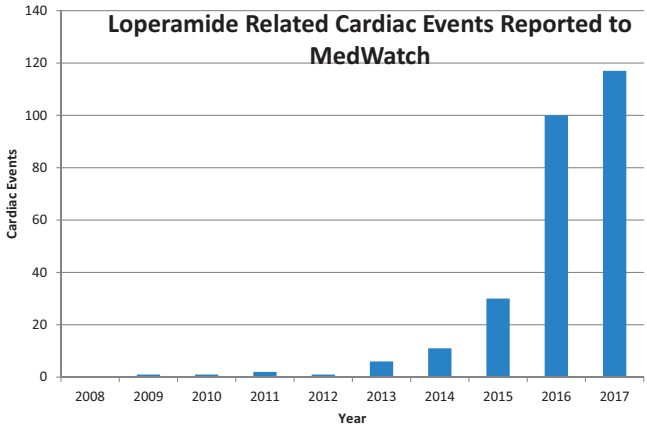

Figure 1.

of multi-drug exposure. There was an increase in cases from 2014 to 2017, with 11 in 2014, 30 in 2015, 100 in 2016, and 117 in 2017 (Figure 1). In cases where dose was reported, the median dose was 288 mg ($n = 133$). Concomitant cimetidine use was reported in 9.7% of cases. There were 62 deaths reported, with 97% reported after 2012. Only 7.4% of cases were reported by a healthcare professional.
Discussion: Loperamide related cardiac events are increasing based on cases reported to MedWatch. We observed a 10-fold increase in cases from 2014 to 2017. Additionally, nearly all deaths were reported after 2012. A major limitation of this study is the possibility of duplicate cases that may overestimate the true number of adverse events. It cannot be determined if the increase is related to increasing loperamide abuse or increasing awareness of loperamide toxicity.
Conclusion: Adverse events reported to MedWatch secondary to loperamide are increasing. Reports of toxicity in the literature, lay press, and an FDA advisory in June 2016 have increased awareness of the risks of loperamide abuse. Although reports to Medwatch have increased dramatically, healthcare professionals represent a minority of these reports.

KEYWORDS Loperamide; misuse; cardiac toxicity

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108. "Chasing the Dragon" with Fentanyl Patch Gel

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Background: Fentanyl patch abuse using unusual methods has been described. "Chasing the dragon" is a slang phrase that refers to inhaling the vapor from heated drugs such as morphine, heroin, oxycodone or opium. The substance is heated and the vapor is "chased" with a tube through which the user inhales. We present a novel method of fentanyl patch abuse that had fatal consequences in a man who "chased the dragon" using gel from a fentanyl patch. "Chasing the dragon" with a fentanyl patch gel has not previously been described in the medical literature.
Case report: A 26-year-old male with history of substance abuse had not emerged from his bathroom. His grandmother was beating on the door and became panicked since he was not responding. She unlocked the door and found him dead on the ground. He had a lighter in one hand, a piece of foil in the other hand and blood pooled around his face. On the bathroom floor was aluminum from the back of a fentanyl patch with burnt residue on it. There was also a pen tube and a pack of Actavis® Fentanyl Transdermal System 100 mcg/h patches. Text messages on his cell phone revealed that he illicitly bought fentanyl patches from his friend for $300. An autopsy was performed and postmortem toxicology testing of femoral blood revealed a fentanyl concentration of 9.4 ng/ml. Cause of death was acute fentanyl toxicity.
Discussion: The evidence in this case shows that our patient "chased the dragon" with gel from a fentanyl 100 mcg/h patch. The Actavis® Fentanyl Transdermal System 100 mcg/h patch contains 10 mg of fentanyl gel. "Chasing the dragon" with fentanyl patch gel first involves intentional compromise of the transdermal delivery system resulting in uncontrolled drug delivery. This is an extremely dangerous practice because the entire patch contains 1000 times the dose listed on the package and that dose is meant to diffuse across the skin per hour. Therefore, the abuser is inhaling an unknown but massive dose at once. Studies have demonstrated that the pharmacokinetic profile of single doses of inhaled fentanyl is comparable to the intravenous route. Three users in the Erowid experience vaults described how to successfully extract gel from a fentanyl patch and inhale its vapors. The users stress the importance of using a tiny amount of fentanyl gel; the amount that would fit on the head of a pen or in a printed "o." The medical literature does not report any cases of "chasing the dragon" with fentanyl patches.
Conclusion: We report the first case of "chasing the dragon" with fentanyl patch gel. This is a novel method of fentanyl patch abuse that had fatal consequences.

KEYWORDS Fentanyl; patch; abuse

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109. Emergency department recidivism in alcohol withdrawal patients after discharge with or without chlordiazepoxide

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Background: Oral chlordiazepoxide is a long-acting benzodiazepine commonly utilized for alcohol withdrawal treatment. However, no studies have described the outcomes in prescribing monotherapy chlordiazepoxide in patients discharged from the emergency department (ED). The aim of this study was to evaluate 30-day ED recidivism in alcohol withdrawal patients discharged with an outpatient chlordiazepoxide prescription versus those discharged without.
Methods: ED admissions for alcohol withdrawal from 2014 to 2017 were retrospectively identified from electronic medical records at an academic tertiary medical center. Patients $\geq$18 years age and discharged from the ED with an ICD-9 or ICD-10 for alcohol withdrawal were included. Collected clinical data included: patient demographics, chief complaint for ED visit, history of alcohol consumption, severity of alcohol withdrawal, administration of benzodiazepines in the ED setting, ED length of stay, ED recidivism for any chief complaint, and chlordiazepoxide prescription and fill information. Of 216 patient encounters, 112 were included in the treatment group and 68 included in the control group. Thirty-six encounters were excluded due to

Table 1. Baseline demographics.

	Discharged with Outpatient Prescriptions ($n = 112$)	Discharged without Outpatient Prescriptions ($n = 68$)	p-Value
Age (mean years ± SD)	43.3 ± 11.4	45.4 ± 10.9	.50
Male gender, *n* (%)	90 (80.4)	56 (82.4)	.96
Ethnicity			
African American, *n* (%)	20 (17.9)	23 (33.8)	.74
Caucasian, *n* (%)	87 (77.7)	43 (63.2)	.76
Other, *n* (%)	5 (4.5)	2 (2.9)	.92
BAC upon ED admit (mean concentration ± SD)	0.18 ± 0.16	0.15 ± 0.15	.51

Table 2. Thirty-day recidivism to the ED.

	Discharged with Outpatient Prescriptions ($n = 112$)	Discharged without Outpatient Prescriptions ($n = 68$)	p-Value
30-day recidivism to the ED with EtOH complaint, *n* (%)	23 (20.5)	17 (25.0)	.92
30-day recidivism to the ED with non-EtOH complaint, *n* (%)	18 (20.2)	12 (23.5)	.94
Admission to floor following first ED recidivism for EtOH complaint, *n* (%)	6 (26.1)	4 (23.5)	.95

BAC: Blood alcohol content; EtOH: Alcohol.

incorrect ICD-9 or ICD-10 codes, eloped patients, inpatient admission, and repeat encounters.

Results: The majority of patients presenting to the ED for alcohol withdrawal in this study were middle-aged, male Caucasians. When comparing baseline demographics of the 112 patients discharged from the ED with chlordiazepoxide prescriptions to those without, there were no statistically significant differences among the groups (Table 1). Ninety-five (85%) of chlordiazepoxide patients presented to the ED with a chief complaint of alcohol withdrawal, compared to 54 (79%) in the control group. Thirty day recidivism to the ED for both alcohol ($p = .92$) and non-alcohol complaints ($p = .94$) did not differ when comparing treatment group with the control group (Table 2). Median time to first 30-d ED recidivism for an alcohol withdrawal complaint was 7 d in the chlordiazepoxide and 10 d in the control group ($p = .83$). Median time to first 30-d ED recidivism for non-alcohol withdrawal complaint was 9 d in the chlordiazepoxide group versus 5.5 d in the control group ($p = .51$). Admission to the floor following first ED recidivism for alcohol complaint was similar between both groups (Table 2). Of the 112 patients discharged with chlordiazepoxide prescriptions, 40 (36%) patients filled the prescription. Sixty-eight percent of those patients filled chlordiazepoxide the same day, with a mean fill date of 2 d (SD 4.7) following ED discharge. In patients who filled their chlordiazepoxide versus those who did not, there was no difference in baseline characteristics. Patients who received chlordiazepoxide had a longer median time to first 30 d ED revisit for alcohol withdrawal (12 d versus 6.5 d) and non-alcohol withdrawal complaints (12 d versus 6 d), but this was not statistically significant.

Conclusion: When comparing patients discharged with a prescription for chlordiazepoxide to those who were not, 30-day recidivism for both alcohol complaints and non-alcohol complaints did not differ. Poor adherence with filling the chlordiazepoxide prescription may have caused similar recidivism between groups. If patients filled the chlordiazepoxide prescription, the median time to return visit was twice as long.

KEYWORDS Chlordiazepoxide; alcohol withdrawal; emergency medicine

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110. Massive 72-h binge of "whip-its" resulting in functional B12 deficiency with myeloneuropathy and pancytopenia

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Background: Nitrous oxide ("Laughing Gas") is used as both an anesthetic and a recreational drug of abuse. Historically, nitrous oxide-induced functional B12 deficiency has occurred after long-term sedation of tetanus patients or after years of chronic recreational abuse. This is the first case of acute, short-term nitrous oxide abuse resulting in severe functional vitamin B12 deficiency with myeloneuropathy and pancytopenia.

Case report: Seventeen-year-old female presented to a tertiary pediatric hospital with 2 d of painful, pruritic rash on her trunk and legs; bilateral leg weakness with unsteady gait; fatigue; mouth pain; anorexia; and dry cough after abusing one nitrous oxide canister ("whip-its") every hour for 72 consecutive hours. This binge was her second-ever exposure to nitrous oxide. Her first-time was 1 month prior, after which she developed oral ulcers. She denied sensory deficits, sick contacts, or recent travel. Physical exam revealed temperature 36.8 °C, pulse 110, respirations 20, blood pressure 84/62, and 99% saturation on room air. She appeared mildly dehydrated, with tender oral ulcerations. Lung sounds were coarse without crackles. Skin showed blanching macular truncal rash with diffuse bilateral petechiae and excoriations on her legs. She had dysmetria with heel-to-shin and finger-to-nose. Lower extremities had 4/5 strength and 2+ reflexes. Gait was unsteady. Romberg was not assessed secondary to weakness. Cranial nerves and sensation were intact. She had no lymphadenopathy, organomegaly, nor meningismus. Labs showed WBC 3.53 × 103/mcL, Hgb 9.8 g/dl, reticulocyte count 0.49%, Plt 88,000, 2.6% bands, 5.3% metamyelocytes, 1.8% myelocytes, ANC 0.83 × 103/mcL; CRP 4.7 mg/dl; ESR 95 mm/h. Cerebrospinal fluid glucose and protein were normal, and negative for HSV1, HSV2, tuberculosis, enterovirus, varicella-zoster, cytomegalovirus, Epstein-Barr, parvovirus, Rickettsial, syphilis, and HIV. Blood, urine, and CSF cultures were negative. Oral ulcer PCR was positive for HSV1. Methylmalonic acid was 2163 nmol/l (normal 87–318 nmol/l) and homocysteine was 85.8 mmol/l (normal <10.4 mmol/l), both of which were consistent with nitrous oxide-induced functional B12 deficiency. Treatment included 4 d of intramuscular B12 (cyanocobalamin) and empiric acyclovir. By day 6, strength improved to 5/5; gait and oral ulcers improved clinically; and pancytopenia, rash, and fatigue resolved. She was discharged on oral B12 with outpatient follow-up.

Case discussion: Cases of chronic nitrous oxide abuse have led to truncal and extremity rashes, neurological symptoms, pancytopenia, and myeloneuropathy from functional B12 deficiency secondary to irreversible oxidation of cobalamin, typically after years of abuse. This case is notable for severe myeloneuropathy and myelosuppression with laboratory confirmation of functional B12 deficiency after massive acute exposure from only her second lifetime usage of nitrous oxide. Oral ulcers were consistent with HSV re-activation secondary to myelosuppression, with likely exacerbation from nitrous oxide-induced tissue hypothermia.

Conclusion: This case illustrates that nitrous oxide-induced functional B12 deficiency may occur after massive short-term exposure and may be treated successfully with intramuscular B12. In case reports of long-term chronic exposure, absence of sensory deficits, Romberg sign, and Babinski sign – similarly noted in this patient – may be associated with favorable reversal of toxicity.

KEYWORDS Nitrous oxide; vitamin B12; myeloneuropathy
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111. Perinephric stranding and hydronephrosis associated with brodifacoum mediated coagulopathy in the setting of inhalational synthetic cannabinoid use

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Background: In the spring of 2018 a large regional poison center (RPC) became aware of many patients who had become exposed to brodifacoum through smoking synthetic cannabinoids (SCs). Previous animal and human reports have recorded hydronephrosis in brodifacoum poisoning. Human and animal pathology reports have also shown brodifacoum to concentrate in the kidney, liver and blood. We report a series of patients who presented with an acquired coagulopathy in the setting of synthetic cannabinoid use who also had perinephric stranding or hydronephrosis on computed tomography (CT) scans of the abdomen without evidence of mechanical ureteral obstruction or infection.
Methods: We performed a retrospective review of RPC cases from March 11 to April 18, 2018 of cases coded as exposures to THC homologs. Our case definition is suspected SC use, international normalized ratio (INR) >3, no alternative explanation of coagulopathy, no documented infection, no documented mechanical obstruction, and a documented CT abdomen. Trained investigators abstracted the following data: presenting serum creatinine (Cr), the presence of hydronephrosis on CT, the presence of perinephric stranding on CT, and the presence of hematuria.
Results: A total of 168 cases were searched with 26 cases meeting inclusion criteria. Of the patients documented as having a CT abdomen, 5 had no documented results while 12 had no noted hydronephrosis or perinephric standing. Five had hydronephrosis only, two had perinephric stranding only and two had both findings. One additional patient, while not counted as having hydronephrosis or perinephric stranding, presented with a CT scan that was documented as "negative w/potential recent passed kidney stone". All of the patients with perinephric stranding or hydronephrosis presented with hematuria. Five of the nine patients with hydronephrosis or perinephric stranding had an average Cr of 1.1 (range 0.57–2.1) and 4/9 patients had a Cr documented as normal. Of the patients with hydronephrosis or perinephric stranding, an expanded serum anticoagulant screen was confirmed for brodifacoum and difenacoum in three patients, and brodifacoum and bromadiolone in one patient. One patient had an expanded SC screen test positive for 5F-AMB-PINACA metabolite. The patients with findings of hydronephrosis or perinephric stranding were evaluated at seven distinct medical facilities in two distinct metropolitan areas 130 miles apart.
Conclusions: We have identified 9 cases of hydronephrosis or perinephric stranding on CT in patients exposed to brodifacoum through contaminated SCs. Hydronephrosis or perinephric stranding is not an uncommon finding in this series of patients. The clinical significance of these findings is unknown.

KEYWORDS Hydronephrosis; brodifacoum; synthetic cannabinoids
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112. Risk factors for discharge against medical advice in patients with opioid use disorder

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Background: Substance use is a known risk factor for leaving the hospital against medical advice (AMA), however little is known about patients with opioid use disorder (OUD) who are discharged AMA compared to patients with conventional discharge (CD). We sought to characterize and identify medication-specific and other risk factors for AMA discharge in patients hospitalized with OUD.
Methods: Using ICD-9 codes in a large urban health system, we identified electronic health records of a cohort of patients with OUD. Patients were categorized by discharge type: AMA or CD, and all medications administered were reviewed. Relevant medication histories were categorized by dose and type: opioid pain reliever, non-opioid pain reliever, and administration of medication-assisted treatment (MAT): methadone and buprenorphine. This study was reviewed and approved by the Institutional Review Board.
Results: One thousand one hundred and eighty-eight patients with OUD were identified over a 12-month period (January 1, 2016–December 31, 2016). Patients were 59% male; average age of 42 +/−12 years. Nine patients expired during their admission and were excluded from further analysis. Seventy-seven (6%) patients were discharged AMA, whereas the overall AMA rate for the health system is 0.4%. Median length of stay for the AMA group was 3.6 d versus 5.5 d for the CD group ($p<.0001$). OUD patients discharged AMA compared to CD patients did not differ by age (41 versus 42 years, $p=.18$) or gender (59 versus 61% male, $p=72$). AMA patients were less likely to receive an opioid overall (74% versus 84%, $p=.03$) and received fewer doses of opioid pain reliever per day (2.3 versus 2.9 doses $p=.04$). They were more likely to be on a detox service (22% versus 9%, $p=.0006$). Methadone administration was not different between AMA and CD 52% versus 47% $p=.41$ and buprenorphine use was low overall (0% versus 2.1%).
Discussion: Patients admitted to the hospital with OUD are at increased risk of AMA discharge. Lower doses of opioids per day and not receiving treatment with any opioids are factors associated with AMA discharge. Methadone administration was similar in both groups and there was minimal use of buprenorphine. Limitations include small sample size and retrospective, single center methodology.
Conclusion: Patients with opioid use disorder admitted to the hospital are at risk for discharge AMA. Further evaluation should assess the impact of treatment of opioid withdrawal symptoms with opioids, dose and duration of MAT and other symptomatic treatments to mitigate risk of AMA discharge.

KEYWORDS Opioid; opioid use disorder; discharge against medical advice
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113. Acquired coagulopathy secondary to brodifacoum-laced synthetic cannabinoids

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Background: The tasteless, odorless superwarfarin brodifacoum is a 4-hydroxycoumarin pesticide, inhibiting Vitamin K epoxide reductase-dependent coagulation factor production. Exposure occurs via ingestion, inhalation, or skin contact. Toxicity induces hemorrhages as Vitamin K-dependent coagulation factors deplete. Treatment involves Vitamin K-dependent coagulation factor replacement. Brodifacoum's prolonged half-life necessitates several months of monitoring. We describe a patient presenting with retroperitoneal hemorrhages and hematuria; work-up revealed a Vitamin K factor-dependent coagulopathy secondary to brodifacoum-laced synthetic cannabinoids.

Case report: A 25-year-old southeastern Missouri male presented to our emergency room with gross hematuria, retroperitoneal hematomas, abdominal cramping, nosebleeds, easy bruising, nausea/vomiting, and weakness. There was no trauma or bleeding disorder history. He ate a balanced diet. He denied medication or drug use, including marijuana and synthetic cannabinoid receptor agonist (SCRA) products. Vital signs were stable. Basic testing showed acute kidney injury, hemoglobin of 6.5 g/dl, and normal platelets. Coagulation studies revealed a prothrombin time/internationalized normalized ratio (PT/INR) $>$ 10 and elevated partial thromboplastin time (PTT). Liver testing was normal and disseminated intravascular coagulation screening negative. Toxicology screens were negative, including salicylates. Human immunodeficiency virus/hepatitis testing was negative. Medical toxicology was consulted and recommended high-dose Vitamin K and sending an anticoagulant panel for brodifacoum and related compound detection. Hematology was consulted. PT/INR and PTT mixing studies corrected fully. Lupus anticoagulant screening was negative. Coagulation factor testing was performed (Table). This matched Vitamin K-dependent factor deficiency. With high-dose intravenous phytonadione, the coagulopathy corrected; the INR downtrended to 1.3 and PTT to 38.2. Neither normalized fully. Lipophilic vitamin levels were normal, ruling out malabsorption. Qualitative anticoagulant testing detected brodifacoum. On further questioning, the patient admitted to smoking SCRAs 3 weeks prior. Upon regional poison control center consultation, we learned of several recent Midwest cases of SCRA-related brodifacoum poisoning. With treatment, the patient's bleeding resolved and labs normalized. He agreed to avoid SCRAs and take high doses of oral Vitamin K with outpatient bloodwork.

Case discussion: Our patient demonstrated brodifacoum toxicity, with life-threatening hemorrhages 3 weeks post-exposure. Specific coagulation factor deficiencies consistent with Vitamin K inhibition were found. His anticoagulant poisoning panel detected brodifacoum, confirming Vitamin K antagonist toxicity. Untargeted liquid chromatography quadrupole time-of-flight mass spectrometry toxicology analysis revealed SCRA AB-FUBINACA metabolite 3 (N-[[1-[(4-fluorophenyl)methyl]-1H-indazol-3-yl]carbonyl]-L-valine) with further confirmations to follow. Several brodifacoum coagulopathy cases have arisen in the Midwest, predominantly in Illinois near Chicago, with suspected SCRA batches laced with brodifacoum. It is unknown if brodifacoum lacing was intentional or accidental. Any patient with SCRA use and unexplained hemorrhages with coagulopathy may have superwarfarin toxicity. Rapid Vitamin K/coagulation factor administration reverses the coagulopathy. Given brodifacoum's half-life, long-term oral Vitamin K and coagulation monitoring are needed. Therapy continues until coagulation profile normalization.

Conclusions: Brodifacoum toxicity causes hemorrhages due to Vitamin K-dependent coagulation factor depletion. Treatment entails Vitamin K-dependent coagulation factor replacement. Providers should maintain high indices of suspicion for brodifacoum toxicity in patients with unusual bleeding and coagulopathy without a clear etiology.

Supplemental Table

Table. Coagulation factor level testing, levels highlighted in red are abnormally low.

Factor	Level
II	**3 U/dl**
V	88 U/dl
VII	**3 U/dl**
VIII	314 U/dl
IX	**1 U/dl**
X	**17 U/dl**

NB: If in-line with text, table to be placed under "Case report" section, after paragraph three text "(table)".

KEYWORDS Brodifacoum poisoning; superwarfarin toxicity; synthetic cannabinoid receptor agonists (SCRAs)

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114. Changes with time in the novel psychoactive substances identified in British patients presenting with severe clinical toxicity.

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Objective: The United Kingdom (UK) Identification Of Novel psychoActive substances (IONA) study aims to link clinical features with analytical findings in patients presenting with severe toxicity after suspected novel psychoactive substance (NPS) use. Here we present analytical findings for 359 patients recruited between March 2015 and November 2017 and examine temporal changes in the substances identified.

Methods: With ethical approval, patients ($\geq$16 years) presenting to participating hospitals with severe acute toxicity (according to specific definitions) after suspected NPS exposure were recruited with informed consent. Those lacking capacity were included with the agreement of an appropriate relative/representative but were able to confirm/refuse their own consent on recovery. 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 in substances identified were examined by comparing data from patients recruited over 5 time periods (Table), each of 6 months duration, except that data were combined for 2015 due to limited numbers recruited in that first year.

Table 1. Changes with time in numbers (%) patients with at lest one positive sample for the most common NPS groups and the five most common). Data presented over 6 months blocks, except 2015.

	2015	2016 (early)	2016 (late)	2017 (early)	2017 (late)	TOTAL
n	55	100	58	99	47	359
Any NPS	44 (80%)	77 (77%)	39 (67%)	48 (48%)	24 (51%)	232 (65%)
Any conventional	38 (69%)	76 (76%)	52 (90%)	87 (88%)	43 (91%)	296 (82%)
SCRA*	24 (44%)	53 (53%)	20 (34%)	25 (25%)	12 (26%)	134 (37%)
NBOMe	12 (22%)	8 (8%)	12 (21%)	10 (10%)	5 (11%)	47 (13%)
Cathinone	6 (11%)	11 (11%)	11 (19%)	7 (7%)	2 (4%)	37 (10%)
SCRA* type						
5F-ADB	0 (0%)	29 (29%)	12 (21%)	14 (14%)	11 (23%)	66 (18%)
FUB-AMB (AMB-FUBINACA)	0 (0%)	12 (12%)	6 (10%)	15 (15%)	10 (21%)	43 (12%)
MDMB-CHMICA	11 (20%)	8 (8%)	7 (12%)	7 (7%)	2 (4%)	35 (10%)
5F-NPB-22	1 (2%)	19 (19%)	4 (7%)	2 (2%)	0 (0%)	26 (7%)
5F-PB-22	3 (5%)	19 (19%)	1 (2%)	0 (0%)	0 (0%)	23 (6%)

*Synthetic cannabinoid receptor agonist.

Results: By the data cut-off point (April 23, 2018) clinical and analytical data were available for 359 participants (median age 33 years, range 16–70 years; 291 or 81% male). The most common NPS groups identified were Synthetic Cannabinoid Receptor Agonists (SCRAs), NBOMe compounds and cathinones; the most common SCRAs were 5F-ADB and FUB-AMB (also called AMB-FUBINACA, Table). Over the course of the study there was a reduction in the proportion of patients where an NPS was detected in at least one sample. This was contributed to by reductions for SCRAs, NBOMe compounds and cathinones. Over the same time there was an increase in the proportion of patients with at least one sample in which a conventional drug of misuse was detected. The patterns of temporal changes differed between the most commonly identified SCRAs, with reductions seen for MDMB-CHMICA, increases followed by reductions for 5F-NPB-22 and 5F-PB-22, and increases without subsequent reductions for 5F-ADB and FUB-AMB.

Conclusions: The substances involved in patients presenting with severe toxicity suspected to be caused by NPS exposure have changed over the course of the study. Legislation directed at controlling NPS (including the UK's Psychoactive Substances Act, which became law in May 2016) may have contributed, but other factors may also have had a role, including law enforcement actions based on existing legislation.

KEYWORDS Novel psychoactive substances; drug control; synthetic cannabinoid receptor agonists

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115. Little blue fentanyl pills: a case series of patients presenting with fentanyl toxicity after exposure to illicit "M30" pills

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Background: Despite the recent national focus on opioid addiction and the danger of illicit fentanyl, there is a paucity of data about the potential morbidity of counterfeit pills contaminated with synthetic opioids. Additionally, there are no commonly available testing methods to reliably identify the presence of fentanyl in a patient sample. We have seen an increase in patients exposed to counterfeit "M30" pills, which resemble 30 mg oxycodone tablets but may contain varying quantities of fentanyl. We present a case series of nineteen such patients.

Table 1. End organ damage with subcategories.

End organ damage	# of patients (total =19)
Any	16 (84.2%)
Respiratory	12 (63.1%)
Aspiration Pneumonitis/Pneumonia	6
Pulmonary Edema	11
ARDS	4
Pneumothorax	1
Cardiovascular	7 (36.8%)
Dysrhythmia (SVT, atrial fibrillation)	1
Ischemia	6
Cardiac Arrest	2
Renal	6 (31.6%)
AKI	4
Rhabdomyolysis	3
Hepatic	4 (21%)
Transaminitis	4
Hyperbilirubinemia	1
Elevated PT	3
Neurologic	3 (15.7%)
Seizures	2
Anoxic Injury	1
Hearing Loss	1
Neuropraxia	1
Hematologic	1 (0.05%)
DIC	1

Case reports: Between June 2017 and April 2018 our medical toxicology service cared for 19 patients who had been exposed to an illicit "M30" pill. Eighteen were men, and ages ranged from 15 to 46 years, with a median age of 22 years (IQR 17–28). Exposure was primarily through ingestion, though 5 reported insufflating the pill. Fourteen patients were found apneic or with agonal respirations. Of those, two were pulseless requiring CPR. All but one received naloxone pre-hospital, and doses varied widely, with an average of 4.4 mg given. Most (15/18) had some response to naloxone. Ninety-five percent of patients were admitted to the ICU. End-organ injury occurred in 84% of patients (see Table 1 for details). Seven patients required intubation. Two patients were placed on ECMO due to severe Acute Respiratory Distress Syndrome (ARDS). All patients had a standard drug immunoassay as well as a urine gas chromatography/mass spectroscopy (GC/MS) as part of their clinical care. Additionally, pills obtained from three different patients were analyzed by the Arizona Department of Health Services. Results may be found in Table 2. Total length of hospitalization ranged from 1 to 24 d (median 3, IQR 1.5–4.5). While two patients were discharged to inpatient rehab due to overall deconditioning, the remainder were discharged home.

Discussion: Our medical toxicology service cared for 19 patients exposed to one "M30" pill purchased on the street. The large proportion of patients admitted to the ICU as well as the high frequency of end-organ injury emphasize the potential morbidity

Table 2. Results of urine testing.

Patient	Immunoassay positive for opiates or oxycodone?	GC/MS positive for fentanyl?	Pill obtained?	Results of pill analysis
1	*Yes (oxycodone only)*	*Yes*	No	
2	No	No	No	
3	No	No	No	
4	No	*Yes*	No	
5	No	*Yes*	No	
6	No	No	*Yes*	Fentanyl, clonazepam, methamphetamine
7	No	No	No	
8	No	No	*Yes*	Fentanyl, heroin
9	No	No	No	
10	No	No	No	
11	No	*Yes*	No	
12	No	*Yes*	No	
13	*Yes (opiates only)*	*Yes*	No	
14	*Yes (opiates and oxycodone)*	*Yes*	No	
15	No	*Yes*	No	
16	No	No	No	
17	*Yes (opiates and oxycodone)*	No	No	
18	No	No	No	
19	No	No	*Yes*	Fentanyl

of these pills, which is consistent with likely fentanyl contamination. Final outcomes were overall encouraging, though that likely owes to the young age and overall health status of our cohort. All patients had a history consistent with illicit M30 exposure. Only 3 tested positive for opiates on a standard urine immunoassay. Even when GC/MS was obtained, 5 had confirmed fentanyl levels above the reportable cutoff, and 3 more were confirmed only through specific ion searching. Additionally, the 3 patients whose pills were analyzed and found to contain fentanyl all had negative immunoassays and GC/MS, again emphasizing the inaccuracy of most available and even advanced testing methods.

Conclusion: We conclude that M30 pills, though marketed as oxycodone, are potentially dangerous sources of fentanyl sold on the street, with the potential for significant morbidity requiring intensive care. Testing for fentanyl is often unreliable, even when GC/MS is obtained. Providers should be aware of this potentially deadly emerging trend and should not rely on commonly available testing for diagnostic certainty.

KEYWORDS Fentanyl; M30; opioid

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116. Efficacy and safety of topical capsaicin for cannabinoid hyperemesis syndrome in the emergency department

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Background: Cannabinoid hyperemesis syndrome (CHS) is a disorder of cyclic and recurrent nausea, vomiting, and abdominal pain associated with high-frequency and extended-duration marijuana use. Symptoms are often refractory to conventional therapies including anti-emetics, opioids, and benzodiazepines. Capsaicin, an agonist of transient receptor potential vanilloid 1 (TRPV1), has limited data supporting its efficacy in CHS.

Objectives: The primary objective was to assess if utilization of capsaicin for emergency department (ED) management of CHS decreased ED length of stay (LOS) as compared to a visit for CHS without capsaicin. Secondary objectives included a cost analysis, rescue therapies, time-to-ED return, and adverse events.

Methods: This retrospective analysis evaluated the safety and efficacy of topical capsaicin for patients presenting with CHS to 11 EDs within a large university health system between June and December 2017. Emergency department LOS was selected for the primary objective as it is a patient-centered outcome and was the most consistent parameter available retrospectively to evaluate efficacy. Inclusion criteria: age 18–89-years-old with a history of marijuana use, symptoms suggesting CHS (e.g., improvement with hot water exposure and/or recurrent episodes of nausea, vomiting, and abdominal pain), and were treated with topical capsaicin. Patients served as their own controls; therefore, included patients had a prior ED presentation for CHS in which capsaicin was not utilized. Wilcoxon signed rank was used to evaluate continuous data and McNemar's test for categorical data. This study was approved by the IRB.

Results: Forty-three patients met the inclusion criteria within the study period. ED LOS was reduced between visits by a median of 22 min (201 versus 179 min, $p = .33$). The most common presenting symptoms were nausea/vomiting (100%) and abdominal pain (85%). Forty-three percent of patients reported home symptom relief with hot water exposure, and patients most frequently used marijuana on a daily basis (55%). Patients received fewer additional medications if capsaicin was utilized (4 versus 3 doses, $p = .015$), and 67% of visits where capsaicin was utilized required no further treatment prior to discharge. There was a trend toward reduced opioid usage when patients received capsaicin (15 versus 7 total doses). Forty-two percent of patients did not have a repeat CHS presentation to the ED after receiving capsaicin for an additional 3 months after the study period ended. Of the patients that re-presented to the ED, time to return was delayed when capsaicin was administered (8.2 versus 10.7 d). Total medication cost was 2.2 times more expensive (median cost difference of $3.26) in the capsaicin group. There were no significant adverse events reported with capsaicin administration.

Conclusions: Overall, there is a trend towards reduction in ED LOS when capsaicin is utilized for CHS. Patients also received a reduced number of medications which could be attributed to the majority of patients requiring no further intervention after capsaicin administration. While medication costs for visits utilizing capsaicin were minimally more expensive, the utility of capsaicin as an over-the-counter (OTC) product may empower at home therapy with OTC products, decreasing long-term healthcare exposure, and costs.

KEYWORDS Capsaicin; marijuana; hyperemesis

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117. Buprenorphine Induction Via Telemedicine to Emergency Department Patients

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Background: In 2016, New York expanded legislation to prohibit commercial insurance companies from declining reimbursement for telemedicine services when they would have otherwise been covered if provided in person. We have previously described our use of telemedicine for toxicology encounters including billing

and reimbursement data. These encounters involved diagnosis and disease management in poisoning, triage and clearance support, antidote administration, and assistance with opioid withdrawal. In this abstract we describe our use of telemedicine to treat opiate withdrawal and to remotely support buprenorphine induction in the ED and hospital setting.

Methods: Toxicology telemedicine support consisted of Zoom® Meeting software utilized in conjunction with a password-protected and encrypted IPad for the toxicologist and similar hardware and software platform where the patient was located. Telemedicine encounters involved use of on-call toxicology residents (rotating Emergency Medicine residents) assisting from the bedside of the patient. The actual consultation was performed utilizing a real-time audio/video connection with the assistance of the rotator who held the camera and relayed information during the exam. Telemedicine was initiated based on the toxicologist's discretion and when they were otherwise unavailable bedside (e.g. while traveling) but could perform the encounter remotely. In the case of buprenorphine induction it was also performed when the ED provider reported unfamiliarity with buprenorphine and requested advice on withdrawal management and induction dosing.

Results: From January, 2017 to December, 2017 three patients (2 male/1 female; 24–35 years) received toxicology consultation via telemedicine for the treatment of opioid withdrawal. IVDU-associated cellulitis, general complaint of opiate withdrawal and request for help getting into chemical dependency treatment, and fever with generalized weakness, later diagnosed as caused by IVDU-associated endocarditis, were the reasons for presentation. In each case patient's were interviewed, examined and opiate dependence and degree of withdrawal was determined via telemedicine. Two of the three were immediately treated with buprenorphine; the 3rd had buprenorphine induction the following morning as an opioid had previously been administered in the ED. Initial buprenorphine/naloxone dosing was 2/0.5 mg followed by 8/2 mg continued BID for 2 patients and ½ QID for one. Two individuals were subsequently seen bedside and bridged with buprenorphine to ongoing treatment after hospital care.

Discussion: We previously described telemedicine reimbursement rates of $203/h. In addition to reimbursement telemedicine represents opportunity to extend medical experience and skill to underserved settings. It has been proposed to support opiate dependent patients in rural areas, which often lack enough X-waivered physicians experienced in addiction treatment. Based on our experience it can also be used to remotely support these patients in ED or hospital settings when the toxicologist is not available for direct bedside care. This may be of particular importance as visits from opiate-related complications, including overdose, continue to rise.

Conclusion: Telemedicine was performed using simple and accessible technology and software platforms which allowed for reimbursed consultation when the toxicologist was not available for bedside care. The initiation and management of buprenorphine for patients in the ED and hospital setting may be a particularly useful and important example of the use of telemedicine for extending Medical Toxicology practice.

KEYWORDS Telemedicine; buprenorphine; opiate withdrawal

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118. Pharmacogenomic analysis of a patient with severe hepatotoxicity and hemolysis after acetaminophen overdose despite early N-acetylcysteine therapy

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Background: Early N-acetylcysteine (NAC) therapy after acute acetaminophen (APAP) overdose generally prevents severe hepatotoxicity. DNA sequencing allows detailed investigations of unexpected toxic responses to xenobiotics.

Case report: A 19-year-old, 69 Kg woman purchased a bottle of APAP/diphenhydramine tablets and promptly ingested 86.5 g APAP/4.325 g diphenhydramine. She arrived at an emergency department within 70 min where time and ingested amount were confirmed with receipt of purchase and pill counts. She vomited and received activated charcoal. IV NAC commenced <2 hr post-ingestion. Plasma APAP concentrations 1.7 and 4 h post-ingestion were 562 and 333 mg/l, respectively. Initial labs: AST 14 IU/l; ALT 32 IU/l; bilirubin 0.5 mg/dl, prothrombin time 14.7 s, and hemoglobin 10.7 g/dl. Despite NAC continued for 145 h, peak values of AST 9774 IU/l, ALT 8668 IU/l, bilirubin 11.8 mg/dl, and PT 53.9 s occurred over 4 d post-ingestion. Hemolysis produced anemia with nadir hemoglobin of 6.8 g/dl and low haptoglobin on day 4 treated with transfusion of 1 unit red cells. No renal failure ensued and 260 h post-ingestion studies showed AST 35 IU/l; ALT 714 IU/l (falling), bilirubin 1.5 mg/l, and hemoglobin 12.2 g/dl.

Methods: Blood DNA was processed for Next-Generation Whole Exome Sequencing on the Illumina HiSeq 2500 platform with average data outputs of 30 Gb and conventional mapping to the GRCh38p12 reference genome. Initial efforts focused on genes directly and indirectly involved in xenobiotic metabolism and transport, including *ALDH6A1*, *AHR*, genes for enzymes of the gamma glutamyl cycle, CYP450s, ABC proteins, various SLC proteins, UGTs, SULTs, GSTs and *G6PD*. Plasma APAP, APAP-metabolites and APAP-Cys adducts were serially measured.

Results: The following potentially relevant variants were identified: (1) pathogenic *G6PD* mutation (<10% activity); (2) rare *ABCB1* missense variant; (3) one extra copy of *CYP2E1*; (4) heterozygous Gilbert's disease (promoter *UGT1A1*); (5) heterozygous for synonymous base substitution in glutathione synthase (*GSS*) of unknown significance; (6) gain of several copies of *SULT1A1*; and (7) loss of one *AHR* copy. Plasma APAP fell to 128 mg/l at 9.4 h and rose again to 164 mg/l at 19.9 h post-ingestion.

Discussion: G6PD deficiency in erythrocytes produces decreased concentrations of reduced glutathione (GSH), causing hemolysis following APAP overdose. However, G6PD deficiency extends to liver, with hepatocyte enzyme activity 15–50% normal. Total hepatocyte GSH levels are maintained both through reduction of dimers by NADPH, generated via G6PD, as well as by *de novo* synthesis through the gamma glutamyl cycle. The five previous reports of hemolysis after APAP overdose with G6PD deficiency haven't described unexpected hepatotoxicity. Previous reports suggest patients with Gilbert's disease (homozygous) might shunt more APAP through oxidative metabolism. *AHR* drives transcription of several genes, including *UGT1A1*, *GSTA2*, and several CYP450s, but heterozygous deficiencies have not been proved to result in disease to date. An *ABCB1* missense mutation may decrease p-glycoprotein (PG) expression. While APAP isn't a PG substrate, PG levels rise in liver injury and may be important for export of secondary cellular toxicants. Phenotypic responses to APAP overdose may result from multigenetic variations. The

combination of described genetic variants in our patient suggest a multigenetic predisposition to hepatotoxicity, despite lack of established risk factor for each variant, alone. However, there have been no well-designed and adequately powered studies examining any of these factors after overdose.
Conclusion: Hemolysis in our patient was explained by G6PD deficiency. However a combination of genetic variations pertaining to APAP metabolism and response to toxic metabolites may have predisposed her to unexpected hepatotoxicity, and reports like this may point to common variants contributing to hepatotoxicity. Putative contributions of all identified genetic variants, alone or in combination, to this clinical phenotype continue to be investigated.

KEYWORDS Acetaminophen; hepatotoxicity; pharmacogenomics

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119. Five years of physo: a retrospective review of the safety and efficacy of physostigmine use at an Academic Tertiary Care Hospital

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Background: Physostigmine is a carbamate acetylcholinesterase inhibitor used for antimuscarinic toxicity. Once a mainstay of treatment for overdoses with anticholinergic symptoms, safety concerns reported in the 1980s resulted in a paradigm shift away from its use toward supportive therapies. More recent publications have suggested that physostigmine is more efficacious than alternative strategies for antimuscarinic poisoning, significant adverse effects are uncommon, and excessive caution is largely unfounded. Our practice is to administer 1–2 mg over 5–10 min to adults with symptoms suggestive of anticholinergic toxidrome (e.g. agitated delirium), barring contraindications such as bradycardia or conduction abnormalities.
Methods: We performed a retrospective chart review of all patients administered physostigmine at a single institution between March 5, 2011 and July 31, 2016. Electronic medical records were reviewed and data were entered into a REDCap database. Data included demographics, exposure history, symptoms, and details of physostigmine administration (dose, response, and adverse effects). Descriptive statistics were used to analyze the results.
Results: A total of 231 patients received physostigmine during the study period. Median age was 37 years (range 22 months–93 years) and 52% were female. Fifteen distinct antimuscarinic substances were identified (see Table 1) with diphenhydramine, quetiapine, and cyclobenzaprine being the most common drug exposures. The most prevalent CNS manifestation reported overall was delirium ($n = 189$, 82%). Agitation was commonly seen in diphenhydramine exposure (49/61, 80%), whereas coma was more common in quetiapine (29/43, 67%). Forty-eight patients received physostigmine in the Post Anesthesia Care Unit (PACU) for delirium where antimuscarinic exposures were absent. Overall, a single dose of physostigmine was administered to 148 patients (64%); 83 patients (36%) received repeat doses ranging from 1 to 5 additional doses. Three patients received physostigmine continuous infusions. The most common initial dose was 2 mg (160/231, 69%), although 1 mg was also common (68/231, 29%), especially among PACU patients. In patients in whom delirium was documented prior to physostigmine, 63% (119/189) had resolution after administration. For patients with agitation or coma, 69% (103/149) and 79% (54/68) had resolution after physostigmine, respectively. There was recurrence of anticholinergic symptoms in 134 (58%) patients after the first dose, despite only 83 receiving additional doses. Adverse effects were uncommon, occurring in just 12 patients (5%), with 8 patients vomiting (3 received antiemetics), 3 patients with seizure (2 received benzodiazepines), and 1 experienced isolated sinus bradycardia (patient also received metoprolol IV for hypertension – no intervention required).

Table 1.

Drug	*n*	Delirium *n* (%)	Agitation (*n*, %)	Coma (*n*, %)
Diphenhydramine	61	59 (97%)	49 (80%)	10 (16%)
Other (e.g. PACU)	66	50 (76%)	46 (70%)	3 (5%)
Quetiapine	43	31 (72%)	21 (49%)	29 (67%)
Cyclobenzeprine	30	21 (70%)	17 (57%)	15 (50%)
Unknown	19	15 (79%)	12 (63%)	6 (32%)
Hydroxyzine	12	12 (100%)	7 (58%)	6 (50%)
Olanzepine	7	5 (71%)	5 (71%)	4 (57%)
Benztropine	8	7 (88%)	4 (50%)	3 (38%)
Promethazine	5	5 (100%)	4 (80%)	2 (40%)
Clozapine	4	3 (75%)	1 (25%)	2 (50%)
Doxylamine	4	4 (100%)	4 (100%)	3 (75%)
Tricyclic antidepressants	2	2 (100%)	2 (100%)	0 (0%)
Atropine	1	1 (100%)	1 (100%)	0 (0%)
Datura (Jimson Weed)	1	1 (100%)	1 (100%)	0 (0%)
Dicyclomine	1	1 (100%)	0 (0%)	0 (0%)
Donnatol (atropine, hyoscyamine, scopolamine)	1	1 (100%)	1 (100%)	0 (0%)
Scopolamine	1	1 (100%)	1 (100%)	1 (100%)
Trihexphenidyl	1	1 (100%)	1 (100%)	0 (0%)

Discussion: This is one of the largest cohorts of physostigmine use to date. Our results are consistent with previous studies that have concluded that physostigmine is both safe and effective for the treatment of anticholinergic toxidrome in appropriate patients. Incidence of significant adverse effects such as seizures and bradycardia were low. We observed favorable outcomes, yet there is room for improvement, as there were still 51 patients with recurrence of symptoms who did not receive additional doses.
Conclusions: Physostigmine was efficacious in reversing anticholinergic signs and symptoms with a low incidence of side effects. Avoidance of physostigmine out of concern for adverse effects is likely unwarranted.

KEYWORDS Physostigmine; anticholinergic; safety

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120. It's Not Lupus: Management of a Severe Hydroxychloroquine Poisoning In The Era of Medication Shortages

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Introduction: Hydroxychloroquine (HCQ) is a medication used for malaria treatment and as an anti-inflammatory treatment chiefly for lupus. Since anti-inflammatory doses are lower than antimalarial doses, cases of acute severe toxicity from

hydroxychloroquine poisoning have declined. We report a case of a large acute overdose on hydroxychloroquine and discuss latest modality of treatment.
Case report: A 16-year-old girl who overdosed on 45 tablets of 200 mg (a total of 9 g) of hydroxychloroquine as a suicide attempt 40 min prior to presentation to her local emergency department. Vital signs included a heart rate of 130 and blood pressure 153/99 mm Hg. She was awake and alert. Her initial electrocardiogram had a rate of 109, QRS of 77, and QTc of 430. After 1 h in the ED, the patient became hypotensive and progressed to pulselessness with a wide complex tachydysrhythmia. CPR was started and she was intubated, defibrillated twice at 300J, and received intravenous epinephrine and sodium bicarbonate. During her resuscitation, diazepam was administered at a dose of 2 mg/kg as an IV bolus followed by an infusion of 2 mg/kg/day. Post-resuscitation, she was given a total of 80 mcg of phenylephrine and a high-dose norepinephrine infusion which failed to resolve her hypotension; high-dose epinephrine infusion was given shortly afterward and normalized her blood pressures, and on arrival to our facility, she was mildly hypotensive despite vasopressors. She received lipid emulsion therapy six h after her overdose, which resulted in an immediate improvement in blood pressure of 30 mm Hg systolic. Her serum potassium was as low as 1.6 mEq/l and despite potassium administration remained low for 17 h after. Roughly nine h after starting the diazepam infusion, hospital stores of diazepam were depleted. We elected to start the patient on high dose phenobarbital since it is a CYP3A4 inducer; she remained on a phenobarbital infusion receiving 1.56 g total in 24 h until diazepam infusion could be resumed. The initial measured HCQ level was 3405 ng/ml 15 h post ingestion. She was started on furosemide infusion on the 3rd day post ingestion for volume overload and augmentation of drug excretion. Her last serum HCQ level was 773 ng/ml 8 d post ingestion. She had a complicated ICU course, remaining intubated for 2 weeks prior to extubation, and was eventually discharged to an inpatient psychiatric facility.
Conclusion: The standard treatment for hydroxychloroquine acute toxicity has been high dose diazepam and epinephrine since 1988, although these medications may not be as widely available as they were thirty years ago. We present a case that shows high dose benzodiazepines are still an effective treatment for HCQ poisoning and that phenobarbital can used when diazepam is not available. The superiority of epinephrine to norepinephrine and phenylephrine in this case may suggest that beta adrenergic agonists are more effective in treating hypotension in hydroxychloroquine overdose. Use of intravenous lipid emulsion, though unproven, could be considered for refractory shock.

KEYWORDS Hydroxychloroquine; diazepam; lipid emulsion

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121. Novel overdose by venetoclax: a case report

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Background: Venetoclax is an antineoplastic agent indicated for relapsed or refractory chronic lymphocytic leukemia with 17p deletion. Specifically, it inhibits BCL-2, an anti-apoptotic regulatory protein which is overexpressed in CLL cells. During clinical trial testing, adverse effects occurred more frequently when venetoclax dose was rapidly increased, the most serious of which was tumor lysis syndrome. A step-wise protocol for dose escalation is recommended when initiating venetoclax therapy. Here we describe the first known case of an acute intentional overdose by venetoclax.
Case report: A 68-year-old man was brought to the Emergency Department by his wife 4 h after ingesting 800 mg of his venetoclax in a self-harm attempt. He was admitted to another hospital for 2 weeks to slowly increase his dose of venetoclax to 100 mg/day and discharged 2 d prior to this presentation. Initially he was mildly tachycardic and had some nausea, but physical exam was unremarkable. Initial diagnostic testing was significant only for an elevated LDH of 503 U/l and lactate of 3.4 mmol/l. Of note, his LDH was 653 U/l upon discharge from his prior hospitalization. Due to the known risk of tumor lysis syndrome, he was admitted to the intensive care unit. A hemodialysis catheter was placed prophylactically, should he need emergent hemodialysis. Serum chemistry, uric acid, phosphorous and LDH were drawn every 2 h for 24 h to surveil for laboratory signs of tumor lysis syndrome. Ultimately, he developed no laboratory findings of tumor lysis syndrome and remained hemodynamically stable. The second day of his admission he was started back on venetoclax at 100 mg/day, and eventually escalated 6 d later to 400 mg/day on discharge.
Discussion: This is the first described case of an intentional overdose of venetoclax. This patient ultimately did well, perhaps owing to his dose escalation, relieving his tumor burden and decreasing the risk of development of tumor lysis syndrome. Further studies are needed to determine the potential toxicity of this exposure.

KEYWORDS Venetoclax; antineoplastic; overdose

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122. Suicide by Proxy: Fatal Methemoglobinemia After Caregiver Administration of Sodium Nitrite

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Background: Sodium nitrite ($NaNO_2$) is a commonly used industrial and agricultural chemical that can cause severe methemoglobinemia if ingested. Here we report a case of a 31-year-old male with a history of quadriplegia secondary to a C-spine injury, who purchased bulk sodium nitrite online.
Case: He informed his primary care giver that what he had purchased was a dietary supplement and convinced her to mix estimated 7 g in water and administer it to him in what was actually a suicide attempt. He presented to the Emergency Department grossly cyanotic with an O_2 sat reading 86% receiving 100% oxygen on a non-rebreather mask a blood pressure was 71/40 with a heart rate of 66. The patient was awake and speaking with providers on his initial presentation. A methemogolbin fraction drawn on arrival was a shocking 82%. An initial dose of 100 mg of methylene blue was administered as the patient had no history of G6PD and Transfusion Medicine was consulted regarding the need for exchange transfusion. Despite early treatment with methylene blue, the patient decompensated, requiring intubation, and suffered PEA arrest. The patient was resuscitated with ACLS protocol including CPR and epinephrine and an additional dose of 100 mg of methylene blue. A methemoglobin fraction drawn a mere 6 h after receiving methylene blue showed a drop to a fraction of 10% and because of this the Transfusion Medicine service felt he would not benefit from exchange transfusion. Despite successful resuscitation, the patient suffered

profound hypoxic brain injury and his family opted to pursue comfort measures after a prolonged ICU stay.
Discussion: We wish to report this case to illustrate the severe features of methemoglobinemia and discuss management options including methylene blue, oxygen therapy and exchange transfusion as treatment for the condition. We also discuss a possible trend among depressed patients purchasing bulk chemicals online to utilize in suicide attempts.

KEYWORDS Methemoglobinemia; sodium nitrite; suicide attempt

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123. The effect of changing paracetamol (acetaminophen) overdose size on hospital admissions and costs in Australia

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Background: Paracetamol (acetaminophen) is the most common substance taken in intentional overdoses in Australia. The majority of paracetamol overdoses are impulsive, and previous studies have shown that many people take what is available in the household. Overdose size correlates well with risk of hepatotoxicity and need for treatment. This study aims to examine how the frequency and size of Australian paracetamol overdoses have changed with time, and the effect of any changes on hospital admissions and costs.
Methods: Paracetamol overdose frequency and size was analyzed using data from Australia's largest Poisons Information Center (PIC, taking 50% of the nation's poisoning calls). Intentional overdoses with paracetamol, 2004–2017 were extracted and free text dose and substance fields were interrogated to determine ingestion size. Yearly distributions were compared using a Kruskal-Wallis test, and cumulative frequency histograms. This was compared to nationwide hospital admissions data held by the Australian Institute of Health and Welfare (AIHW). Hospital admissions can be used as a surrogate for people with levels above the treatment line or with toxicity. Data from 1998–99 to 2014–15 was extracted for admissions under ICD-10 codes T39.1 (poisoning by 4 − Aminophenol derivatives) and K71 (Toxic liver disease). Number of separations and average length of stay was analyzed.
Results: There were 23,772 intentional paracetamol exposure calls to PIC over the 14-year period, with an 80% increase, 2004–2017. From 2004 to 2017, the median (IQR) number of tablets ingested has increased from 15 (10–24) to 20 (10–32). This was a statistically significant change in distribution of overdose size (Kruskal-Wallis H test = 56.03, $p < .0001$). Nationwide admissions for paracetamol poisoning have increased by 51% (4213 to 6372) and average length of stay has increased from 2 d to 2.7 d, 1998–1999 to 2014–2015. Admissions for toxic liver injury have increased 449% (65–357) over the same period. Based on the standard costings per bed day, it is estimated that Australia spent $34 million AUD on paracetamol admissions in 2014–2015, compared to $17 million in 1998–1999, and $19 million in 2003–2004 (first year of PIC data collection).
Conclusions: The number and size of paracetamol ingestions reported to Australia's largest poisons center has increased significantly. Hospital admissions and length of stay for paracetamol poisoning have also substantially increased. The increase in toxic liver injury cannot be definitively linked to paracetamol, however it is estimated that approximately 50% of toxic liver disease is due to paracetamol. Thus it is hypothesized that the increasing size of overdose seen in PIC data is resulting in increasing admissions, need for N-acetylcysteine, and hepatotoxicity. These results also have economic repercussions, with an approximate doubling of the estimated expenditure on treating paracetamol poisonings. Australia, like the US, has large quantities of paracetamol available without a prescription or pharmacist consultation. UK studies have shown that a reduction in over-the-counter paracetamol pack size reduces overdose size, hepatotoxicity and deaths. Similar measures could be employed in Australia to curb increasing harms from paracetamol overdose.

KEYWORDS Paracetamol (acetaminophen); health economics; intentional poisoning

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124. Delayed seizure from isoniazid overdose after empiric pyridoxine administration

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Background: Isoniazid (INH) is a relatively uncommon, yet potentially life-threatening ingestion. Benzodiazepine-refractory seizures secondary to isoniazid are known to be successfully treated with pyridoxine administration. Often onset of symptoms are rapid due to the pharmacokinetics of this medication. We present a case of empiric pyridoxine administered close to INH peak plasma levels with first seizure delayed by several hours.
Case report: A non-English speaking 15 year-old girl presented to an emergency department approximately an hour after suspected suicidal ingestion of her mother's isoniazid. She was somnolent, responsive to pain with presenting vitals of blood pressure 109/57, pulse 64, and pulse oximetry 100% on room air. She could not provide history initially as interpreter services were being accessed. Intravenous pyridoxine 5 g was given prophylactically. The patient's mother arrived and stated that up to 70 tablets of her 300 mg INH prescription were unaccounted for. There was no reported co-ingestion. Patient was transferred to a pediatric hospital for overnight observation. Approximately 6 h post-ingestion she had a tonic-clonic seizure and received a total of 6 mg lorazepam and an additional 2 g pyridoxine, depleting the hospital supply. An additional 3 g were obtained from an outside hospital and administered. Her mental status cleared and she had no further seizure activity.
Discussion: This patient reportedly had access to 21 g of isoniazid and therefore may have not received the recommended empiric dose-equivalent pyridoxine upon initial presentation. Seizures often develop early in the clinical course of toxicity given the rapid absorption and time to peak plasma concentration. Isoniazid is metabolized via acetylation to inactive metabolites, and rate of metabolism can vary due to genetic polymorphisms. Average half-life ranges from 1 to 5 h. Given the elimination half-life of pyridoxine is approximately 15–20 d, isoniazid will be excreted more quickly than the large dose of pyridoxine used for such cases. Although many experts suggest a gram-for-gram dose of pyridoxine to counteract the toxicologic mechanisms of isoniazid overdose, it is currently recommended to administer 5 g of pyridoxine intravenously to a patient suspected of INH overdose of unknown quantity. It is possible that empiric prophylactic doses of pyridoxine can slow the rate of glutamate accumulation and decreased GABA production without complete inhibition of this process, and

thus result in delayed seizures. No similar published cases were found in the literature.
Conclusion: Prolonged observation periods are warranted for isoniazid ingestions despite administration of the antidote, especially when the amount ingested is unknown. Toxicologists and poison center staff can aid in communication to hospitals anticipating admission of these patients to acquire adequate supply of pyridoxine in the event of delayed or prolonged symptoms.

KEYWORDS INH; pyridoxine; intentional ingestion

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125. Massive enoxaparin overdose partially reversed with low doses of protamine

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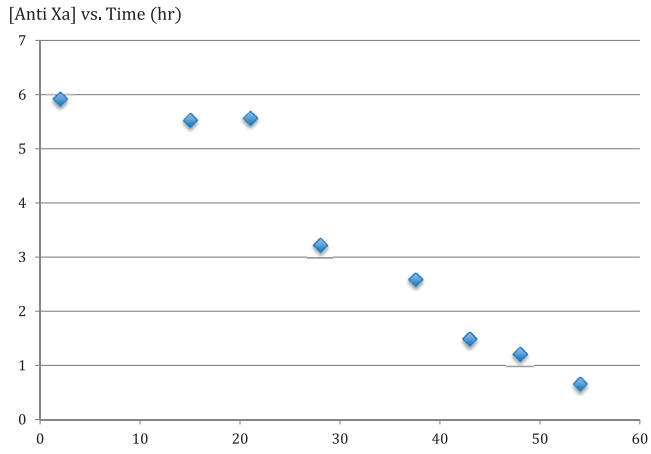
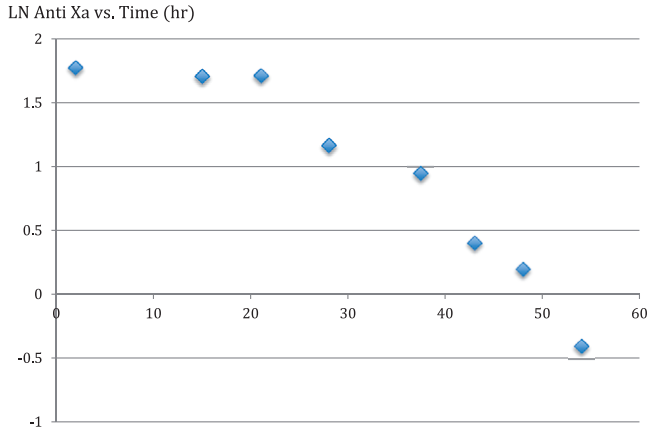
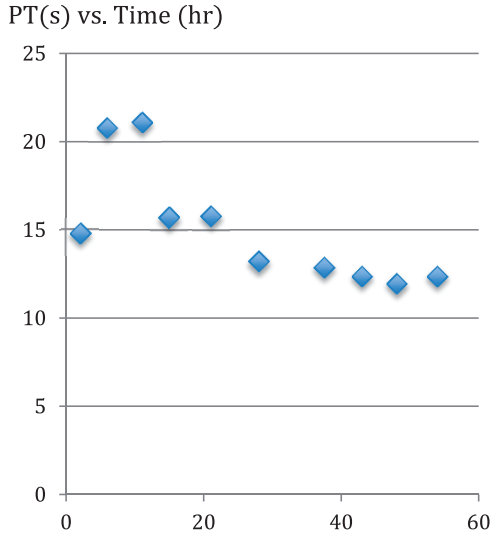
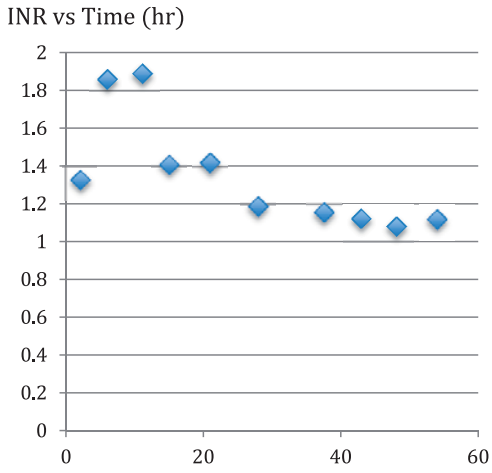
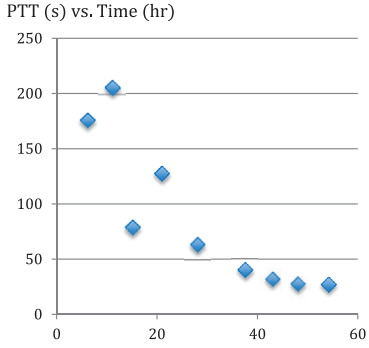
Background: Low molecular weight heparin (LMWH) overdoses are rarely described in the literature. While protamine is the treatment of choice for reversal of unfractionated heparin, its clinical efficacy in LMWH overdoses is less clear and reported with variable success. We report a single case of a massive enoxaparin overdose treated with small amounts of protamine.
Case report: A 25-year-old man with a history of antiphospholipid antibody syndrome, pulmonary embolism, borderline personality disorder, presented to the emergency department after intentionally injecting himself with 31 vials of 80 mg of enoxaparin (total of 2480 mg) in multiple areas of his body over the course of 1 h, and self-inflicted lacerations over his left forearm. His initial vital signs were notable for mild tachycardia of 107 bpm. Exam demonstrated multiple areas of ecchymosis over injection sites in his abdomen, calves and right inner thigh, as well as multiple superficial vertically oriented lacerations with blood oozing over the volar aspect of his left forearm. His initial laboratory findings were: hemoglobin of 16.6 g/dl, platelets of 168 per μL, creatinine 1.0 mg/dl, PT 14.8s, INR 1.33s, aPTT >120s, and an anti Xa 5.93 IU/ml (therapeutic range 0.5–1 IU/ml). Approximately 6.5 h post injection, 25 mg of protamine was given for concern for compartment syndrome to left arm. Subsequent evaluation by hand surgery determined low suspicion for compartment syndrome. At 11 h post overdose, the aPTT rose to 206s prompting an additional 50 mg of protamine. Fifteen minutes post protamine injection the aPTT decreased to 79s, then rose again at 21 h post overdose to 127s before decreasing. The anti-Xa levels peaked at 5.93 on arrival and plateaued for the first 21 h before decreasing. Kidney function remained unchanged, but patient's hemoglobin decreased by 6 g/dl without any obvious sources of bleeding besides superficial hematoma over injection sites and left forearm.
Case discussion: Protamine binds to heparin and preventing the formation of a heparin-antithrombin III complex. LMWHs however are anti-Xa inhibitors with only modest anthrombin inhibition (a ratio of approximately 14:1 for enoxaparin). Additionally the reduction in sulfate charge of LMWHs may also minimize the neutralization by protamine sulfate. Protamine therefore may only partially reverse the anticoagulant effects of enoxaparin. Treatment options in enoxaparin overdoses range from observation to treating with doses of up to 250 mg of protamine. Guidelines suggest protamine should be given a 1:1 mg of enoxaparin with a max dose of 50 mg as larger quantities protamine may worsen anticoagulation. Yet given the rarity of massive LMWH overdoses, there is still significant controversy in dosing of protamine. In this case, anti-Xa levels remained











elevated for 21 h and were not affected by protamine administration. Furthermore, the aPTT decreased and rebounded hours later, consistent with previous reports.
Conclusions: We present a case of a massive enoxaparin overdose treated with observation and small doses of protamine with a good outcome. The efficacy and optimal dose of protamine for LMWH overdoses needs further study.

KEYWORDS Enoxaparin; low molecular weight heparin; protamine

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126. More than an upset stomach: the life-threatening consequences of massive ibuprofen overdose

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Background: Ibuprofen has a wide range of systemic toxicities in the setting of massive overdose. We describe a case of a 29-year-old woman with an overdose of ibuprofen who developed hypothermia, shock, alerted mental status, acute liver failure, and profound metabolic acidosis requiring hemodialysis.

Case report: A 29-year-old woman presented to the emergency department (ED) with altered mental status 10 h after taking approximately 300 tabs of 200 mg ibuprofen. The ED providers noted somnolence and disorientation on presentation. Her initial vital signs were: blood pressure, 109/63 mmHg; pulse, 111 beats/min; respiratory rate, 17 breaths/min; temperature, 98° F; and bedside glucose, 89 mg/dl. During her ED course, she became hypothermic to 93.0° F (rectal) and decreasingly responsive. She was intubated for airway protection. Her initial laboratory studies showed: serum creatinine, 1.4 mg/dl; blood urea nitrogen, 17 mg/dl; and an anion gap metabolic acidosis (AGMA) with anion gap (AG) of 17 and venous pH of 7.23; lactate, 1.2 mmol/l. Urinalysis was negative for ketones. Acetaminophen, acetylsalicylic acid, and ethanol were all negative. Her initial liver function tests were all within normal limits. Initial urine toxicology drug screen was positive for barbiturates; a subsequent screen was negative. On hospital day (HD) 2, her AG increased to 26 and pH decreased to 7.11. She was started on a continuous intravenous infusion of sodium bicarbonate at 30 mEq/h. Her serum ibuprofen concentration on HD 3 was 330 mcg/ml (therapeutic range 10–50 mcg/ml). During admission, she developed acute oliguric kidney failure and required renal replacement therapy on HD 4. She also developed acute hepatotoxicity; her peak aspartate transaminase (AST) concentration was >717 U/l (laboratory maximum upper limit); alanine transaminase (ALT) 1873 U/l; bilirubin, 5.0 mg/dl, and INR 1.9. A liver transplant center was contacted for evaluation, but her mental status began to improve by HD 4 and liver function ultimately improved. She became hypotensive only after her transaminases began to rise, briefly requiring norepinephrine. Over the course of her 14-day hospital stay, her hemodynamic status, liver function, and kidney function all improved. She was transferred to a psychiatric unit for management of major depression on HD 15.
Case discussion: Most cases of acute ibuprofen overdose involve mild to moderate gastrointestinal distress and a self-limited acute kidney injury. This case illustrates the rare but serious potential consequences of massive NSAID overdose. Ibuprofen, as a propionic acid, can directly lead to profound elevated AGMA that usually precedes metabolic acidosis from acute kidney injury. Hypothermia, CNS depression, and hepatotoxicity, all seen in this case, have also been described previously, although rarely together, and the mechanisms are not well elucidated. Interestingly, a false positive urine assay for barbiturates has been described in the setting of ibuprofen use.
Conclusion: Ibuprofen is widely used in clinical practice and readily available in large quantities without a prescription. Although uncommon, systemic toxicity in cases of massive ibuprofen overdose is possible and may be delayed. Providers encountering cases of ibuprofen overdose should be cognizant of the clinically important consequences described in this case.

KEYWORDS Ibuprofen; NSAID; overdose

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127. Characterization of oral factor Xa inhibitor exposures reported to US Poison Centers

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Background: The oral factor Xa inhibitor class has gained widespread use for many indications. Due to the lack of specific reversal agents and inability to reliably monitor anticoagulation,

Effect	Adult Intentional	Adult Unintentional	Pediatric (<6 yr)
Death, *n* (%)	0 (0%)	13 (1.3%)	0
Major, *n* (%)	4 (1.9%)	46 (4.8%)	1 (0.3%)
Moderate, *n* (%)	44 (21.1%)	122 (12.7%)	10 (3.3%)
Minor, *n* (%)	35 (16.7%)	110 (11.4%)	14 (4.7%)
No effect, *n* (%)	126 (60.3%)	672 (69.8%)	274 (93.3%)
Total, *N* (%)	209 (100.0%)	963 (100.0%)	299 (100.0%)

Medical Outcomes of Exposure			
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Total, *N* (%)	209 (100.0%)	963 (100.0%)	299 (100.0%)

Most Prevalent Major Effects of those with Major Effects or Death (*n* = 64)	
Major Effect	Incidence
Bleeding, *n* (%)	24 (37.5%)
PT prolonged, *n* (%)	22 (34.3%)
Other, *n* (%)	15 (23.4%)
Death, *n* (%)	13 (20.3%)
Coagulopathy, *n* (%)	10 (15.6%)
Intracranial bleed, *n* (%)	10 (15.6%)
Blood per rectum, *n* (%)	9 (14.1%)
Hypotension, *n* (%)	9 (14.1%)
Tachycardia, *n* (%)	7 (10.9%)

toxicity from overdose or incidental exposure is difficult to monitor and outcomes from exposure are not well defined.

Objective: To characterize the clinical effects and medical outcomes in intentional adult exposures and unintentional adult and pediatric exposures reported to U.S. poison centers.

Methods: This retrospective study utilized data from the National Poison Data System (NPDS) comprised of calls to U.S. poison centers. Inclusion criteria were all human patients with exposure to the oral factor Xa inhibitor class from July 1, 2011 to December 31, 2016. As medical outcome of exposure was a primary outcome in this study, only those cases within NPDS that were followed to known outcome were included.

Results: There were 1486 total oral factor Xa inhibitor exposures followed to known outcome. Of the 1486 patients, 1181 (79.5%) were adult, and 297 (20.0%) were pediatric (age <6 y). Intentional exposures were 210 (14.1%) of the population. Only 9 (4.3%) of the intentional exposures developed major effects. Within the 297 pediatric exposures, 1 (0.3%) had a major effect, 10 (3.4%) had moderate effects and 285 (95.6%) had minor or no effects. Thirteen (0.8%) fatalities were reported. Review of detailed fatality reports revealed that all of these occurred while patients were taking the medication as prescribed. Reported major effects included bleeding, PT prolongation, coagulopathy and death.

Conclusions: The majority of oral factor Xa inhibitor exposures resulted in minor or no effects in pediatrics patients and intentional adults overdose. All deaths were seen in intentional use. This effect may be due to reporting bias, as no specific antidote is available, poison centers were often contacted for reversal recommendations in the case of life threatening bleeds. This study is limited by its retrospective nature, passive reporting and reliance on caller information. Additional research is needed to characterize the natural history of toxicity from intentional overdose or pediatric exposure and possible clinical effects or lab abnormalities that may occur.

KEYWORDS Anticoagulant; novel; overdose

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128. Massive apixaban overdose with blood concentrations managed conservatively without bleeding: a single case report

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Background: Apixaban is a factor Xa inhibitor indicated for treatment and prevention of multiple thromboembolic states. Significant bleeding from acute apixaban overdose seems to be uncommon however the safety and pharmacokinetics of apixaban in massive ingestions is underreported. We report a single case of a massive overdose of apixaban that was managed conservatively and without the occurrence of significant bleeding.

Case report: A 76-year-old man with a past medical history of chronic heart failure, non-insulin dependent diabetes, atrial fibrillation and taking apixaban 5 mg twice daily, presented to the emergency department (ED) 10 h after a reported ingestion of 60–70 of his home pills. His other medications include carvedilol, cetirizine, furosemide, glimepiride, hydralazine, isosorbide dinitrate, sitagliptin and tamsulosin. On initial presentation, he was alert and had a normal physical examination. His Initial vital signs were: BP, 112/97 mmH; HR, 68 beats/min, RR, 26 breaths/min; temperature, 97.4 °F; O_2 Sat, 96% on room air; weight, 88.5 Kg. Initial blood tests demonstrated an INR of 12; platelets, 152, 000 cells/mm3; hemoglobin, 10 g/dl; creatinine, 1.77 mg/dl; and antifactor Xa <0.2 IU/ml. Of note, the Antifactor Xa assay was calibrated for unfractionated heparin. The patient was given 60 g of activated charcoal and 4 units of fresh frozen plasma prophylactically. His initial apixaban blood concentration was 4000 ng/ml. Repeat apixaban concentrations were 3000 ng/ml and 2200 ng/ml at 7 and 14 h, respectively (Figure 1). During the patient's hospital course, he did not develop any evidence of clinical bleeding nor had a decrease in hemoglobin concentration. Repeat INR at 7 hrs post admission was 7.9, and he was not given any additional fresh frozen plasma. On hospital day 3, he was medically cleared and transferred to psychiatry.

Discussion: We report the case of a massive apixaban overdose that was managed conservatively. Consistent with prior case reports, our patient remained well and without evidence of bleeding despite a massive apixaban overdose documented with serial apixaban concentrations. The INR of this patient was elevated initially and consistent with one previous case report. Presumably, this is the reason the providers administered 4 units of FFP although the patient was not bleeding. While the

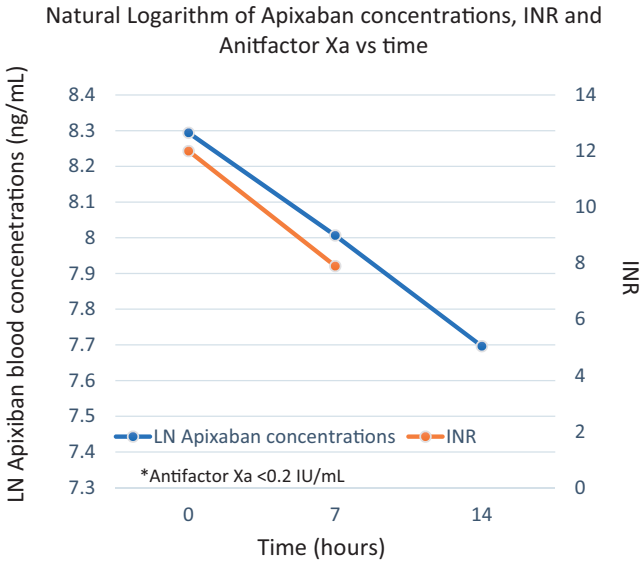

Figure 1. Natural Logarithm (LN) of Apixaban concentrations, INR, and Antifactor Xa assay results. †20 mg oral Apixaban results in a concentration of 500 ng/mL in human volunteers.

administration of FFP may show a modest improvement in laboratory values, there is no evidence that FFP controls apixaban associated bleeding. The Antifactor Xa activity was not elevated likely due to its calibration for unfractionated heparin. Although there were a limited number of apixaban concentrations obtained, apixaban appears to follow first-order elimination kinetics with a half-life of 14 h. This apparent half-life is slightly longer than prior reports and may be due to impaired renal function in our patient.

Conclusion: Despite a massive apixaban overdose documented with serial apixaban concentrations, apixaban was not associated with significant bleeding in this case report. Additional patient data are necessary to determine if overdoses of apixaban can be treated with supportive care alone.

KEYWORDS Apixaban; overdose; anticoagulation

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129. Fetal demise from a suicide attempt with diphenhydramine

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Background: Diphenhydramine is a sedating antihistamine used to treat nausea, motion sickness, cough, insomnia, and allergic reactions. It is readily distributed throughout the body, and is a competitive antagonist of histamine at the H1 receptor. Onset of action following oral administration occurs in 15–30 min, with peak concentrations occurring in about 2–4 h. The FDA classified the drug safe for use during pregnancy based on animal studies. Most products taken during pregnancy are over-the-counter medications. Studies show that diphenhydramine is used by 3.6% of pregnant women.

Case report: Emergency Medical Services (EMS) consulted the Poison Center (PC) on a 22-year-old gravida 3, para2, 20–5/7 week gestation woman who ingested 200 tablets of 25-milligram diphenhydramine 30 min prior to calling EMS. Initial survey found the patient to be alert, reporting paresthesia to lips and fingertips. Vital signs at the scene were BP 120/69, HR 160, RR 16, O_2 saturation with oxygen was 100%. The lung sounds were clear. She started seizing during the initial assessment and was transported to the emergency department once stabilized. Upon arrival, she underwent rapid sequence intubation and was placed on a ventilator. The QRS interval was 0.182 s. She was treated with midazolam, lorazepam, and twice with 100 mEq of sodium bicarbonate. She seized 3 times. PH on the initial VBG was 6.8, lactic acid 21.8 mmoL/l, and the urine drug screen was positive for tricyclic antidepressants and benzodiazepines. The blood gas improved after intubation and sodium bicarbonate. ABG showed pH of 7.37, pO_2 37, HCO_3 21.4. Other labs were CPK 55 U/l, MYOG 129 ng/ml, CKMB <0.2%, troponin <0.03 ng/ml. ED staff attempted to lavage the patient unsuccessfully. The physicians decided against activated charcoal due to the delay in its administration. Four hours after the initial call, the ultrasound showed the fetus having an agonal rhythm. Attending physicians suspected that fetal demise was imminent. A few days later, the patient had a spontaneous passing of a stillborn fetus. The fetus and placenta were delivered intact with no gross abnormalities.

Case discussion: Diphenhydramine is considered safe during pregnancy although it does have the ability to cross the placenta to the fetus. The patient showed classic anticholinergic toxidrome symptoms. GI: nausea, vomiting, neurological: confusion, seizures, delirium, and coma, cardiovascular: tachycardia, ventricular arrhythmias, prolonged QRS interval. The QRS interval prolongation seen in antihistamine overdoses is mediated by myocardial sodium channel blockade.

Conclusion: Providing care to a pregnant seizing patient is challenging; there are two patients to manage; the gravid mother and the fetus. Although diphenhydramine is considered safe for use during pregnancy, it can cause seizures, which may lead to hypoxia, fetal distress, and possibly fetal demise in overdose.

KEYWORDS Diphenhydramine; teratogen; fetus

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130. A fatal ranolazine overdose

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Background: Ranolazine (Ranexa®) is an antianginal agent prescribed for persistent symptomatic coronary vascular disease. In therapeutic dosing, it has a favorable safety profile. However, after an overdose, ranolazine can cause severe clinical effects. We present a fatal case of ranolazine overdose after a suicide attempt.

Case report: A 65-year-old woman with a history of Turner's syndrome, schizophrenia and bipolar disorder reported taking 50 of her brother's 1000 mg ranolazine 45 min prior to Emergency Department admission. The patient's prescribed medications were mirtazapine, quetiapine, gabapentin, trazodone, and rivaroxaban, but she denied other overdose. At presentation, the patient was awake and oriented with an unremarkable physical examination. Vital signs at triage were BP 103/67, HR 94, T 98.7° F, RR 20, SpO_2 98%. Laboratory values were within normal limits. Acetaminophen, salicylate and ethanol levels and urine drug screen were all negative. Initial EKG showed HR 88, QRS 85 msec and QTc 472 msec. The patient received 50 gm of activated charcoal 1 h after ingestion. One hour later, her SBP fell to 89, and an EKG showed QTc 505. The patient's blood pressure responded initially to IV fluids, 1 gm of IV magnesium and 1 gm of IV calcium gluconate, but her BP continued to fluctuate, requiring

norepinephrine infusion, and 6 L of IV fluid in the first few hours. At 8 h after admission, she became somnolent, diaphoretic, hypoxic and hypotensive with mean arterial pressure in the 40s–50s mmHg. The patient was intubated and was found to have pulmonary edema. Within the next hour, the patient had recurrent diffuse myoclonic activity (potentially seizures), became bradycardic, then experienced PEA arrest and expired, despite a prolonged attempt at resuscitation, including IV glucagon administration. The ranolazine concentration in the patient's serum was 50 mg/l (therapeutic level: 0.4–6.1 mg/l). Gabapentin, mirtazapine, quetiapine and trazodone were quantified at therapeutic or subtherapeutic levels.

Discussion: To our knowledge, this case is the first published report of a fatal ranolazine overdose in a human, with laboratory confirmation. Only a few previously reported cases highlight hypotension and seizures as severe manifestations of overdose. Toxicity may occur via multiple mechanisms. The most likely mechanism is inhibition of the delayed inward sodium channel current (iNa), which in turn decreases intracellular calcium concentration, reducing cardiac contractility and output. In addition, ranolazine causes prolonged QTc by activating delayed rectifier potassium channels, and it inhibits β -oxidation of fatty acids at supratherapeutic dosing. Animal models also suggest weak alpha and beta inhibition. And a FDA memorandum warned of convulsions in chronic administration of high doses of ranolazine in dogs. Optimal treatments for overdoses are unclear, but IV calcium, aggressive use of inotropes and vasopressors, and possibly high dose dextrose and intravenous lipid emulsion may be beneficial. Administration of IV fluids should be carefully monitored due to the risk of precipitating cardiogenic pulmonary edema.

Conclusion: Ranolazine overdose can result in severe toxicity, including intractable hypotension, cardiac conduction disturbances and seizures. Early recognition and aggressive treatment of its complications are imperative.

KEYWORDS Ranolazine; serum level; fatality

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131. Completed and attempted suicides with psychopharmaceuticals in Switzerland

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Background: Approximately 150 individuals annually die from self-poisoning in our country. Self-poisoning is the most often applied method of self-harm in survived suicide attempts, and the third most frequent in completed suicides. Less than 10% of suicide attempts are successful. Psychopharmaceuticals are frequently used for suicidal self-harm, a group of substances with a high potential for severe outcome. Due to the specific way of data acquisition, poisons centres data massively underreport fatal cases, whereas medical examiner data underreport survived cases, with negligible overlap. Therefore, in our study, suicide attempts reported to the national poisons centre were combined with cases reported by the national institutes of legal and forensic medicine with the aim to compare letality of substances and substance groups used in suicides and suicide attempts.

Methods: Anonymized human cases of self-poisoning with suicidal intention (referred to as "suicide attempts") from 2000 to 2010 were extracted from the national poisons centre case database (with medical follow up and high causality) and from the National Science Foundation project "Suicides, a national survey" (medical examiners' database, referred to as "completed suicides"). Because the medical examiners' database does not include all cases of suicidal death when compared with the national mortality register, the numbers extracted from the medical examiners' database were corrected with a factor of 1.9 (= ratio of the national mortality register numbers and the medical examiners' database numbers for 2009–2010). In the present study, only cases with exposure to psychopharmaceuticals (antidepressants, mood stabilizers, sedatives, antipsychotics) were included while exposures with strong narcotics incl. barbiturates and opiates/opioids were particularly excluded.

Results: Of the 23174 poisons centre cases with suicide attempts from 2000 to 2010, 9929 (42.8%) subjects used psychopharmaceuticals. Five thousand six hundred and twenty-six (56.7%) of these suicide attempts were single substance exposures, while 4303 (43.3%) subjects used two or more substances. In the medical examiners' database (uncorrected numbers) there are 6497 cases of which 963 (14.8%) had committed suicide by self-poisoning with medications as the main method of suicide, and 379 of those used exclusively one or several psychopharmaceuticals. One hundred and fifty (39.6%) of completed suicides were single substance exposures, while 229 (61.7%) subjects used two or more substances. The percentage of completed suicides per all suicidal exposures (i.e. attempted plus completed) was calculated only in single drug exposures. It was 6.8% for all classes of psychoparmaceuticals combined, 6.3% for antidepressants, 6.5% for mood stabilizers, 7.9% for sedatives, and 5.2% for antipsychotics. For single agents, the highest percentages (>10%) of completed suicides were seen with doxepine (34.3%), midazolam (21.6%), flunitrazepam (19.2%), trimipramine (17.6%), clomethiazole (15.5%), clomipramine (15.3%), clozapine (15.1%), zolpidem (14.5%), oxazepam (11.6%), and levomepromazine (11.0%).

Conclusions: In attempted or completed suicides psychopharmaceuticals are an important fraction in the group of medication-related cases. Victims in completed suicide used more frequently multiple drugs than in attempted suicide. The percentage of cases with specific drugs which are found in completed suicides can be an indicator of increased risk for a fatal outcome in suicidal self-harm thus giving clues for measures in the field of suicide prevention.

KEYWORDS Epidemiology; suicide; psychopharmaceuticals

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132. Prime eligible and only $17.00 on Amazon®: fatal sodium azide poisoning.

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Background: Sodium azide is a well-known mitochondrial poison primarily used in industry as a chemical preservative and also found as a propellant within some automobile airbags. Poisoning leads to refractory hypotension followed by severe lactic acidosis and death. We report a case of rapid fatality following ingestion of approximately 40 g of industrial sodium azide purchased from an internet supplier.

Case report: A 22-year-old male (90.7 kg) with a history of drug abuse, multiple visits to rehab, and extensive psychiatric history including multiple prior suicide attempts called his mother threatening suicide. The patient was found by EMS in the backseat of a vehicle having vomited once. A bottle of sodium azide purchased online was found in the trunk area of the vehicle. The patient presented to the emergency department via emergency medicine services approximately 60–90 min after intentional ingestion of 40 g of sodium azide. Initial vital signs in the emergency department were: blood pressure, 119/50 mmHg; heart rate, 114 beats/min; respiratory rate, 32 breaths/min; oxygen saturation, 96% on room air; and temperature, 34.6 C. Initial labs were grossly normal, including an anion gap of 11. Exceptions included an elevated ALT of 70 Units/l and elevated blood glucose of 162 mg/dl. Physical exam was notable for diaphoresis, tachycardia, and tachypnea with rales. Approximately 30 min after arrival, the patient's cardiac rhythm developed atrial fibrillation with rapid ventricular response. He required intubation for deterioration of mental status with Kussmaul respirations. Repeat laboratory evaluation 2.5 h after presentation revealed an anion gap of 20 with CO_2 of 14 mEq/l, lactate greater than 15 mmol/l, potassium of 6.6 mEq/l, and blood glucose of 254 mg/dl. Repeat vital signs continued to deteriorate with systolic blood pressure in the 80's; HR, 50 beats/min; temperature, 34.3 C. At approximately 4.5 h following time of ingestion, the patient experienced ventricular fibrillation and cardiac arrest. Cardiopulmonary resuscitation was attempted, but the patient expired. Case investigation and history were consistent with a suicidal ingestion of sodium azide so an inspection was performed at the medical examiner (ME). Comprehensive toxicology screen performed by the ME was negative for drugs, volatiles, and carbon monoxide. Sodium azide is not included in the drug screen and there were no readily available reference labs for analysis. Given his historical findings, clinical course, and otherwise negative workup, cause of death was determined to be sodium azide toxicity by the ME.
Case discussion: To date, the largest reported ingestion of sodium azide survived is 1 g. Our patient ingested approximately 40 g (441 mg/kg). Based on this patient's massive ingestion and no known antidote, there was an assumed 100% chance of mortality. Early recommendations were made for transfer for possible extracorporeal membranous oxygenation, however the family declined transfer.
Conclusions: This case represents a classic example of sodium azide poisoning that resulted in early tachycardia, followed by hypotension, hyperglycemia, severe lactic acidosis and death by approximately 4.5 h. Toxicologists and emergency providers should be aware of the ease of availability of such fatal toxins via the internet.

KEYWORDS Sodium azide; fatality; internet

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133. Efficacy and outcomes of lipid resuscitation on OP poisoning patients: a systematic review and meta-analysis

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Objective: Organophosphorus(OP) pesticide is still widely consumed in developing countries, leading to numerous accidental or suicidal poisoning each year. Lipid emulsion is commonly used in OP poisoning patients but few studies about OP were reported. Our meta-analysis aimed to illustrate the efficacy and outcomes of lipid resuscitation on OP poisoning patients.
Methods: A systematic search for associated studies was conducted in Pubmed, EMBASE, MEDLINE, Cochrane Library and Chinese National Knowledge Infrastructure. Collected data was pooled using Revman5.3. Outcomes include prognosis (cured rated and mortality rate), hepatic function (serum ALT, AST, TBIL level), serum acetylcholinesterase (AchE) level and respiratory function (rate of respiratory muscular paralysis).
Results: Seven randomized controlled studies consisting of 630 patients meeting inclusion criteria were identified. Lipid emulsion helps to improve cured rate [OR = 2.54, 95%CI (1.33, 4.86), $p = .005$] and lower the mortality rate [OR=0.31, 95%CI (0.13, 0.74), $p = .009$]. Serum ALT, AST and total bilirubin (TBIL) in patients undergoing lipid resuscitation are lower than those in control groups [ALT, SMD = −1.52, 95%CI(−2.64, 0.40), $p = .008$; AST, SMD = −1.66, 95%CI(−3.15, 0.16), $p = .03$; TBIL, SMD = −1.26, 95%CI (−2.32, 0.20), $p = .02$]. Serum AchE level is increased in patients treated with lipid emulsion [SMD =2.15, 95%CI(1.60, 2.71), $p < .00001$]. Rate of respiratory muscular paralysis is lower in patients undergoing lipid resuscitation than those in control groups [OR =0.19, 95%CI(0.05, 0.71), $p = .01$].
Conclusion: Based on the relatively low quality RCT reports in Chinese, lipid resuscitation seems likely to help to improve the clinical conditions, including the organic functions and prognosis of OP patients. Future multiple center and large sample RCTs are still needed.

KEYWORDS Lipid resuscitation; organophosphorus pesticide; meta-analysis

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134. Increased incidence of alleged adolescent suicidal ingestions reported to the National Poison Data System (NPDS) from 2008 to 2017

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Objective: National trends of alleged adolescent suicidal ingestions reported to the National Poison Data System (NPDS) from 2008 to 2017.
Background: Mental health is a growing public health concern. Suicide is reported as the third leading cause of death among early adolescents (10–14 years of age) and second leading cause of death among older adolescents (15–19 years of age). Although intentional poisonings make up only 15% of death by suicide, they likely reflect a larger majority of non-fatal suicide attempts. Unfortunately, information on non-fatal suicide attempts is currently limited. Better understanding of current trends in self harm attempts by ingestion could provide actionable information regarding prevention in susceptible demographics. The aim of this study is to characterize intentional suicide ingestions reported to the Nation Poison Data System (NPDS) by regional poison centers in the United States from 2008 to 2017.
Methods: The National Poison Data System (NPDS) was queried for all alleged intentional suicide exposures for males and females, aged 10–14 and 15–19 years for the period January 1, 2008–December 31, 2017. The number of exposures, severity of

Table 1. Summary of adolescent exposures reported to NPDS, 2008–2017.

	Total Cases (All severity)	Moderate	Major	Death*	Total Exposures (Mod., Major, or Death)
Male	148,813	36,552	4916	123	41,591
(10–19 years)		(24.6%)	(3.3%)	(0.1%)	(27.9%)
10–14 years	21,966	4818	512	10	5340
		(21.9%)	(2.3%)	(0.0%)	(24.3%)
15–19 years	126,847	31,734	4404	113	36,251
		(25.0%)	(3.5%)	(0.1%)	(28.6%)
Female	467,016	98,923	10,402	194	109,519
(10–19 years)		(21.2%)	(2.2%)	(0.0%)	(23.5%)
10–14 years	120,906	24,317	2324	33	26,674
		(20.1%)	(1.9%)	(0.0%)	(22.1%)
15–19 years	346,110	74,606	8078	161	82,845
		(21.6%)	(2.3%)	(0.0%)	(23.9%)
All Genders	615,829	135,475	15,318	317	151,110
(10–19 years)		(22.0%)	(2.5%)	(0.1%)	(24.5%)

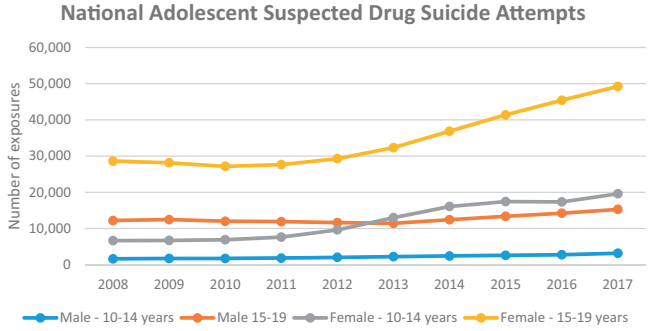

Figure 1. National adolescent suspected drug suicide attempts.

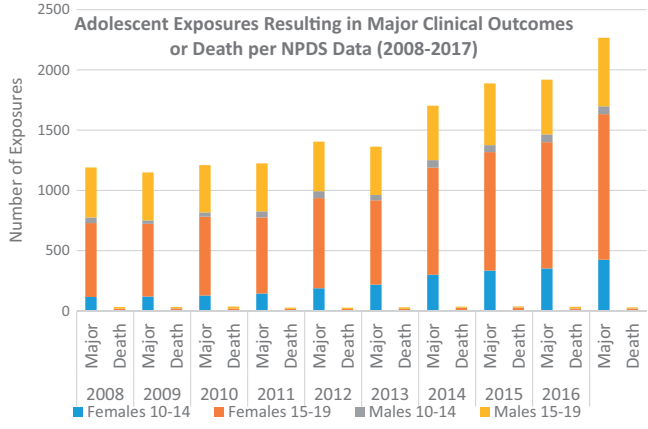

Figure 2. Adolescent exposures resulting in major clinical outcomes or death per NPDS data (2008–2017).

exposure outcomes, and generic codes for substances reported were evaluated for each age group and gender.

Results: A total of 615,829 exposures were identified, including 151,110 (24.5%) significant exposures leading to moderate clinical outcomes, major clinical outcomes, or death. There were 467,016 (75.8%) female exposures. A summary of aggregate NPDS data over the 10 year period is shown in Table 1. Between the years 2008 and 2017, adolescent (age 10-19 years) self-harm attempts by ingestion rose 78%. Female exposures increased by 95% while male exposures rose by 33%. Figure 1 illustrates suicide attempts per year by age group and gender. Younger female adolescents (10–14 years) had the greatest increase (195%) over the 10 year period queried. Exposures leading to major clinical outcomes and death are shown in Figure 2. Exposures leading to major clinical outcomes increased 92.8% between 2008 and 2017, with female exposures leading to major clinical outcomes increasing 124%. Of special concern, there was a 270% increase in young, female adolescent exposures resulting in major clinical outcomes. Fatal exposures remained stable over the ten year period. The three most common xenobiotics reported in adolescent exposures were non-steroidal anti-inflammatory drugs and acetylsalicylic acid (24.2%), acetaminophen (22.4%), and antidepressants (22.2%). The three most common xenobiotics reported in fatal exposures were benzodiazepines (15.9%), atypical antipsychotics (14.7%), and bupropion (8.4%).

Conclusions: Although adolescent deaths have not risen according to NPDS over the past 10 years, exposures, including those leading to moderate and major toxicity have increased significantly. Female adolescents have seen an especially sharp rise in self harm attempts by ingestion. The etiology of the recent rise in suicide attempts by ingestion in adolescents is unclear. NSAIDs, ASA, acetaminophen, and antidepressants were likely the most common xenobiotics involved in adolescent exposures given their ubiquity and ease to access. While overall exposures to benzodiazepines were low (6.6%), they were disproportionately represented in fatal outcomes.

KEYWORDS Adolescent; suicide; NPDS

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135. Lack of seizures in patients presenting to the ED with suspected benzodiazepine toxicity reversed with flumazenil

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Background or objectives: Flumazenil, a competitive antagonist at the benzodiazepine (BZD) receptor, reverses the central nervous system (CNS) depression in BZD overdose. Controversy surrounds the antidote as it has been associated with seizures; hence, its use has been discouraged in patients with chronic BZD use or abuse, history seizure disorders, history of pro-convulsant co-ingestion, a long QTc, or hypoxia. A recent study demonstrated no seizures in all patients administered low doses of flumazenil for suspected BZD toxic in the emergency department (ED) setting. Thirty-five percent of patients in this cohort had contraindications to flumazenil. The objective of this pilot study is to describe the rate of seizures in ED patients receiving low doses of flumazenil for suspected BZD overdose and describe any contraindications. The secondary objectives include a documented improvement in CNS depression and mean effective dose.

Methods: The study design was a descriptive, retrospective chart review of 5 academic EDs in a single Canadian city. The data was accessed electronically through Sunrise Clinical Manager®. All patients were included if they presented from January 1, 2014 to May 31, 2015 with CNS depression from a suspected BZD overdose and received <1 mg flumazenil given in multiple divided doses. Patients were excluded if there was inadequate chart documentation of administration or effect of flumazenil. Two abstractors compiled all of the chart data and consensus was achieved when contradictions arose through conversation. The primary outcomes included the presence of seizure in the immediate time following flumazenil administration, and the presence of contraindications to its use. Contraindications included patients with chronic BZD use (Rx daily for past 3 months), BZD

Table 1. Contraindications to flumazenil.

Contraindication	Total (19)
Chronic BZD* use or abuse	6 (31.57%)
Pro-convulsant coingestion	4 (21.05%)
	2 methamphetamine
	1 dextroamphetamine
	1 cocaine
	1 bupropion
Seizure history	4 (21.05%)
Seizure in the ED** prior to flumazenil	2 (10.53%)
QTc prolongation	2 (10.53%)
Hypoxia	1 (5.26%)

*BZD = benzodiazepine, **ED = emergency department

abuse, co-ingestion of known pro-convulsants, seizure disorders, seizures prior to flumazenil administration, a QTc >500, or hypoxia (SpO_2 <88%). Secondary outcomes included physician or nurse documentation of any increase in GCS, or a description of a patient that has an improvement in CNS depression, and the average effective dose.

Results: A total of 62 patients met inclusion criteria. Nine patients were excluded due to lack of documentation. The average age was 58.7 years (range 15–95 years). Males accounted for 54.7% (29/53) of included patients. The average total dose of flumazenil administered was 0.24 mg. Primary outcomes: No patients suspected of BZD overdose in the ED setting who received flumazenil subsequently had a seizure. A total of 19 patients had contraindications to flumazenil including 4 patients with 2 contraindications each (Table 1). Pro-convulsant co-ingestants included methamphetamine, dextroamphetamine, cocaine, and bupropion. Secondary outcomes: A documented no change in CNS depression post-flumazenil occurred in 9 of 53 (17.0%) patients. Whereas 44 of 53 (83.0%) patients had a documented increase improvement of CNS depression following flumazenil. The mean effective dose was 0.23 mg (range 0.1–1 mg).

Conclusions: No seizures occurred in patients when flumazenil was administered to patients with suspected BZD toxicity in the ED, despite several contraindications being present. Many patients also had a clinically significant improvement in mental status following flumazenil administration by an ED physician. Further research delineating the role of flumazenil in the ED is warranted.

KEYWORDS Flumazenil; benzodiazepine; overdose

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136. Rapid-onset hyperthermia and hypercapnea preceding rigor mortis and cardiopulmonary arrest in a DNP overdose

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Background: 2,4-Dinitrophenol (DNP), a chemical sold online as an illicit weight loss agent, has resulted in 70 published deaths over 102 years. DNP uncouples oxidative phosphorylation, resulting in a hypermetabolic state and excess energy released as heat. Clinical effects include hyperthermia, tachycardia, methemoglobinemia and acute onset rigor mortis. We present a detailed account of a patient with confirmed DNP toxicity and death, including the highest ever documented temperature following a DNP ingestion.

Case report: A healthy 26-year-old male weighing 118 kg presented 12 h after intentional ingesting 2.6 g of DNP that he obtained online as a "Shrub and Plant Fertilizer". The patient was in acute distress with GCS 15, hyperthermic at 38.4 °C, tachycardic at 162, hyperpneic at 44, and diaphoretic (Figures 1 and 2). Resuscitation began with multiple boluses of normal saline. A bedside echocardiogram demonstrated a hyperdynamic heart. Initial laboratory evaluation demonstrated a normal venous blood gas, a potassium of 5.8 mmol/l, lactate of 3.8 mmol/l, and a CK of 435 U/l. Due to respiratory fatigue and following considerable planning, the patient was intubated on first pass using sodium bicarbonate, etomidate, and rocuronium. Activated charcoal was then administered via confirmed nasogastric tube. The initial end tidal CO_2 ($ETCO_2$) measured 69 mmHg, but despite aggressive ventilation maximizing minute ventilation, it increased rapidly to 130 mmHg. An arterial blood gas revealed a pH of 7.14, CO_2 of 103 mmHg and a bicarbonate of 33 mmol/l. After intubation core temperature was 39.9 °C; cooling was initiated utilizing a combination of iced wet towels with frequent changes, fanning and misting. Despite these efforts, the patient's core temperature rose to a maximum of 43.1 °C at 61 min after arrival.

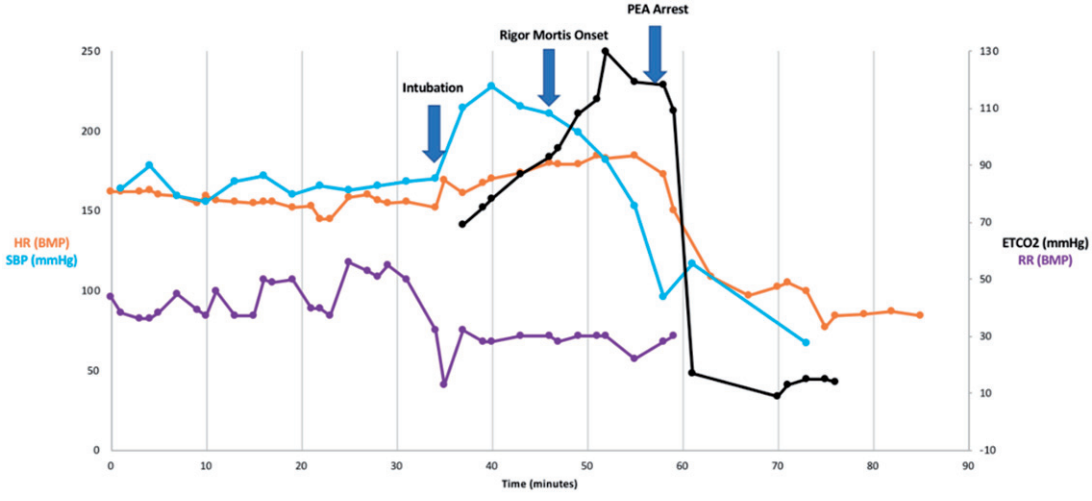

Figure 1. Vitals and end tidal CO_2 vs time.

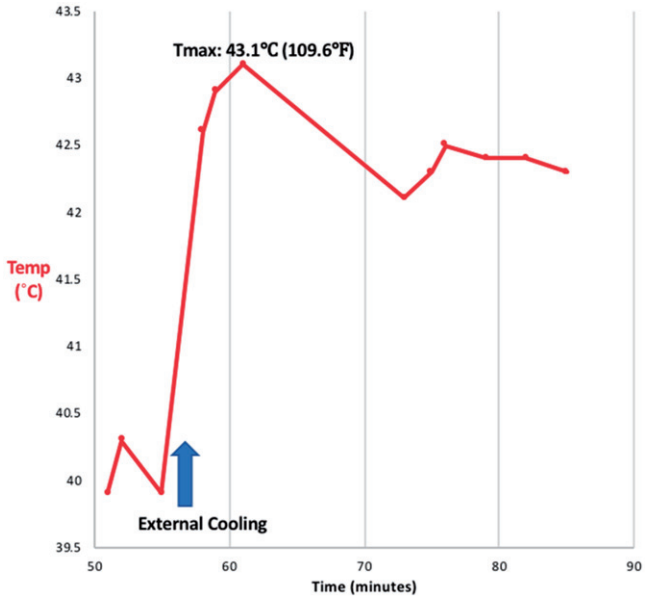

Figure 2. Temperature versus time.

The patient concurrently became rigid, and trismus occluded his endotracheal tube despite attempts with jaw spreader and corkscrew devices and direct 2-person manual mandibular retraction. A sudden, precipitous drop in $ETCO_2$ from 130 mmHg to 17 mmHg was detected, heralding pulseless electrical activity (PEA) arrest. Cardiopulmonary resuscitation was initiated, but chest compressions and ventilation soon became ineffective due to the patient's degree of rigidity. Hydroxocobalamin (5 g) was administered during post-arrest resuscitative efforts without effect. The patient expired within 87 min of presentation to the ED, approximately 807 min from ingestion. DNP was measured by UV-Vis spectroscopy in postmortem specimens. DNP was present in blood and quantified at 5.8 mg/ml in urine.

Case discussion: Death by DNP overdose has been previously described, however, we provide the most detailed account available to chronical a patient's course, vital sign changes, and pre-terminal events. Compressions and ventilation became impossible post-intubation due to full body rigor mortis, which preceded PEA arrest, suggesting a slight delay to cardiac rigor. Given a 12-h delay to peak toxicity in our patient as in others, absent clinical toxicity should not delay aggressive gastrointestinal decontamination and maximal supportive cares. This case suggests that progressive hyperthermia and $ETCO_2$ may be predictive of mortality in DNP overdose.

Conclusions: Accelerated hyperthermia and hypercarbia heralds PEA arrest, rigor mortis, and death following DNP overdose; early onset peripheral rigor mortis appears to precede cardiac arrest after DNP exposure.

KEYWORDS 2,4-dinitrophenol; DNP; overdose

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137. Intentional abuse and misuse of *Sophora secundiflora*

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Background: *Sophora secundiflora* (Texas mountain laurel) is native to Texas, New Mexico, and northern Mexico and is used as a landscape plant in various states. The 'mescal beans' of *S. secundiflora* are purported to be hallucinogenic, although they do not contain mescaline. The severe adverse effects of an ingestion have been attributed to the plant alkaloid cytisine, a partial agonist of nicotinic acetylcholine receptors. There is at least one case in the literature of a person ingesting *S. secundiflora* seeds for intoxication. The purpose of this study was to describe outcomes after intentional abuse and misuse of *S. secundiflora* reported to poison centers.

Methods: Cases of *S. secundiflora* ingestions reported to a large, statewide poison center network during 2000–2017 where the exposure reason was intentional abuse or misuse. The distribution of cases was determined for various factors related to patient demographics, exposure circumstances, management, and outcome.

Results: Of 741 total *S. secundiflora* ingestions reported, 44 (16.8%) were reported as intentional. Of these 44 ingestions, 79.5% were reported to involve intentional misuse and 20.5% intentional abuse. Seeds were reported in 93.2% of the cases, flowers in 2.3%, and unknown plant part in 4.5%. Of the 33 cases where the number of seeds ingested was reported, 81.8% involved one seed, and 12.1% involved two seeds; 16 seeds were reported ingested in one case. The patient age distribution was 20.5% children ($\leq$12 years), 50% adolescents (13–19 years), and 29.5% adults ($\geq$ 20 years); 79.5% of the patients were male. The ingestion site was the patient's residence (65.9%), school (15.9%), public area (11.4%), and other (6.8%). The patient was managed on site in 47.7%, already at or en route to a healthcare facility in 27.3%, referred to a healthcare facility in 20.5%, and other sites in 4.5% of the cases. The distribution by medical outcome was 18.2% no effect, 25% minor effect, 22.7% moderate effect, 25.0% not followed-minimal effects possible, 4.5% unable to follow-potentially toxic, and 4.5% unrelated effect. The most frequently reported clinical effects were gastrointestinal (54.5%) – vomiting (34.1%), nausea (29.5%), abdominal pain (22.7%), and neurological (25%) – vertigo (6.8%), lethargy (9.1%), numbness and tremor both (4.5%); no instances of hallucination were reported. The most common treatments were dilution (25%), IV fluids (18.2%), antiemetics (15.9%), cathartic (13.6%), and activated charcoal (13.6%).

Discussion: Of the cases of intentional abuse and misuse of *S. secundiflora* reported to this poison center network, most involved ingestion of seeds, usually a single seed. Half of the patients were adolescents, and the majority were male. Equal proportions of the patients were managed on-site and at a healthcare facility. Over two-thirds of the ingestions resulted in at most minor effects. The most frequently reported clinical effects were gastrointestinal and neurological. All patients recovered with no clinical sequelae. There were no fatalities.

Conclusion: *S. secundiflora* ingestions resulted in mostly gastrointestinal findings with no hallucinations reported. The majority of medical outcomes were at most minor.

KEYWORDS Sophora secundiflora; texas mountain laurel; cytisine

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138. ED TEE, tissue perfusion monitoring, and clinical examination guiding ED resuscitation of a massive caffeine ingestion

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Table 1. Selected laboratory values through initial stabilization and hemodialysis.

Time	11:42	12:15	15:13	17:30	21:40	2:20	2:41
Sodium (mEq/l)	135			141	141		138
Potassium (mEq/l)	2.5			3.7	3.4		2.6
Chloride (mEq/l)	102			105			99
Bicarbonate (mEq/l)	19			19			29
Creatinine (mg/dl)	0.61			0.41			0.2
Glucose (mg/dl)	222			150	124		
Lactate (mmol/l)	3.8		4.3	2.3		0.7	
Magnesium						1.4	
Venous pH	7.54						
Venous pCO_2	22						
Troponin I (mcg/l)	0.011						
Acetaminophen (mcg/ml)		49				0	
Salicylate (mg/dl)		0.3					
Caffeine (mcg/ml)		187.5		57		6	
Theophylline (mcg/ml)		6				0	

Background: Profound caffeine toxicity is a rare, life-threatening toxidrome whose management is complex, requiring attention to clinical status and exam. Depressed cardiac function and vasoplegia mandate resuscitation guided by multimodal monitoring. We present a case of profound caffeine toxicity managed collaboratively by emergency and toxicology staff, with excellent outcome and foreshortened hospital stay.

Case report: A 21-years-old woman presented to a rural hospital after being found unconscious in a shower <10 min after she was last seen normal, surrounded by empty bottles of caffeine, hydrocodone-acetaminophen, zolpidem, and alprazolam. Approximately 28 g of caffeine were unaccounted for; other medications exposures were uncertain. Presenting vitals were pulse 153, blood pressure 107/70, temperature 95.6F. Naloxone and flumazenil resulted in no improvement; endotracheal intubation followed. Gastric lavage revealed pill-like contents. Intravenous midazolam 10 mg, potassium chloride 15 mEq, and metoprolol 5 mg were administered, achieving heart rate control but worsening hypotension (systolic pressure 70). She was emergently transferred to a tertiary care center. En route 400 ml crystalloid, 20 mg midazolam, and 10 mg vecuronium were administered for hypotension and agitation. She arrived tachycardic and warmly perfused; extremity examination suggested vasodilation. Transthoracic cardiac ultrasound revealed poor lusitropy. Anticipating worsening illness, a transesophageal ultrasound (TEE) probe was placed by emergency physicians, displaying real-time cardiac function to guide interventions. Peripheral perfusion monitoring revealed stO_2 of 90%, cerebral perfusion of 60% with the patient at 30 degrees. Presenting acetaminophen level was 49 mcg/ml, caffeine 187.5 mcg/ml, and theophylline 6 mcg/ml. EKG revealed sinus tachycardia at a rate of 105, with t-wave flattening, small u-wave and normal intervals. Figure 1 includes vitals and interventions. Esmolol was titrated and phenylephrine initiated with continuous TEE, stO_2, invasive arterial pressure monitoring, and examination guiding resuscitation. A dialysis catheter was emergently placed; the patient underwent 3 h of hemodialysis (HD) at 400 ml/min against a 3 mEq/l potassium bath. Post-dialytic caffeine remained at 57 mcg/ml; a second, 4-h HD run at 350 ml/min followed. Final caffeine and theophylline levels were 6 mcg/ml and undetectable, respectively. Intravenous n-acetyl cysteine was initiated. Serum potassium nadired (2.5 mEq/l) at presentation. Table 1 includes further laboratory data. Extubation occurred on hospital day (HospD) #3, transfer from intensive care (ICU) on HospD#4, and discharge to inpatient psychiatry on HospD#6. No further toxic sequelae occurred.

Case discussion: Over 3200 cases of caffeine unrelated to energy drinks were reported to national Poison Centers in 2016. While massive caffeine overdose remains rare, complex pathophysiology may challenge clinicians. Adenosine antagonism, phosphodiesterase inhibition, hypokalemia, and catecholaminergic surge, coupled with blood brain barrier permeability, conspire to present numerous life threats including hypokalemia, tachydysrhythmias, seizures, and hemodynamic instability. In this case aggressive multimodal monitoring was implemented early with toxicology input and complimented physical exam to guide management of acute diastolic dysfunction, systemic hypotension, and disparate peripheral and cerebral perfusion presumed secondary to vasoplegia. Aggressive early monitoring resulted in expedited hemodialysis and optimized patient outcome while minimizing ICU time.

Conclusions: In cases of profound methylxanthine toxicity, toxicologists may facilitate early aggressive multimodal monitoring initiated in the ED to improve patient care and outcomes, while optimizing length of hospitalization.

KEYWORDS Caffeine; methylxanthine; overdose

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139. Tween/teen intentional self-harm incidence: a poison center's 18-year review of data

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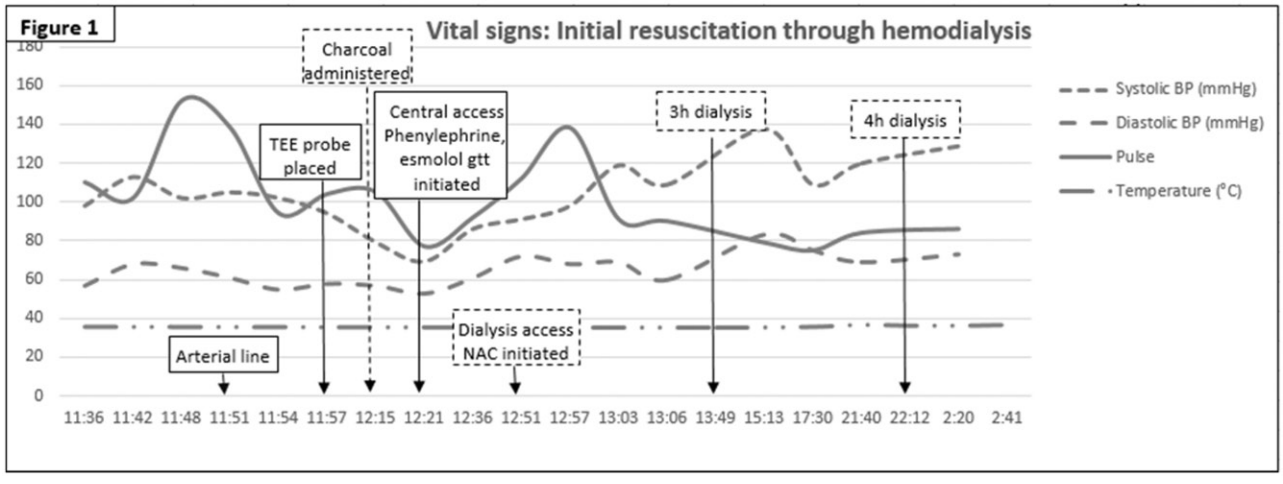
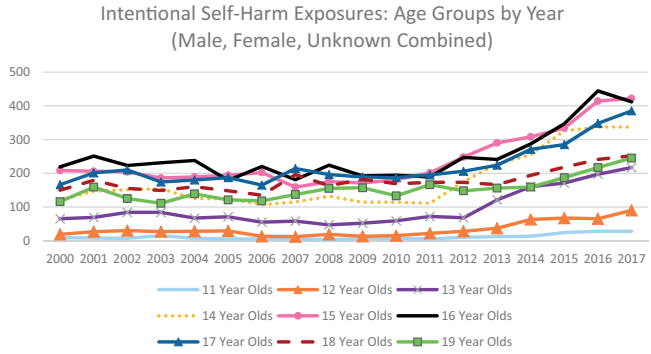
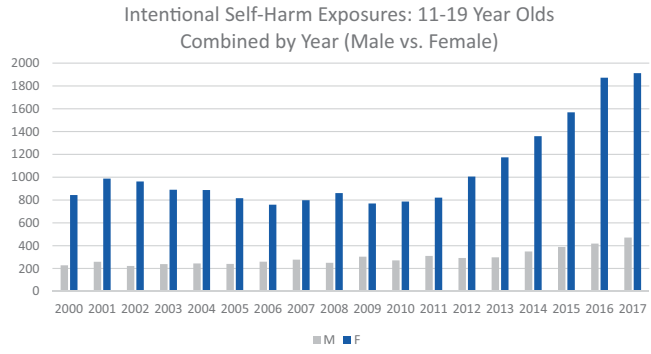


Figure 1. Vital signs: initial resuscitation through hemodialysis.





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Background: According to the Centers for Disease Control and Prevention, suicide is the second leading cause of death for youth between the ages of 10 and 24 years in the United States. Furthermore, intentional overdose or poisoning is a common modality of self-harm among adolescents. Identifying trends can help with future mitigation of such behavior.
Methods: A retrospective review of all intentional exposures for self-harm reported to a single poison center from January 1, 2000 to December 31, 2017 for children ages 11-years-old to 19-years-old. A ToxiCALL® data search was conducted using the following search criteria: Year Code; Call Type: Exposure; Reason for Exposure: Suspected Suicide; Caller State: Single State; Species: Human; Age.
Results: A total of 24,436 intentional exposures in children 11–19-years-old were reported from 2000 to 2017, with an overall increase in reported exposures of 122.6% during this time. The largest increase during this time period, 553.8%, was seen in 12-year-old females. For males, the largest increase, 316.7%, was seen in the 14-year-old age group. For the majority of age groups, the total number of self-harm cases tended to be higher for females than for males. However, the percentage increase was greater for males in the 14, 15, and 16-year-old age groups as compared to females from 2000 to 2017 (316.7% versus 163.3%; 185.2% versus 90.6%; 97.8% versus 84.4%, respectively).
Conclusion: Further evaluation of what factors have contributed to this increase in cases, why certain ages have seen larger increases than others, and what substances are being used for self-harm would be valuable to better understand how education and other efforts may affect suicide attempt rates. Additional study is also warranted to determine if a similar increase in adolescent self-harm cases has been noted by other U.S. poison centers.

KEYWORDS Self-harm; youth; trends
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140. Trends and characteristics of oxycodone exposures reported to the U.S. Poison Centers, 2011–2017

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Background: Between1991 and 2013, there was a three-fold increase in prescribing of opioids in the United States. According to the Substance Abuse and Health Services Administration, there were 182,748 visits to emergency departments (ED) related to oxycodone products in 2010. Between 2009 and 2014, there has been a 49%decrease in the initiation of oxycodone misuse according the National Survey of Drug Use and Health. This study aims to examine the national trends inoxycodone exposures reported to U.S. poison centers (PCs).
Methods: TheNational Poison Data System (NPDS) was queried for all closed, human exposuresto opioids from 2011 to 2017 using the American Association of Poison ControlCenter (AAPCC) generic code identifiers for oxycodone. We identified anddescriptively assessed the relevant demographic and clinical characteristics. Oxycodone reports from acute care hospitals and EDs were analyzed as asub-group. Trends in oxycodone frequencies and rates (per 100,000 humanexposures) were analyzed using Poisson regression methods. Percent changes fromthe first year of the study (2011) were reported with the corresponding 95% confidence intervals (95% CI).
Results: Therewere 119,263 oxycodone exposures reported to the PCs from 2011 to 2017, withthe calls decreasing from 19,165 to 14,859 during the study period. Among theoverall oxycodone calls, the proportion of calls from acute care hospitals andEDs increased from 46.2% to 55.6% from 2011 to 2017. Multiple substanceexposures accounted for 54.1% of the overall oxycodone calls and 70% of thecalls from acute care hospitals and EDs. The most frequent co-occurringsubstances reported were benzodiazepines (21.2%), and hydrocodone (5.1%). Residencewas the most common site of exposure (94.2%) and 59.2% cases were enroute to the hospital when the PC was notified. Tachycardia and respiratorydepression were the most frequently demonstrated clinical effects. Naloxone wasa reported therapy for 19.9% cases, with this therapy being performed prior to PC contact in most cases. Demographically, 54.9% cases were females,and the most frequent age groups were 20–39 years (32.6%) and 40–59 years(28.6%). Suspected suicides (36.7%) and intentional abuse (11.4%) were commonlyobserved reasons for exposure, with these proportions being higher in casesreported by acute care hospitals and EDs (57.5% and 13.4%, respectively). Approximately20% of the patients reporting oxycodone exposures were admitted to the criticalcare unit (CCU), with 10% of patients being admitted to non-CCU. Major effects were seen in 6.1% cases and the case fatality rate for oxycodone was1.3%, with 1476 deaths reported. There were 546 deaths reported within acutecare hospitals and EDs during the study period. The frequency of oxycodoneexposures decreased by 22.5% (95% CI: −24.2%, −20.8%; $p < .001$), and the rate of oxycodone exposures decreased by 14.1% (95% CI: −22.6%, −5.3%; $p = .009$).
Conclusions: PCdata demonstrated a decreasing trend of oxycodone exposures, which may in partbe attributed to the reformulation of this medication with abuse-deterrentproperties in 2010. However, the increase in the calls from the acute-

carehospitals and EDs indicates higher severity of such exposures along with coingestants.

KEYWORDS Oxycodone; overdose; NPDS

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141. Massive fatal abrin poisoning by injection

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Background: Seeds from the tropical plant Abrus precatorius contain abrin, a highly toxic protein (MW=~64 kilodaltons) with an estimated human fatal dose of 0.1—1.0 mcg/kg. It is a type II ribosome-inactivating protein like ricin. Abrin induces toxicity through RNA N-glycosidase activity that alters the 3′ end of the 28S rRNA of the 60S ribosomal subunit preventing elongation and protein synthesis. Exposures are associated with abdominal pain, vomiting, and diarrhea leading to fluid loss and electrolyte disturbances. Endothelial damage may lead to widespread tissue edema and patients may develop hemorrhagic gastroenteritis, increased intracranial pressure, demyelination, and multi-organ failure culminating in death. We report the first known human case of abrin toxicity by injection.
Case reports: A 35-year-old suicidal man purchased ~150 A. precatorius seeds online, ground them, mixed them into water, and administered one third of this solution subcutaneously and intramuscularly into multiple extremity sites. Upon emergency department presentation he was awake, alert, and mildly tachycardic with otherwise normal vital signs. He had marked erythema and edema in his right forearm and milder irritation localized to the injection sites on his left shoulder and right leg. Magnetic resonance imaging revealed fasciitis and myositis. Initial laboratory studies were remarkable for initial white blood cell count of 41,600/mm^3. Orthopedics and general surgery services evaluated him for possible compartment syndrome and necrotizing fasciitis. Charcoal hemoperfusion was discussed early but was unavailable. On hospital day two he developed decreased mentation and autonomic dysregulation, including episodes of supraventricular tachycardia for which he was chemically cardioverted. Labile blood pressure at times required alternately nitroglycerin infusion and epinephrine, among other vasoactive medications. He developed generalized tonic-clonic seizures and was intubated for airway protection. He was provided continuous renal replacement therapy on day three in an attempt to remove the toxin and treat his anuric renal failure. After developing skin blebs he underwent right forearm extensor fasciotomy for concerns of necrotizing fasciitis, however infection was not found. An EEG obtained that evening showed minimal cerebral activity. On the morning of day four the intensive care team was able to contact the patient's parents who agreed to no further resuscitation, and he expired shortly thereafter. Blood and urine samples were sent to the Centers for Disease Control and Prevention (CDC) and the state laboratory. Urine sampling confirmed abrin exposure. CDC results are pending at this time.
Discussion: Abrin poisoning has been of increasing interest due to its extreme toxicity and potential use as a bioterrorism weapon. In this first reported human case of abrin injection, death resulted within 3 d after a massive self-administered dose. It remains unknown if there are clinical differences between abrin toxicity by ingestion versus injection. There exist no established therapeutic countermeasures against abrin exposure other than supportive care. Due to its relatively large molecular weight, extracorporeal removal by charcoal hemoperfusion was used in one published case of toxicity, but this method was not available to our patient. Abrin antitoxin antibodies are under investigation as a possible antidote.

KEYWORDS Abrin; jequirity; ricin

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142. Severe metformin toxicity with highest recorded surviving level treated with aggressive extracorporeal therapy

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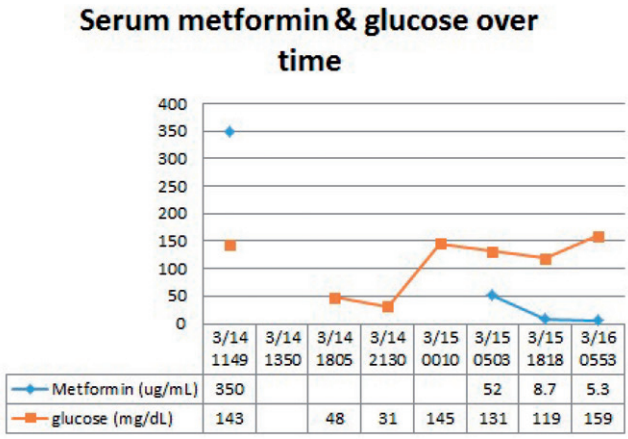
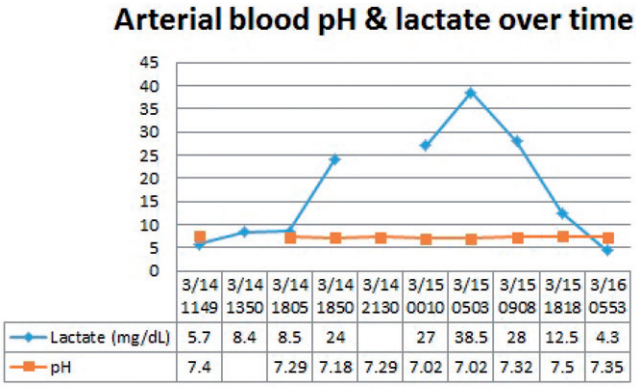
Background: Metformin poisoning can cause marked lactic acidosis and fatalities following massive ingestions. Severe metformin toxicity has been treated successfully with intermittent hemodialysis (HD). In a systematic review of acute metformin overdose, patients with low pH, high lactate, and high metformin concentrations were found to have a high rate of mortality. We report a case with markedly elevated metformin levels, low pHs, and high lactates that survived following aggressive extracorporeal management.
Case report: A suicidal 19-year-old male with previous history of depression presented to the Emergency Department (ED) with severe vomiting after ingesting 360 tabs of 500 mg metformin. He was initially hemodynamically stable with pH 7.4, lactate 5.7 mmol/l, and creatinine of 1.4 mg/dl. Serum metformin concentration obtained at time of arrival was 350 mcg/ml. Despite two l of normal saline, his lactate rose to 8.5 mmol/l and pH dropped to 7.29 with serum bicarbonate 10 mmol/l and serum glucose of 48 mg/dl at 6 h post presentation. Intravenous dextrose and sodium bicarbonate infusion were started. His lactate rose to 24 mmol/l at 7 h after presentation. Following a 4-h session of HD started at 8 h following presentation, laboratory values revealed: pH 7.02, bicarbonate 8 mmol/l, lactate 27 mmol/l, glucose 31 mg/dl. The patient became agitated and confused, ultimately requiring intubation and mechanical ventilation. On arrival to tertiary care center 17 h after initial presentation, his pH was 7.02, lactate 38.5 mmol/l, glucose 131 mg/dl (on D10 infusion at 200 ml/h to maintain euglycemia) and he required vasopressor support with norepinephrine to maintain a mean arterial pressure (MAP) > 65. Metformin concentration at this time was 52 mcg/ml. Patient was started on high-dose continuous renal replacement therapy (CRRT) which continued for 2.25 h after which he had improving pH to 7.15 and lactate of 34 mmol/l. He then had two consecutive 3-h HD sessions. Following HD, his lactate dropped to 19 mmol/l, pH rose to 7.38, and he was weaned off vasopressor support as well as sodium bicarbonate infusion. Serum metformin concentration following HD was 8.7 mcg/ml. The patient was continued on CRRT therapy for the next 29.5 h and repeat HD session was not performed given his improving clinical status. Metformin concentration following CRRT was 5.3 mcg/ml. Metformin half-life and clearance on CRRT were calculated as 16.2 h and 30.6 ml/min respectively. The patient was discharged on hospital day 10 with full neurologic recovery.
Discussion: We present a case of massive metformin ingestion leading to severe metabolic acidosis with elevated lactate, recurrent hypoglycemia, and hypotension that was treated with dextrose, norepinephrine, and sodium bicarbonate infusions as well as both HD and CRRT. The presenting metformin level of 350 mcg/ml represents the highest documented level in a surviving patient.





Conclusion: Aggressive supportive care and the use of various extracorporeal therapies remain the staples of therapy in severe metformin toxicity. CRRT is less efficacious than HD in metformin removal, but may have a role to play between HD sessions if a prolonged session is not available.

KEYWORDS Metformin; hemodialysis; intentional

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143. Successful ECMO for massive venlafaxine overdose

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Background: There is a growing body of literature on the role of Extracorporeal Membrane Oxygenation (ECMO) in severely poisoned patients, who would otherwise be unlikely to survive. In particular, veno-arterial (VA) ECMO can be used in patients with refractory hypotension from cardiogenic shock. Venlafaxine is a selective serotonin-norepinephrine-dopamine-reuptake inhibitor that, in large overdoses, can be associated with cardiac channelopathy. In this report, we describe a case of severe acute cardiac channelopathy from venlafaxine with VA-ECMO rescue leading to intact neurologic recovery. Additionally, this is the highest reported venlafaxine level in the literature to date.

Case report: A 24-year-old female presented after being found somnolent in her bathroom with open pill bottles. Reported ingestion was 13.5 gm venlafaxine ER, 9 gm bupropion, 450 mg aripiprazole, 3.5 mg clonazepam, and two to three bottles of wine. Per EMS report, the patient responded to 4 mg naloxone. Urinary drug screen was positive for amphetamines and blood alcohol level was 207. Approximately 3 h after arrival, she had a seizure, which resolved with lorazepam. Two hours later, she seized again, after which she received 1000 mg of levetiracetam and was intubated for airway protection. After remaining stable on the ventilator for 13 h, she rapidly deteriorated. She had frequent seizures and developed hypotension requiring norepinephrine. Electrocardiogram (ECG) showed QRS 216 and QTc 620. She was placed on a midazolam infusion of 4 mg/h. Sodium bicarbonate was administered, which narrowed the QRS interval, however, the blood pressure decreased. Intravenous lipid emulsion was administered without improvement. Soon after, the patient had a bradycardic cardiac arrest requiring chest compressions prior to return of spontaneous circulation. The patient was emergently placed on VA-ECMO via femoral cannulation. She was also started on continuous renal replacement therapy (CRRT) for acute renal failure secondary to hypotension. Echocardiogram performed the following day showed left ventricular ejection fraction of less than 10% and "moderate to severely reduced" right ventricular systolic function. Medication serum levels were obtained almost 24 h after patient presentation and after administration of lipid emulsion (see Table). The level of venlafaxine was higher than any other value that we have been able to find in our search of the literature. ECMO catheters were removed approximately 24 h after placement. Mental status and vital signs continued to improve and she was transferred to a medical floor 8 d after initial presentation. The patient was eventually discharged and was neurologically intact.

Case Discussion: This patient had a massive ingestion of various psychoactive, vasoactive, and cardioactive substances that did not respond to aggressive critical care interventions including mechanical ventilation, anti-epileptics, vasopressors, sodium bicarbonate, and intravenous lipid emulsion. ECMO was initiated after the patient arrested to allow organ perfusion while medications metabolized in concert with CRRT. The patient recovered on ECMO with no significant sequella.

Conclusions: This case demonstrated that full recovery from venlafaxine induced cardiogenic shock is possible with the assistance of VA-ECMO, even with serum levels greatly exceeding those previously documented in the literature.

KEYWORDS Venlafaxine; ECMO; overdose

Medication	result (ng/ml)	Reference Range (ng/ml)
venlafaxine	31034	100–500
desmethylvenlafaxine	2982	200–400
aripiprazole	732.3	109–585
lisdexamphetamine	<10	10–200
bupropion	<20	50–100
hydroxybupropion	871	600–2000
methocarbamol	<2 mcg/ml	peak 26–41 mcg/ml

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144. One persistent man: multiple suicide attempts with *Abrus precatorius* seed ingestion

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Background: Jequirity bean (*Abrus precatorius*), prevalent in Asia, consists of abrin containing seeds. The beans have previously been purchased online for suicidal ingestions. The toxin causes gastrointestinal injuries with reports of nervous system demyelination. We describe a 38-year-old male patient, with a history of depression, anxiety and multiple sclerosis, who attempted suicide on three occasions with A. precatorius seeds.
Case series: On initial presentation, the patient ingested twenty to thirty *A. precatorius* seeds purchased online. EMS reported that he experienced nausea, emesis, tachycardia (Heart Rate (HR): 110) and diaphoresis 20 min post exposure. Presenting to the emergency department (ED) 5 h after ingestion, he had ongoing emesis which was managed with ondansetron and IV normal saline. Twenty-four hours after ingestion, the patient's vital signs normalized and he tolerated oral fluids. Forty-two hours after ingestion, he experienced significant abdominal pain and bloody diarrhea. Abdominal X-ray revealed a distended sigmoid colon with bowel wall thickening. His colitis resolved 5 d later. On day 7, he became delirious which persisted for 6 d before he was cleared medically. A few weeks later, the patient again ingested 20 *A. precatorius* seeds. He presented to the ED with nausea and fatigue 2.5 h after ingestion. Within 24 h of ingestion, he experienced diarrhea, sinus tachycardia (HR 140–150) and delirium. At 48 h, the patient's diarrhea resolved but his delirium persisted. The patient was transferred to psychiatry on day 7, and on-going psychosis/delirium continued for another two weeks prior to medical clearance. Sixteen months later, the patient ingested sixty ground-up seeds. He presented to the ED 9 h after ingestion with abdominal cramps, emesis, bloody diarrhea (with visible beans fragments) and hypotension (systolic blood pressure 78). Whole bowel irrigation was performed. At 16 h post ingestion, melena-like, malodorous stool was noted. He was treated with IV fluids, ondansetron and hydromorphone. On day 5, the patient was admitted to the ICU due to a deteriorating level of consciousness (Glasgow Coma Scale: 7), decreased tone in all extremities, up-going Babinski reflex with mydriasis (4–5 mm). The patient had a normal head CT scan, an abnormal EEG with moderate encephalopathy showing a predominant theta rhythm, and a brain MRI showing new evidence of minimal enhancement within peripheral anterior pons lesion consistent with new active demyelination. He was treated with levetiracetam prophylactically. On day 11, his neurological and gastrointestinal symptoms resolved and he was medically cleared.
Case Discussion: To our knowledge, repeated *A. precatorius* ingestion has not previously been reported. The progressive increase in number and grinding of seeds likely contributed to the patient's longer lasting gastrointestinal symptoms and more severe neurological deficits on the third admission. Given the patient's pre-existing Multiple Sclerosis, we can only speculate that his brain demyelination is related to the repeated *A. precatorius* ingestions.
Conclusions: Repeated *A. precatorius* ingestions in the same patient provides a unique opportunity to better understand the clinical course of the ingestion. Collectively, our patient's admissions illustrate the time course and a progressive dose response for abrin toxicity.

KEYWORDS Abrus precatorius; poisoning; demyelination

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145. The effect of plasmapheresis on the elimination half-life of colchicine in a case of fatal overdose

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Background: Colchicine toxicity carries a high mortality rate. There is no antidote and few interventions that may be of benefit beyond aggressive supportive care. There are case reports of plasmapheresis used in colchicine overdose, but limited data on its toxicokinetic effects. We present a fatal case of colchicine toxicity with pre- and post-plasmapheresis levels of whole blood colchicine.
Case report: A 14-year-old girl presented to a community emergency department and was subsequently transferred to a tertiary care center 36 h after a reported overdose of an unknown amount of colchicine. The colchicine was prescribed to the patient's father for gout, but he had consolidated several months of refills leading to an unknown pill count prior to ingestion. Over 60 tablets of colchicine were found in the pill bottle at the time of presentation. The patient had initially presented with nausea and vomiting and was found to have multiorgan failure including renal, hepatic and cardiac. In the pediatric intensive care unit (PICU), she was subsequently intubated for airway protection due to shock. Bedside echocardiography revealed an ejection fraction of 10–15%. Activated charcoal was deferred by the PICU due to poor perfusion. Rifampin was administered for CYP3A4 induction and continued for 5 d in total. She was then placed on extracorporeal membrane oxygenation (ECMO) due to circulatory failure, as well as continuous renal replacement therapy (CRRT), on day 1 of hospitalization. Plasmapheresis was performed, with whole blood colchicine levels of 5.2 micrograms/ml and 4.7 micrograms/ml at 41 and 65 hrs, respectively, available as a post-hoc analysis. The elimination half-life was calculated to be 165 h. On hospital day 7, the patient was found to have a large intracerebral infarct with hemorrhagic conversion and midline shift, likely secondary to carotid artery cannulation during initiation of ECMO. After discussion with family regarding prognosis, she was removed from supportive care on hospital day 8 and subsequently expired.
Case Discussion: The normal elimination half-life of colchicine is 15 h. Toxicokinetic data is limited on colchicine toxicity, as the majority of studies associated with mortality are based on the ingestion dose, which was not available in this case. The initial level of 5.2 micrograms/ml is within the known toxic range of 3.0–24 micrograms/ml, but is further confounded by the delayed presentation in this patient. The half-life of colchicine was likely prolonged in this patient both due to the presumably large dose of ingestion as well as impaired excretion secondary to renal failure. Although there were several interventions to shorten this half-life in addition to plasmapheresis, including CYP3A4 induction, there was no significant effect. Colchicine has significant distribution into red blood cells after 24 h, which may account for the lack of efficacy due to a delayed onset in this patient.
Conclusion: The elimination half-life of colchicine was found to be 165 h during plasmapheresis compared to a normal elimination half-life of 15 h. Plasmapharesis is unlikely to benefit cases of delayed colchicine toxicity.

KEYWORDS Colchicine; plasmapheresis; toxicokinetics

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146. Mercury rising: 6 month course of toxicity after acute mercuric chloride ingestion

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Background: Mercuric chloride ($HgCl_2$) causes acute severe gastrointestinal and nephrotoxicity with lethality frequently occurring at doses of 1–4 g. We discuss issues regarding decontamination, chelation, enhanced elimination, and prevention of secondary exposure of healthcare workers.
Case report: An otherwise healthy 44-year-old man admitted to ingesting 10 g of mercuric chloride ($HgCl_2$) in a suicide attempt. He presented with hypersalivation, hypertension, tachycardia, and with copious brown emesis and watery diarrhea. Treatment was initiated with 50 g of activated charcoal, orograstric lavage, and whole bowel irrigation. Abdominal radiographs demonstrated no radiopaque material. Dimercaprol was ordered at 3 mg/kg every 4 h intramuscular, but was unavailable for administration until 6 h after patient presentation. The patient refused IM dimercaprol after the third dose due to pain. He was admitted to the intensive care unit where all body fluids were collected in hazardous waste containers. Strict contact precautions were implemented despite toxicology recommendations. Anuric renal failure with a peak creatinine of 10 mg/dl occurred. The patient experienced hepatic injury with a peak AST of 686 IU/dl and muscle injury with a peak creatine kinase of 3028 IU/dl. Initial whole blood and urine mercury levels were <160 μg/l. After one week of hemodialysis his renal function returned to pre-injury levels. He was discharged on oral dimercaptosuccinic acid (DMSA), but required multiple readmissions and retreatment with DMSA over the following 6 months. His long term course was complicated by persistant altered mental status, esophageal dismotility, aspiration, pyloric stenosis, and malabsorption. Six months post ingestion his whole blood and urine mercury levels remained >160 μg/l.
Case discussion: This case demonstrates acute tubular necrosis, metabolic acidosis, and caustic gastrointestinal injury after HgCl2 ingestion. The case was complicated by difficulty securing chelators, concerns about secondary exposure, and patient non-compliance with chelation.
Conclusions: Deliberate self-harm mercuric chloride ingestion may result in severe sequelae, prolonged and intensive treatment course, and complicated logistics of obtaining antidote and disposing of waste products.

KEYWORDS Heavy metals; chelation; dialysis

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147. Intravenous zoletil poisoning

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Background: Zoletil is a combination of zolazepam and tiletamine, and is a veterinary anesthetic for dogs, cats, wild animals, and zoo animals. Tiletamine hydrochloride is an arylminocycloalkanone dissociative anesthetic, while zolazepam hydrochloride is a nonphenothiazine diazepinone. It is very rare for tiletamine/zolazepam to be directly injected into the vein.
Case reports: A 39-year-old male came to the hospital with decreased consciousness. When the patient was brought in, his GCS was 6, while initial vital signs showed 120/80 mmHg blood pressure, 90/min pulse rate, 28/min breathing rate, 36.9 °C body temperature, and 98% O_2 saturation. His physical examination showed an isocoric 3 mm pupil, while the pupillary light reflex was normal, and nothing abnormal was found. The medical team suspected this case to be a suicide poisoning and found a 50 ml syringe and a receipt for an animal anesthetic in his bag. It was confirmed by the place of purchase that he had purchased 6 vials of zoletil 50 (tiletamine hydrochloride 125 mg, zolazepam hydrochloride 125 mg). One hour after the patient's arrival, his breathing weakened and the O_2 saturation decreased to 85%. The medical team carried out an intubation and provided 7 L/min oxygen, and the ABGA was pH 7.19, PaO_2 257.2 mmHg, $PaCO_2$ 71.1 mmHg, HCO_3 – 28.0 mmol/l, and SaO_2 99.9%. Mechanical ventilation was applied in order to assist with ventilation. Twenty hours after the patient's arrival, he regained consciousness and the intubation and mechanical ventilation was removed. The total poisoned dosage was 1500 mg of tiletamine/zolazepam (21.4 mg/kg). The patient was transferred to the department of neuropsychiatry after 3 d of being brought to the hospital.
Case discussion: This drug induces anesthesia very quickly, causing the breathing rate of the injected animal to double for 15 min after the injection, tidal volume to decrease to less than half of control values, and pO_2 to decrease. Poisoning reports in humans are very rare and are usually related to drug abuse. Syncope, decreased mentality, and involuntary movement were some of the accompanying symptoms.
Conclusions: Acute zoletil intoxication is generally abuse for recreational purposes, but acute poisoning due to a large amount of zoletil in a suicide attempt causes severe symptoms of poisoning. It is mandatory for doctors in the emergency department to be able to decide the appropriate stage for intubation by repeatedly evaluating the condition of the respiratory tract and breathing.

KEYWORDS Poisoning; zoletil; tiletamine

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148. Phenazopyridine induced methemoglobemia successfully treated with ascorbic acid reported to a regional poison control center

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Context: Methemoglobin is produced by the oxidation of the normal ferrous ion in the heme complex to the ferric form which does not combine with oxygen. This reduces the ability to deliver oxygen throughout the body by shifting the oxygen dissociation curve to the left, and results in diminished oxygen unloading in the tissues and causes hypoxia. There are many different medications, including phenazopyridine, that have the potential to cause methemoglobinemia, especially in an overdose setting. Methylene blue is the first line treatment for induced methemoglobinemia, however ascorbic acid may be considered in other scenarios, due to its ability to act as an oxidant. There are few cases discussed in literature, and the optimal dosing remains unclear.
Case presentation: A 20-year-old, 6-week pregnant, 57 kg female with suicidal intent ingested 20 tablets of 95 mg phenazopyridine 4 h prior to coming to the emergency department. Upon arrival she complained of nausea, vomiting, and diffuse abdominal pain.

Her initial vitals were heart rate 76, respiratory rate 18, blood pressure 131/71, oxygen saturation 96% on room air and temperature of 98.6F. About 8 h after arrival, her oxygen saturation dropped to 84% on room air and only improved to 88% with a 100% oxygen nonrebreather mask. She complained of dizziness and dyspnea. A methemoglobin level was checked and found to be 33.8%. Since Methylene blue is pregnancy category X, the treating physician ordered and administered ascorbic acid 1500 mg IV (2.6 mg/kg) every 6 h. An hour after the initial dose, the patient's color improved, dyspnea resolved and oxygen saturation increase to 92% on the nonrebreather. She was given a total of 8 doses of ascorbic acid, totaling 12 g over her stay. Her final methemoglobin level was checked at 23 h post ingestion and was 2.4%.
Conclusion: As presented in this case, ascorbic acid is an effective alternative for methemoglobinemia treatment when methylene blue is contraindicated. It may also be an effective alternative when methylene blue is not readily available or if a patient is glucose-6-phosphate-dehydrogenase (G6PD) deficient. More research on the use of ascorbic acid for methemoglobinemia treatment is needed to determine the optimal dose and scenario that will produce the best clinical outcomes.

KEYWORDS Methemoglobinemia; phenazopyridine; ascorbic acid

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149. Caffeine through the (hemodialysis) filter

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Background: Caffeine (1,3,7-trimethylxanthine) antagonizes central adenosine receptors and releases endogenous catecholamines through beta-adrenergic stimulation, resulting in tachycardia, hypertension and central nervous system stimulation. In overdose, caffeine inhibits phosphodiesterase, causing smooth muscle relaxation and peripheral vasodilation. Caffeine-induced hemodynamic instability is commonly followed by metabolic disturbances. Peak serum concentration is 30–60 min and elimination half-life is 4.5–16 h. Caffeine's low volume of distribution and protein binding make it a candidate for hemodialysis in severely intoxicated patients.
Case report: A 21-year-old, 1.62 m tall, 91.1 kg female presented to a regional hospital emergency department with vomiting 1 h after ingesting 20 caffeine tablets of unknown strength. Initial labs revealed a potassium (K) 2.3 mEq/l, CO_2 14 mEq/l and glucose 141 mg/dl. Initial vital signs were HR 98 bpm, BP 129/65 mmHg, SpO_2 100% on room air, respiratory rate 18 and afebrile. After administration of 1L isotonic fluids and 10 mEq K, potassium was 1.9 mEq/l and CO_2 10 mEq/l. She was transferred to a referral center for initiation of hemodialysis. Sodium bicarbonate therapy was contraindicated given profound hypokalemia. The patient became anxious, confused and restless with vital signs evolving to HR 100bpm, BP 152/95 mmHg, RR 20–30BPM. The patient was acidemic with lactate 10.4 mmol/l and pH 7.22 on arterial blood gas. Potassium was replaced, 50 mEq sodium bicarbonate administered and 2L fluids infused during hemodialysis. After 4 h of hemodialysis using an Optiflux® 160 Dialyzer (300 ml/min blood flow rate, urea clearance 271 ml/min) repeat labs showed pH 7.53, CO_2 21 mEq/l, lactate 6.4 mmol/l and K 3.6 mEq/l. Vital signs improved to HR 77bpm, BP 104/58 mmHg, and RR 16 after hemodialysis. Fourteen hours after presentation her mental status improved to baseline, vital signs remained within normal limits, lactate decreased to 1.6 mmol/l, and repeat CO_2 was 22 mEq/l. On day 3 post-ingestion the patient was discharged. A caffeine level drawn 17 h after dialysis was 19.6 mcg/ml(therapeutic range 1–10 mcg/ml). No additional etiologies of acidosis and electrolyte disturbances were uncovered.
Case discussion: Massive caffeine ingestions have been reported with positive outcomes using hemodialysis; however, they commonly present with initial deterioration in vital signs. Our case displays the potential for severe metabolic disturbances as an indication for early hemodialysis prior to vital sign abnormalities. Initial serum caffeine concentration, A, was estimated at approximately 78 mcg/ml using the formula: $t = [-V^{*}\ln(19.6/A)\ /0.06^{*}k]$, where t is dialysis time required to reach serum caffeine concentration of 19.6 mcg/ml, V is Watson estimate of total body water, and k is 80% of specific dialyzer urea clearance (ml/min) at specified blood flow rate. However, using a conservative estimation of one elimination half-life between conclusion of dialysis and blood draw, the initial caffeine serum concentration may have been as high as 155 mcg/ml. Early initiation of hemodialysis should be considered in all caffeine ingestions presenting with refractory hypokalemia or acidosis, despite absence of hemodynamic instability.
Conclusion: We report significant hypokalemia, metabolic acidosis and hyperlactatemia secondary to caffeine intoxication occurring prior to hemodynamic instability. Severe metabolic derangements in a hemodynamically stable patient may require initiation of hemodialysis. After 4 h of hemodialysis, acidemia and electrolyte disturbances were corrected, allowing for a full and rapid recovery.

KEYWORDS Caffeine; hemodialysis; acidosis

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150. CRRT for metformin toxicity: is it enough?

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Background: Metformin is a biguanide antihyperglycemic medication commonly prescribed to patients with type 2 diabetes. Overdose can cause severe toxicity (typical plasma level greater than [>] 5 micrograms per milliliter [mcg/ml]), and metformin-associated lactic acidosis (MALA) is well-described in the literature. Extracorporeal treatment (ECT) is of benefit in mitigating profound lactic acidosis and in expediting metformin clearance. The Extracorporeal Treatments in Poisoning Workgroup (EXTRIP) describes metformin as a moderately dialyzable xenobiotic and advises use of ECT in patients with severe or refractory lactic acidosis, shock, or decreased mentation. EXTRIP recommends initial treatment with intermittent hemodialysis (HD), however continuous renal replacement therapy (CRRT) is a second-line option when HD is unavailable. HD effectively dialyzes metformin, whereas CRRT removes metformin only about 25% as efficiently; median metformin clearance is 148 ml/min with HD compared to 34 ml/min with CRRT. CRRT has been successful in treating patients with MALA, however some patients have required prolonged courses (> 30 h) of full-dose HD. One study demonstrated only 17% of the amount ingested (3.5 of 10.6 g) was removed after 10.5 h of CRRT. We present a case of metformin toxicity as

evidenced by refractory MALA in which CRRT was ineffective in both correcting lactic acidosis and eliminating metformin.
Case report: A 38-year-old male was brought to the Emergency Department (ED) via ambulance as a trauma activation after he had reportedly ingested an unknown quantity of pills and cut himself in the neck as a suicide attempt during a police standoff at his home. Multiple medications were found on scene, and an intact metformin tablet was identified in the patient's emesis. While surgery evaluated his superficial neck wound, blood testing returned significant for pH 7.02 and lactate 12.7 milligrams per deciliter (mg/dl). The Medical Toxicology service was consulted for concern of MALA. During his hospital course, the patient suffered from worsening lactic acidosis with refractory shock and acute kidney failure despite infusion of sodium acetate and multiple high-dose vasoactive medications. CRRT was initiated and continued for approximately 39 h, with maximum effluent flow rate 56 milliliters per kilogram per hour (ml/kg/h, standard is 20 ml/kg/h). Despite multiple aggressive interventions including lipid emulsion therapy and extracorporeal membrane oxygenation, care was ultimately deemed futile, and the patient expired approximately 60 h after presentation. Plasma metformin levels were drawn and sent to an off-site laboratory for comparison. Level drawn prior to CRRT was 260 mcg/ml, and level after 39 h of CRRT was 46 mcg/ml.
Discussion: MALA is more likely with plasma metformin level >5 mcg/ml, and metformin is considered moderately dialyzable. Our patient's laboratory analysis confirmed that prolonged CRRT did eliminate 82% of the drug, however even after 39 h the amount of residual metformin was still over nine times the potentially toxic dose. In cases of metformin toxicity where ECT is necessary to both treat refractory acidosis and remove the offending agent, HD may prove more efficient than CRRT.

KEYWORDS Metformin; acidosis; dialysis

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151. Severe potassium poisoning after intentional ingestion

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Background: Potassium chloride (KCl) is routinely consumed by the general public as a nutritionally acceptable salt substitute, and it is commonly recommended by physicians for the treatment and prophylaxis of hypokalemia. Oral KCl is a common choice for replenishing and maintaining potassium levels in individuals with ongoing potassium loss. Historically, oral administration of KCl in individuals with normal renal mechanism for potassium excretion was believed to be relatively safe with minimal risk for serious hyperkalemia. We present a case of critical hyperkalemia due to oral KCl ingestion.
Case report: A 41-year-old female reportedly ingested up to 80 tablets of 20 milliequivalent extended release KCl tablets in a suicide attempt. The patient was assessed in the emergency department and noted to be alert and oriented, however she was bradycardic as low as 30 bpm. She was also noted to have electrocardiographic changes including a widened QRS complex and peaked T waves. A diagnosis of hyperkalemia was made and emergent interventions were performed, including administration of intravenous crystalloid, calcium gluconate, dextrose, insulin, and nebulized albuterol. The comprehensive metabolic panel revealed a critical serum potassium level of 10.3 milligrams per deciliter (mg/dl) in the setting of normal renal function (creatinine 1.1 mg/dl). The patient was transferred to a hospital capable of performing hemodialysis (HD). On arrival to the receiving hospital, approximately 4 h after initial presentation, she became pulseless and apneic but was able to be resuscitated. After resuscitation, repeat testing revealed a potassium level still critically elevated at 8.2 mg/dl. Emergent HD was performed. Forty-six hours post ingestion and two rounds of intermittent HD later, the serum potassium level had normalized to 5.0 mg/dl. The patient subsequently made a full recovery.
Conclusion: Oral KCl is generally considered safe for potassium repletion except in patients with substantially reduced glomerular filtration rate. This case illustrated a critically elevated serum potassium level (10.3 mg/dl) following acute overdose in a patient with normal renal function. It is important to maintain a high index of suspicion for life-threatening hyperkalemia in a suicidal patient with reported oral KCl ingestion.

KEYWORDS Potassium; hyperkalemia; critical

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152. Some pains never go away

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Introduction: Propoxyphene was removed from the market in 2010, citing significant cardiac toxicity and numerous deaths; minimal propoxyphene exposures are expected 8 years later. We report a case with major adverse effects from likely propoxyphene/acetaminophen overdose – a prescription filled 9 years prior to ingestion.
Case report: A 21-year-old woman found altered at home was brought to an emergency department unresponsive after three seizures: two en route, each terminated by diazepam. She was missing 6 fluoxetine 20 mg and 3 olanzapine 5 mg tablets, per pill count. Initial vital signs: heart rate (HR) 115bpm, blood pressure (BP) 69/32 mmHg, respiratory rate 28, temperature 97 °F, 99% SpO_2 on 15 ml/min oxygen. Significant laboratory findings: bicarbonate <8 mmol/l and serum acetaminophen (APAP) 89 mcg/ml. Intravenous N-acetylcysteine (NAC) was initiated. She was intubated, sedated with midazolam, and transferred to a tertiary facility. Six hours later, her BP was 90/30 mmHg despite two vasopressors, HR 124bpm. No further seizures were noted, however deep-tendon reflexes were absent and pupils fixed and dilated. EKG showed wide-complex sinus tachycardia with QRS 118 ms (baseline 90 ms), and QTc 494 ms. Labs at this time: pH 6.96, pCO_2 <19 mmHg, pO_2 168 mmHg, serum lactate immeasurably high, and serum salicylate, methanol, and ethylene glycol levels all undetectable; her liver panel was without abnormalities. Infusion of NAC continued along with sodium bicarbonate and antibiotics. She had no seizure history, but with history of an ambiguous pituitary tumor. Within 2 d she developed grade IV encephalopathy, acute renal failure requiring renal replacement therapy, rhabdomyolysis, hypotension refractory to 4 vasopressors, coagulopathy, and hemoccult-positive stool. Electroencephalogram (EEG) showed global cortical dysfunction, and echocardiogram demonstrated normal left ventricular function. Serum APAP 14 h post-presentation was 97 mcg/ml with INR 6.8, AST 270, and ALT 75. Maximum INR 8.4 on hospital day 2 (HD-2) and was down to 1.6 by HD-6 after fresh frozen plasma administration. AST and ALT peaked at 3299 units/l and 3633 units/l, respectively, on HD-5. Transaminases improved to <1000 units/l on HD-9. On HD-3 she regained reflexes and spontaneous movements. Vasopressors were discontinued on HD-5. Two

subsequent EEGs showed no further seizure activity. On HD-6 it was revealed that she had access to an old prescription of propoxyphene/acetaminophen that expired in 2008. She was eventually extubated on HD-9. On HD-14, a long-term dialysis catheter was placed due to persistent renal failure and anuria. Her mental status improved, but she remained amnestic to the events surrounding hospitalization.

Discussion: Our patient was profoundly ill from an initially-unclear process. Although laboratory confirmation of propoxyphene exposure was not obtained, her presentation of seizures, prolonged QRS, hypotension and elevated acetaminophen levels fits with known mechanisms of propoxyphene/acetaminophen. Propoxyphene is a synthetic opioid with sodium channel-blocking properties. Both propoxyphene and its major metabolite, nordextropropoxyphene, contribute to toxicity. The elimination half-life of propoxyphene is 6–12 h – nordextropropoxyphene up to 44 h. Previous studies have proven the futility of hemodialysis to enhance these xenobiotics' elimination, likely because of large volume of distribution and high protein binding.

Conclusion: Although it was removed from the market 8 years ago, propoxyphene can still cause significant toxicity today.

KEYWORDS Propoxyphene; darvocet; overdose

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153. Increased incidence of alleged adolescent suicidal ingestions from 2008 to 2017

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Background: Suicide in Mississippi represents the second leading cause of death for young persons aged 10–24 years per the Centers for Disease Control and Prevention. Statistical data on alleged suicidal attempts by drug ingestions remains difficult to estimate. The aim of this study was to report alleged suicidal attempts and suicides in adolescents reported to the state Poison Control Center (PCC) over a 10-year period. Secondary objectives included comparing trends based on gender and age categories (10–14 years and 15–19 years) and the most common substances reported in alleged suicidal attempts.

Methods: The Mississippi Poison Control Center's reported cases were queried for all alleged suicide exposures for persons aged 10–19 years from 2008 to 2017. The number of exposures, substances reported, and exposure outcomes were evaluated based on gender and two age groups (10–14 years and 15–19 years).

Results: Reported alleged suicide ingestions in adolescents increased steadily by 9.5% each year. Overall, adolescent females increased by 147% in the 10 year period with the majority of these cases representing those aged 15–19 years of age (Figure 1). Adolescent male ingestions only rose by 68% over this period. Females between 15and 19 years of age represented 57.9% of the total cases reported for alleged adolescent suicide attempts between 2008 and 2017. Serious toxicity (defined as death or PCC rating of major or moderate toxicity) was more likely in adolescent males when compared to adolescent females (21.3% versus 15%; $p < .05$). However due to a much larger number of female cases, the absolute number of female ingestions resulting in serious toxicity was greater than the absolute number of males ingestions (533 cases versus 222 cases) (Table 1). In the 10 year period, there were 4 deaths reported. All deaths were in adolescents between the ages of 17 and 19, with three of these fatalities in females. The five most common drug classes involved in these intentional adolescent exposures were aspirin/NSAIDS (15.5%), acetaminophen (14.8%), antidepressants (12.7%), opiates (7.4%), and antipsychotics (7.1%). Of the most commonly reported substances, the relative percent of alleged ingestions involving antidepressants increased the most, while the relative percent of opiates decreased over the 10-year period (Table 2). The following drug categories were present in less than 5% of the adolescent suicidal ingestions: ADHD medications,anticonvulsants-mood stabilizers, antihypertensives, benzodiazepines, diphenhydramine, OTC medications, and ethanol.

Conclusion: Alleged adolescent suicidal attempts from drug ingestion have been steadily rising in Mississippi over the past ten years. The greatest increase is in females age 15–19 years of age, followed by females age 11–14 years of age. Males were statistically more likely to experience signs of significant toxicity. However, the absolute number of exposures resulting in death or PCC ratings of serious toxicities were greater in adolescent females. The most commonly involved substances were non-opioid analgesics (acetaminophen, aspirin and NSAIDS) and antidepressants. This information can be used to help target at-risk groups of adolescents and should prompt further study into the causes of this self-harm.

ADOLESCENT ALLEGED SUICIDAL INGESTIONS (FIGURE 1)

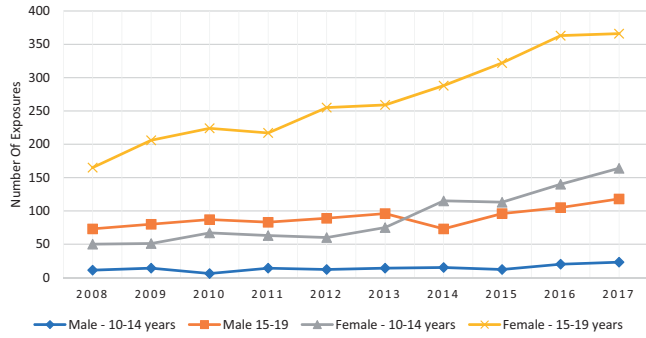

Table 1. Adolescent exposures by severity ratings.

	Total cases (all severity)	Moderate	Major	Death	Significant toxicity (moderate, major, or death)
Male (10–19 years)	1041	194 (18.6%)	27 (2.6%)	1 (0.1%)	222 (21.3%)
Female (10–19 years)	3563	486 (13.6%)	44 (1.2%)	3 (0.08%)	533 (15.0%)
All genders (10–19 years)	4604	680 (14.8%)	71 (1.5%)	4 (0.09%)	755 (16.4%)

Table 2. Relative percent of yearly exposures for top five medication classes.

	Aspirin/ NSAIDS	Acetaminophen	Antidepressants	Opiates	Antipsychotics
2008	22.1%	28.8%	15.4%	14.4%	9.4%
2009	22.2%	24.2%	14.5%	15.1%	10.5%
2010	21.9%	26.6%	17.2%	15.9%	13.8%
2011	19.9%	21.2%	18.3%	13.0%	13.8%
2012	21.9%	20.7%	18.3%	12.5%	13.7%
2013	22.1%	19.8%	21.2%	7.4%	8.6%
2014	23.4%	17.5%	16.9%	6.9%	10.4%
2015	23.2%	18.4%	22.1%	8.5%	6.8%
2016	20.7%	20.7%	18.0%	9.4%	10.0%
2017	24.1%	21.0%	18.8%	8.6%	8.0%

KEYWORDS Adolescent; suicide; Poison Center
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154. Intravenous nicardipine in the treatment of cocaine-induced peripheral vasospasm: a case report

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Background: Cocaine-induced vasospasm is a complication of cocaine abuse. It occurs through mechanisms suspected to be partially dependent on calcium release. Few publications review the management of this condition but most advise the administration of parenteral phentolamine, which is contraindicated in hypotensive patients. We present a case in which intravenous nicardipine was administered due to its documented effect in other vasospastic conditions such as subarachnoid hemorrhage.
Case report: A 32-year-old female cocaine abuser presented with severe pain and discoloration of three extremities. Her systolic blood pressure was 80 mmHg, with a heart rate of 70–110 bpm in sinus rhythm. There was no sign of acute sympathomimetic intoxication otherwise. An abdominal angio-tomodensitometry done to rule out aortic dissection and thrombosis showed diffuse peripheral vasospasm. The patient's vitals remained unchanged during the first 24 h. She received aspirin 460 mg PO, an heparin infusion as per protocol and epoprostenol 0.3 mg IV push-dose followed by an infusion as per protocol. Upon arrival, IV solumedrol 250 mg and 80 mg every 6 h was given for possible vasculitis. Intra-arterial access was obtained by interventional radiology and 2.5 mg of phentolamine was injected followed by 2.5 mg hourly for 16 h with transient (less than 1–2 min) improvement in the symptoms after each dose. A diltiazem infusion at 5 mg/h was subsequently administered for 12 h. The use of aspirin, heparin, epoprostenol, diltiazem and corticosteroids resulted in little to no clinical improvement in the patient's condition. Nitrates were contraindicated due to hypotension. Laboratory analyses (troponin and lactate) stayed within normal range. Thus, a nicardipine infusion at 2.5 mg/h was started 48 h after presentation. There was a delay in obtaining the Health Canada special access authorization and then the medication. Significant improvement in extremity color and pain were noted within the first hour after nicardipine administration. Blood pressures remained unchanged. Radiological confirmation of the vasospasm resolution occurred 16 h after the first administration of nicardipine.
Case discussion: We report the first case of a protracted cocaine-induced peripheral vasospasm treated successfully with a dihydropyridine calcium-channel blocker, nicardipine. Nicardipine is pharmacologically more vaso-selective than non-dihydropyridines which may account for its efficacy in our case. The use of nicardipine in coronary and cerebral vasospasm appears to be an effective treatment option, although no published data demonstrated similar results for cocaine-induced peripheral vasospasm. In our opinion its use was limb-salvaging for our patient.
Conclusions: Nicardipine was effective in reversing the cocaine-induced peripheral vasospasm in this patient when phentolamine was contraindicated due to hypotension. While controlled studies could confirm this benefit, physicians need to be aware that IV nicardipine is an alternative when other therapies fail.

KEYWORDS Cocaine; vasospasm; nicardipine
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155. A rare cause of a rare exposure: elevated serum aluminum levels after intravesical alum instillation for hemorrhagic cystitis

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Background: Acute aluminum toxicity is uncommon but can be fatal. Common symptoms include encephalopathy, myoclonus, and seizure. Intravesical alum instillation is a treatment option for hemorrhagic cystitis and can be a rare cause of acute aluminum toxicity.
Case report: This is a single patient chart review. A 52-year-old female was admitted for hematuria and acute blood loss anemia requiring transfusion of 28 units of packed red blood cells throughout her hospital stay. She had a history of chronic kidney disease as well as endometrial cancer which was treated with radiation resulting in hemorrhagic radiation cystitis which was refractory to typical treatment. Intravesical alum instillations with a 1% aluminum solution were initiated and continued for 9 d. During that time she developed severe septic shock due to a urinary tract infection related to dislodgement of her nephrostomy tubes. She was intubated and started on four different vasopressors to stabilize her blood pressure. Her illness was complicated by acute kidney failure with peak creatinine of 4 mg/dl. Multiple serum aluminum levels were obtained and gradually increased. On day 8 of treatment with alum instillation her level was 48 mcg/l and 6 d later peaked at 182 mcg/l. She recovered from her sepsis and was extubated about the same time the peak elevations in her serum aluminum levels occurred. Since the patient did not display symptoms consistent with acute aluminum toxicity it was decided to monitor her closely and trend her levels. She continued to improve without any encephalopathy, myoclonus, or seizures. Approximately 2 months after cessation of her alum instillations she remained asymptomatic and her level had trended down to 88 mcg/l.
Case discussion: Aluminum is renally cleared and thus patients with kidney disease are prone to acute aluminum toxicity. Serum levels do not correlate well with symptoms and patients have had severe toxicity with levels as low as 17 mcg/l or have been asymptomatic like our patient with a level of 182 mcg/l. Chelation with deferoxamine is the preferred treatment of choice for aluminum toxicity and may need to be combined with hemodialysis in the presence of renal dysfunction.
Conclusion: Our case shows that intravesical alum instillation can cause severely elevated serum aluminum levels. However, these levels poorly correlate to symptoms and outcome. More research is needed to help determine which patients will experience toxicity and which will remain asymptomatic.

KEYWORDS Aluminum toxicity; intravesical alum instillation; hemorrhagic cystitis
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156. Transaminitis caused by trimethoprim-sulfamethoxazole treated with N-acetylcysteine: a case report

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Background: Trimethoprim-sulfamethoxazole (TMP-SMX) is a widely used antibiotic and rarely causes hepatic injuries, but cases of hepatocellular, mixed hepatocellular/cholestatic and cholestatic hepatic injuries caused by TMP-SMX have been reported. These injuries tend to resolve over 2 to 8 weeks and very rarely lead to fulminant hepatic failure. Besides removal of the offending agent, there is no standard treatment of non-acetaminophen (APAP) drug induced liver injury (DILD), although steroids have been administered. Data from Acute Liver Failure Study group suggest that in adults N-Acetyl Cysteine (NAC) may have benefits in the treatment of non-acetaminophen DILI. This report describes a case of TMP-SMX DILI, treated with NAC.
Case report: A healthy 44-year-old female with psoriasis managed with topical fluocinocinde developed fever, nausea, vomiting and a diffuse maculopapular rash 3–4 d after starting a 5 d course of TMP-SMX for a suspected asymptomatic urinary tract infection. (See Picture 1 for the rash.) She had no history of liver disease or alcohol abuse, and her previous transaminase levels were within normal range. Evaluation revealed a hepatocellular pattern of liver inflammation with the following laboratory
Results: Acetaminophen undetectable, Aspartate Aminotransferase (AST) 7137 U/l, Alanine Aminotransferase (ALT) 5149 U/l, total bilirubin of 1.9 mg/dl, alkaline phosphatase of 164 U/l, and International Normalized Ratio (INR) 1.6. Ultrasound of the liver did not show any pathological changes except fatty liver. Two days after completion of this course of TMP-SMX, patient continued to have malaise, nausea, and right upper quadrant pain although her rash had subsided. Repeat tests at that time showed an AST 6916 IU/l and ALT 11,055 IU/l, and intravenous NAC was started. She received 37 h intravenous NAC – a standard 21 h course plus an additional 100 mg/kg over 16 h. She tolerated NAC well without any adverse effect, and her liver function tests improved rapidly over the next 3 d. Her clinical condition improved as well, and she was discharged with an ALT 897 IU/l, an AST of 119 IU/l and INR of 1.14 on hospital day 4. (See Chart 1 for the chronological changes of her ALT laboratory results).

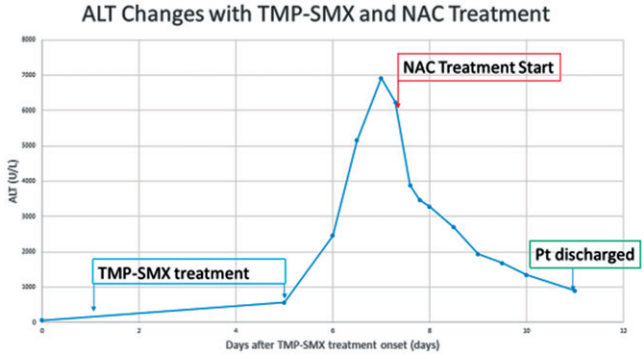

Chart 1.

Case discussion: TMP-SMX is a rare cause of liver injury. (See Table 1 for the previous case reports on DILI by TMP-SMX.) The mainstay of treatment for DILI is withdrawal of the offending agent and supportive care. Steroids have been used in some cases and fulminant hepatic failure has led to hepatic transplant. The use of NAC for TMP-SMX DILI has not previously been described.
Conclusion: This case of TMP-SMX DILI was treated with NAC in addition to usual supportive care. NAC was well tolerated without adverse effect. Whether NAC had any impact on her clinical course is entirely speculative, but it is worthy of further investigation on the effectiveness of NAC treatment in the cases of TMP-SMX DILI.

KEYWORDS Trimethoprim-sulfamethoxazole (TMP-SMX); N-acetylcysteine (NAC); Alanine Aminotransferase (ALT) Test

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157. Loperamide associated torsades de pointes in marginally supratherapeutic dosing, 20 mg daily

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Introduction: Amidst the opioid epidemic, high-dose loperamide has become abused and used to ameliorate opioid withdrawal symptoms. In this context, there is a well-documented risk of developing Torsades de Pointes (TdP). We present a case of loperamide associated TdP, in the context of third degree heart block, at marginally supratherapeutic dosing.
Case presentation: A 64-year-old man presented to the emergency department (ED) with six months of recurrent lightheadedness and syncope on the day of admission. He had chronic diarrhea from Crohn's disease and for a year had been taking 12 mg of loperamide in the morning and 8 mg at night. His only additional medication was simvastatin. In the ED, he was found to be bradycardic to 34 bpm, with a blood pressure of 146/82 mm Hg, respiratory rate 20, Sp02 98% on 2L nasal cannula and afebrile. An electrocardiogram revealed complete heart block with QTc of 523. Twenty minutes after arrival he lost consciousness and his cardiac monitor showed polymorphic ventricular tachycardia (VT) at 220 bpm with concern for TdP. His VT self-terminated after 30 s, he regained consciousness and his bradycardia resumed. Serum complete blood count, electrolytes, renal and liver function, magnesium, phosphorus, thyroid-stimulating

1	year	sources	age	gender	clinical symptoms	treatment	outcome	additional drug exposure
2	2013	Ng, et al	17	M	fever, myalgia and rash	liver dialysis	survived	isotretinoin
3	2010	Bell, et al	9	M	fever, HA, neck pain	med discontinuation	survived	acetaminophen
4	2007	Kouklakis, et al	30	M	cholestatic hepatitis, fever, rash	prednisolone	survived	none
5	2003	Zaman, et al	23	M	Myalgia, fever, rash	liver transplant	survived	none
6	2003	Mainra, et al	24	F	rash, thrombocytopenia	med discontinuation	survived	none
7	2000	Ilario, et al	60	F	fever	med discontinuation	died	phenytoin
8	1989	Alberti-Flor, et al	26	M	maculopapular rash, abdo pain	med discontinuation	died	nitrofurantoin, doxycycline
9	1981	Ransohoff & Jacobs	70	M	jaundice, rash	neomycin	died	acetaminophen

Table 1.

hormone, troponin were unremarkable. Bedside echocardiogram showed normal ejection fraction. His head CT revealed a punctate hyperdensity to the medial left temporal lobe and small hemorrhage. A repeat CT several hours later was unchanged. He received intravenous magnesium, and cardiology was consulted. The patient was stabilized with a temporary transvenous pacemaker and then received permanent pacemaker placement the following day. At admission, his loperamide level was 8.2 ng/ml (prior investigations showed peak plasma concentrations of about 8 ng/ml after a single oral bolus of 16 mg) and his N-desmethyl-loperamide level was 9.8 ng/ml. He was discharged without further complication. Two weeks later, the patient was well with no further episodes of syncope, or presyncope. He was counseled to discontinue loperamide.

Discussion: The maximum approved prescription dose of loperamide is 16 mg, daily. Doses of up to 32 mg daily are typical to treat diarrhea associated with loop ileostomy and short bowel syndrome. Previous cases of loperamide induced cardiotoxicity have reported levels from 2 ng/ml (3 d into hospitalization) to as high as 210 ng/ml. This case is exceptional because it highlights the risk for QTc prolongation and TdP in narrowly supratherapeutic dosing of loperamide. The desmethyl metabolite of loperamide shows weak K+-rectifier current inhibition and may contribute to QTc prolongation. The presence of a therapeutic serum level of loperamide, at the time of Tdp, and in the context of his history, prompted us to counsel him in its cessation for fear of precipitation of further malignant arrhythmia. Third degree heart block increases the risk for TdP in patients with long QTc. This case further underscores that providers should find third degree heart block particularly worrisome as a high risk feature in the setting of drug induced QTc prolongation.

KEYWORDS Loperamide; torsades; QTc

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158. Pediatric deaths associated with over-the-counter cough and cold medication exposures

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Background: In 2008, in response to reports of serious adverse events associated with pediatric over-the-counter cough and cold medication (CCM) exposures, drug manufacturers voluntarily withdrew infant CCMs from the market and released labeling changes instructing caregivers not to use CCMs in children <4-years-old. Later updates advised avoiding CCMs in children <2-years-old, and additional warnings instructed caregivers to not to use certain antihistamines to sedate children. These changes were supported by the Food and Drug Administration (FDA). A comprehensive assessment of pediatric deaths associated with these exposures has not been performed since 2009. The purpose of this report is to describe fatalities associated with exposures to CCMs in children <12-years-old that were detected by a safety surveillance system from 2008 to 2015.

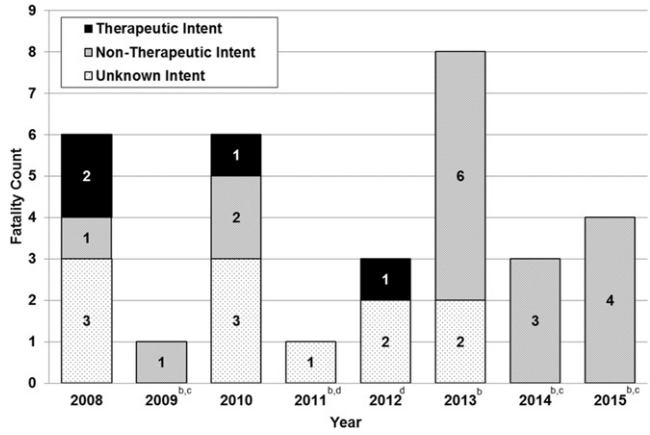

Figure. Annual counts of pediatric deaths potentially related or related to CCMs by event year (2008–2015).[a]
[a]39 fatalities occurred before 2008 or had no event date and were excluded from the figure; [b]No deaths were determined to have therapeutic intent; [c]No deaths were determined to have unknown intent; [d]No deaths were determined to have non-therapeutic intent.

Methods: Fatalities in children <12-years-old reported via the National Poison Data System (NPDS), FDA's Adverse Event Reporting System (FAERS), media reports, English language medical literature, or reports to participating manufacturers were collected from 2008 to 2015, regardless of death date. Case inclusion criteria were oral exposure in the United States to ≥1 of 8 index ingredients: brompheniramine, chlorpheniramine, dextromethorphan, diphenhydramine, doxylamine, guaifenesin, phenylephrine, or pseudoephedrine. A panel of experts reviewed cases to determine if the causal relationship between the exposure and death was "related," "potentially related," "unlikely related," or "unable to determine." Cases judged "related" or "potentially related" were further categorized as having therapeutic, non-therapeutic, or unknown intent and involving a therapeutic dose, overdose, or unknown dose.

Results: Of 172 fatality cases detected, 164 met inclusion criteria and were reviewed by the panel. The panel judged 71/164 deaths (43%) as "related" or "potentially related" while 68 deaths (41%) were judged "unable to determine." This analysis focuses on fatalities involving CCMs determined to be at least potentially related to the death. The majority involved children <2-years-old (55, 77%). The panel determined overdose occurred in 41% ($n = 29$) while an "unknown" dose occurred in 42 cases (59%). No deaths occurred with therapeutic dose. In 32 cases (45%), children received CCMs for a non-therapeutic intent. The frequency of CCM deaths and intent of exposure fluctuated over the study period (Figure). Diphenhydramine (37, 52%), pseudoephedrine (21, 30%) and dextromethorphan (20, 28%) were the most common ingredients determined to be at least potentially related to the death. Diphenhydramine was most commonly used with non-therapeutic intent, whereas pseudoephedrine and dextromethorphan were most commonly used with therapeutic intent. Among at least potentially related fatalities, the most common root cause of exposure was homicide (22, 31%). Sedation was mentioned in 7 (10%) and accidental ingestion was mentioned in 6 (9%).

Conclusions: The majority of deaths associated with exposures to CCMs detected by the surveillance system from 2008 to 2015 occurred in children <2 years of age. Diphenhydramine was the most attributed CCM ingredient in deaths, and most deaths involved non-therapeutic intent. More research is needed on how non-therapeutic use of CCM should be recognized when evaluating concerns for child abuse and neglect.

KEYWORDS Fatalities; cough/cold medication exposures; pediatric
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159. IV acetaminophen causes significant decrease in blood pressure when used to treat pediatric fever but not when used to treat pediatric pain

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Background: Intravenous acetaminophen (IV APAP) is increasingly used in the pediatric emergency and emergency department setting to treat fever as well as painful conditions in children. Both such uses are off-label. Preliminary data in adults suggests that when used to treat fever, IV APAP may result in clinically relevant decrease in blood pressure. In this pilot study, we sought to investigate if this phenomenon occurs in children receiving IV APAP in the emergency department setting.
Methods: This is a retrospective review of electronic medical records of children treated IV APAP in an academic pediatric emergency department with annual census of 250,000. Records of children who received IV APAP were reviewed, and BP prior to and 2 h after receiving IV APAP was compared. Hypotension was defined as any of the following: 20% decrease in systolic BP, diastolic BP, or mean arterial pressure (MAP).
Results: IV APAP was administered 55 times to 50 children, of which 22 administrations were to treat fever, and the other 33 for treatment of afebrile conditions, typically pain. Three patients who received IV APAP to treat febrile seizures were excluded from analysis: Each of these developed hypotension, but had received multiple anticonvulsant medications expected to cause hypotension. The remaining 52 administrations in 47 patients were analyzed: 19 administrations were to treat fever, and 33 to treat afebrile conditions. No patients were hypotensive prior to receiving IV APAP. When administered for fever, 52.6% (10/19) of patients developed hypotension subsequent to IV APAP use. This was almost exclusively diastolic hypotension, with an average decrease of 28.6% (range 22–42 mmHg, 95% CI 23.7–33.5 mmHg). Of patients receiving IV APAP for afebrile conditions, 9% (3/33) developed hypotension, (range 20–36 mmHg; 95% CI 5.2–47.4 mmHg). One patient receiving IV APAP for fever developed both diastolic (23% decrease) and systolic (20% decrease) hypotension.
Conclusions: This pilot study suggests that children receiving IV APAP to treat fever, but not IV APAP used to treat pain, develop a relevant decrease in BP, on average 28.6%. Most children treated with IV APAP developed diastolic, but not systolic hypotension. A single patient treated for fever, 25% ($n = 1$) experienced significant drop in both systolic and diastolic BP. Use of IV APAP to treat fever may result in hypotension. This may be particularly relevant in circumstances in which decrease in BP, such as sepsis or septic shock, is undesirable. We are no studying this phenomenon prospectively.

KEYWORDS Acetaminophen; intravenous; hypotension
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160. Clinical and electrocardiographic features of aconitine poisoning presenting to the emergency department

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Objectives: Aconitine and related alkaloids binds to site 2 of the voltage-sensitive sodium channels at the open state, causing their persistent activation in excitable tissues, including myocardium, nerves and muscles. They are potent cardiotoxins and neurotoxins and can cause life-threatening arrhythmia. In this study, we aimed to characterize the clinical and electrocardiographic features of aconitine poisoning in the emergency department (ED).
Methods: This was a retrospective study of consecutive patients who presented to two EDs in Hong Kong for aconitine poisoning over 11 years from January 1, 2006 and December 31, 2016. Clinical notes, electrocardiogram (ECG), treatment and outcome were reviewed.
Results: During the study period, 17 cases of aconitine poisoning were identified, in which exposure were analytically confirmed in 12 cases. The mean age was 53-years-old and there was no gender preponderance (9 men and 8 women). In the majority of cases (76.5%), aconitne-containing herbs were prescribed by a traditional Chinese medicine doctor. However, 4 patients consumed aconitine without prescription from a registered practitioner. Neurological, cardiovascular and gastrointestinal toxicities were reported in 16 (94.1%), 15 (88.2%), and 8 (47.1%) of the patients, respectively. The most common ECG finding on presentation was junctional rhythm (6 cases), followed by ventricular tachycardia (4 cases), atrial fibrillation with ventricular ectopics (3 cases), sinus rhythm (3 cases), and narrow-complex tachycardia (1 case). Amiodarone was administered in 7 cases (41.2%), lignocaine in 1 case and magnesium sulphate in 3 cases. Three (17.6%) patients required synchronized cardioversion, but ventricular tachycardia was refractory to electrical therapy in 2 cases. Six cases (35.3%) developed shock and 4 cases (23.5%) required inotropic support. Three patients (17.6%) were intubated and put on mechanical ventilation. One patient developed prolonged cardiac arrest longer than 1 h. In total, 7 (41.2%) patients were admitted to the intensive care/coronary care unit. The outcome was major in 8 cases (47.1%), moderate in 5 cases (29.4%), and mild in 4 cases (23.5%). All patients survived after resuscitation and supportive treatment.
Conclusions: Emergency physicians should consider aconitine poisoning as a differential diagnosis in patients who present to the ED with unexplained cardiac dysrhythmia and with a history of recent exposure to traditional Chinese herbal medicine, especially for those with concomitant neurological and gastrointestinal symptoms. Supportive treatment remains the mainstay of treatment but ventricular tachycardia caused by aconitine alkaloids may be refractory to electrical therapy.

KEYWORDS Aconitine; arrhythmia; cardiotoxicity
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161. Acute hemolysis following acetaminophen overdose in a patient with undiagnosed G6PD deficiency

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Author, year	Baseline Hgb	Hgb nadir	Day of nadir	APAP level	APAP dose	Differential
Heintz, 1989	Unknown	5.4 g/dl	Unknown	Unknown	1000 mg	Viral illness
Bartsocas, 1982	Unknown	8 g/dl	1	Unknown	500 mg	Viral illness
Wright, 1996	14 g/dl	9.4 g/dl	4	184 mcg/ml	Unknown	None
Ruha, 2001	13.7 g/dl	7.6 g/dl	8	680 mcg/ml	Unknown	None
Oliver, 2001	9 g/dl	7.4 g/dl	Unknown	Unknown	Unknown	Multiple doses
Sklar, 2002	17 g/dl	13.4 g/dl	4	71 mcg/ml	15 g	None
Phillpots, 2014	11.3 g/dl	9.6 g/dl	1.5	129 mcg/ml	11 g	None
Rickner, 2016	13.6 g/dl	8.6 g/dl	4	72.3 mcg/ml	150 mg/kg	None
Mullins, 2011	14.8 g/dl	6.2 g/dl	7	>200 mcg/ml	Unknown	5-fold NAC OD

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Background: Glucose-6-phosphate dehydrogenase (G6PD) is the enzyme responsible for oxidation of glucose-6-phosphate to 6-phosphogluconolactone in the hexose monophosphate pathway while simultaneously reducing NADP to NADPH. NADPH acts as the electron donor in the reduction of the antioxidant glutathione. Patients with G6PD deficiency are at increased risk of hemolytic anemia secondary to oxidative stress. We report a case of severe hemolysis following acute acetaminophen overdose in a patient with previously undiagnosed G6PD deficiency.
Case report: A 17-year-old Pakistani female presented to the emergency department with a chief complaint of abdominal pain, nausea, and vomiting. Twenty-four hours prior to presentation she had taken approximately 25 acetaminophen 500 mg tablets to treat menstrual pain. Upon arrival, vital signs were: blood pressure, 135/89 mmHg; respiratory rate, 22 breaths/min; heart rate, 96 beats/min; oxygen saturation, 100% on room air; temperature, 36.9 C. Physical exam revealed an ill-appearing female with scleral icterus and diffuse abdominal tenderness worse in the right upper quadrant. Initial laboratory evaluation revealed transaminitis (AST: 2354 Units/l; ALT: 2498 Units/l), elevated bilirubin (4.5 mg/dl), elevated direct bilirubin (0.77 mg/dl), prolonged PT/INR (17.7 s/1.5), lactate was 1 mmol/l, serum phosphorous not available; other components of the basic metabolic panel were normal. Acetaminophen level was <2 mcg/ml. Complete blood count (CBC) revealed a normal hemoglobin (12.7 g/dl) and hematocrit (39.5%). She received intravenous n-acetylcysteine for presumed acetaminophen-induced hepatotoxicity and ondansetron plus famotidine for nausea and vomiting. Peak AST and ALT values occurred 36 h after ingestion at 6480 Units/l and 8217 Units/l, respectively. Total bilirubin continued to increase until day 3 and peaked at 16.4 mg/dl. She remained clinically stable until 48 h after arrival when she experienced near syncope while walking to the restroom. Repeat CBC revealed a hemoglobin of 5.2 g/dl and hematocrit of 17.5%. Lactate dehydrogenase was elevated at 5335 Units/l; direct bilirubin of 4.5 mg/dl, unconjugated bilirubin of 10 mg/dl, conjugated bilirubin of 2 mg/dl; peripheral smear showed Heinz bodies. She was treated for acute anemia with an otherwise uneventful hospitalization and was discharged 10 d after initial presentation. New diagnosis of G6PD deficiency was confirmed through genetic testing.
Case discussion: We identified 10 previously published cases of hemolytic anemia associated with acetaminophen. In nine of the cases, the patients were either known to have G6PD deficiency or were subsequently diagnosed as a result of their acute hemolysis. Two of the reported cases suggested therapeutic use of acetaminophen could lead to hemolysis in the setting of G6PD deficiency, but both patients had an intercurrent illness. Our patient, had acute hemolysis with her hemoglobin nadir occurring at approximately day 4 following overdose; this was the lowest recorded hemoglobin related to acetaminophen induced hemolysis. The mechanism remains unclear but may be depletion of red blood cell glutathione and oxidative stress from systemic NAPQI production. Acetaminophen itself has been implicated, but only in an *ex vivo* study at concentrations equivalent to 6000 mcg/ml.
Conclusions: This case highlights the unique possibility of hemolytic anemia in a patient with G6PD deficiency after overdose of acetaminophen.

KEYWORDS Acetaminophen; hemolysis; anemia

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162. Extracorporeal membrane oxygenation for cardiopulmonary failure following fentanyl analogue overdose treated with high-dose naloxone

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Background: As fentanyl and potent analogues have infiltrated the U.S. heroin supply, many have suggested that reversal with naloxone may require larger doses than previously described. Both opioids and naloxone have been described to cause cardiopulmonary complications. We present a patient with pulmonary edema and cardiogenic shock following an extremely high dose of naloxone for suspected heroin overdose. The patient survived after a period of extracorporeal membrane oxygenation (ECMO).
Case report: A 23-year-old man presented to a rural hospital with coma, respiratory failure, and hypotension after a reported heroin overdose. He received repeated doses of 1–2 mg of IV naloxone, responding with twitching and gasping after each dose. After 1 h he had received a total of 19 mg and he was described as alert and oriented. Shortly thereafter he developed cough and frothy pink respiratory secretions and was emergently intubated. Upon transfer to our hospital he had refractory hypoxemia, respiratory acidosis, and hypotension despite norepinephrine infusion. Transesophageal echocardiography showed globally depressed myocardial function despite additional agents so we initiated venoarterial ECMO. By the following day his cardiac function normalized and the pulmonary edema resolved; ECMO decannulation occurred on hospital day three. During his 23-d hospitalization he developed rhabdomyolysis, nonoliguric acute kidney injury, pneumonia, and left femoral artery thrombosis adjacent to the ECMO cannula leading to compartment syndrome, fasciotomy, and thrombectomy. Although he had complete neurologic recovery his complex surgical wound may ultimately require below-knee amputation. Liquid and gas chromatography with mass spectrometry identified fentanyl and methamphetamine in the patient's urine; no heroin was

detected. Targeted immunoassays for novel psychoactive substances (NPS) revealed ocfentanyl in the urine and furanylfentanyl and acetylfentanyl in the urine and blood. These NPS findings have been previously associated with cyclopropylfentanyl intoxication.
Case discussion: This case highlights several unique aspects of the present state of opioid poisoning. First, while some authors suggest that larger doses of naloxone may be required to reverse coma caused by fentanyl analogues, reports documenting this phenomenon are rare. This patient's coma was definitively linked to fentanyl analogues and he did not meaningfully respond until after a total of 19 mg of naloxone. Second, almost immediately after high-dose naloxone the patient developed severe cardiopulmonary failure. Opioid-related pulmonary edema has been described for over 100 years and some data suggest that precipitation of opioid withdrawal with large doses of naloxone may rapidly increase blood catecholamine concentrations and cardiac afterload causing stress cardiomyopathy and pulmonary edema. Coingested methamphetamine may have contributed to the patient's pulmonary edema by adding to the catecholamine excess. Finally, while ECMO is a promising therapy for refractory shock from poisoning, it is invasive and may result in significant hematologic and vascular complications.
Conclusion: In this case, fentanyl analogue and methamphetamine intoxication treated with high-dose naloxone resulted in resolution of coma followed by pulmonary edema and cardiogenic shock. ECMO support was associated with full neurologic and cardiac recovery, complicated by catheter-related arterial thrombosis, compartment syndrome, and fasciotomy. This case demonstrates multiple emerging aspects of the treatment of opioid poisoning in 2018.

KEYWORDS Fentanyl analogue; naloxone; ECMO

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163. Tyramine on tap – hypertensive crisis with tranylcypromine and draft beer

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Background: Irreversible monoamine oxidase inhibitors (MAOIs) have seen limited use due to potentially lethal food and drug interactions. We report a case of a 51-year-old male on tranylcypromine who developed hypertensive crisis after consumption of craft beer on tap at a microbrewery.
Case report: A 51-year-old male with a history of depression, maintained on tranylcypromine 30 mg daily, presented to the emergency department (ED) in hypertensive crisis. In the previous hour, the patient drank approximately two pints (946 ml) of an American light lager on tap at a local microbrewery and subsequently developed dizziness, palpitations, and severe occipital headache. On arrival, he was extremely anxious and hyperventilating with a blood pressure of 240/120 mmHg, heart rate of 66 bpm, and oxygen saturation of 100% on room air. EKG was normal and troponin negative. The patient received 2 mg IV lorazepam which improved his comfort level but not his blood pressure. A nitroprusside infusion was initiated and titrated to 1 mcg/kg/min with hemodynamic improvement (blood pressure 167/97 mmHg and heart rate 53 bpm). He was easily weaned from the nitroprusside infusion over the next 6 h and discharged the following day without complications.
Case discussion: To reduce the risk of hypertensive crisis, patients taking irreversible MAOIs are required to restrict their intake of foods rich in tyramine as mild reactions can occur after ingestion of only 6 mg and much more severe reactions with 10 mg or more. Shulman and colleagues analyzed more than 100 foods believed to be high in tyramine content, but found low concentrations in all of the beers studied. They concluded one would have to consume at least four bottles (1364 ml) of the beer with the highest tyramine concentration within a 4-h period to reach the maximum allowable limit (6 mg). Subsequently, two case reports appeared in the literature with patients who experienced hypertensive crisis after consumption of much smaller amounts of tap beer. As previous research only included bottled and canned beers, Tailor and colleagues suspected that the draft process may make a difference in respect to tyramine content, and so analyzed 49 beers on tap at local establishments. They reported alarmingly high tyramine concentrations (27.05–112.91 mg/liter) in four samples and suggested that storage and bacterial contamination of the hose from the keg to the tap may provide conditions conducive to the production of tyramine. Small and independent United States craft brewers have tripled over the past eight years to more than 6000 breweries in 2018. With their increasing popularity, beer poses as even greater drug-food interaction risk in this patient population than it has in the past.
Conclusion: Our case is consistent with the clinical course from the two previous reports and supports the absolute restriction of tap beer in patients who take MAOIs. Healthcare providers should be aware of this interaction and provide more specific dietary counseling to their patients on these medications.

KEYWORDS Beer; MAOI; hypertensive crisis

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164. *In Vitro* evaluation of ketamine, fentanyl, and midazolam effects on leukocyte mitochondria membrane potential and mtDNA

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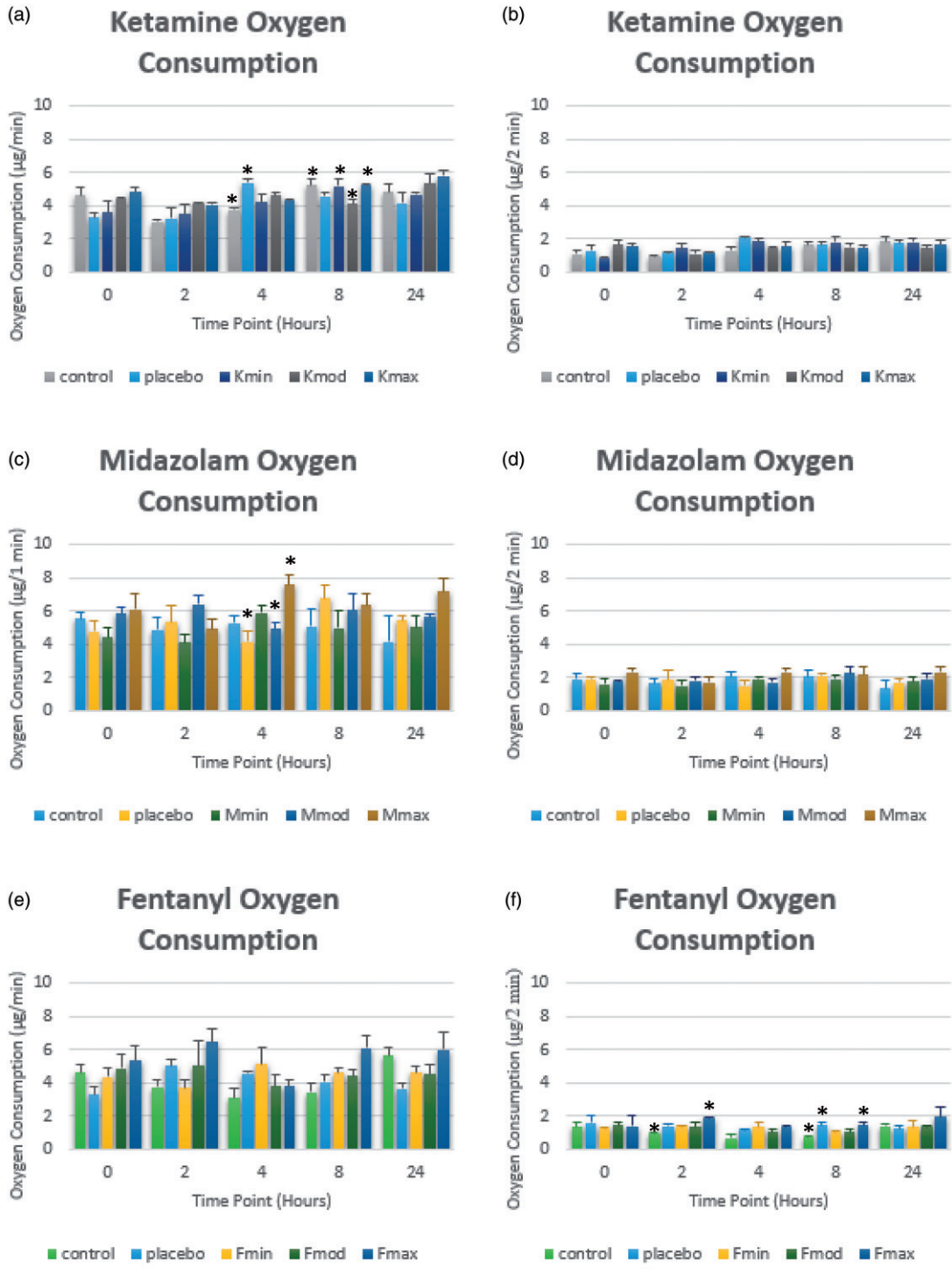
Background: Ketamine has a multitude of treatment potentials. However, animal models and *in vitro* investigations found ketamine caused apoptosis and necrosis related to concentration and duration of exposure. These models exceed therapeutic administration of ketamine. Studying ketamine's effects is challenging; but, lymphocytes provide a surrogate marker to study potential toxic effects of ketamine at clinically relevant doses. This study aimed to evaluate ketamine's effects on whole blood *in vitro*, on markers for cellular apoptosis including leukocyte oxygen consumption, mitochondrial membrane potential ($\Delta\Psi$), and mitochondrial DNA (mtDNA) breakage.

Table 1 Additive medication concentrations.

		Active control	
Concentration	Ketamine (mcg/ml)	Midazolam (mcg/ml)	Fentanyl (ng/ml)
1	1	0.24	2
2	10	2.4	20
3	497.5	24.9	248.8



Graph 1. Oxygen consumption. $p < .05$

Methods: This *in vitro* study used fresh whole blood aliquoted using 6 ml EDTA tubes and maintained at 36 °C for the duration of the study. Five groups compared ketamine's effects to fentanyl or midazolam (active control), 0.9% NaCl (placebo), and a control. Ketamine and active control medications were applied in three concentrations (Table 1). Concentration 1 mimics therapeutic blood concentrations and concentration 3 includes no dilution. All dilutions were done using 0.9% NaCl with maximum 25 µl added. Groups were analyzed at 0, 2, 4, 8, 24 h. Primary outcome was the change in oxygen consumption at 2 h compared to baseline after ketamine concentration 1 exposure. Secondary outcomes include the change in oxygen consumption, $\Delta\Psi$, and mtDNA breakage over time after ketamine exposure compared to baseline or other groups. Measurements were done in triplicate. Oxygen consumption was measured using 25 µL of leukocytes at 1 and 2 min and $\Delta\Psi$ with 100 µL of leukocytes using JC-1 (5′,6,6′-tetrachloro-1,1′,3,3′-tetraethyl-benzimidazolyl-carbocyanide iodide). Finally, mtDNA will be assessed for

breakage on 300 μL of leukocytes using CO_2 3285 bp long fragment, D-loop 2467 bp long fragment, Calicin 2658 bp long fragment primers for PCR. Statistical analysis included descriptive statistics; Student's t-test for parametric data; and intra-group analysis a Paired t-test. Comparison of 3 or more groups used an ANOVA or repeated-measures ANOVA with post hoc Tukey test.
Results: No difference was found from baseline in 1-min oxygen consumption in ketamine concentration 1 at 2 h ($p = .9438$). Oxygen consumption is denoted in Graph 1. Ketamine's concentration 1,2,3's $\Delta\Psi$ differed from midazolam and fentanyl concentration 1,2,3 at 4 h. Ketamine concentration 2 $\Delta\Psi$ differed from ketamine and fentanyl concentration 2 at 8 h. Ketamine concentration 3's $\Delta\Psi$ differed from midazolam concentration 3 at 8 h. At 24 h, concentration 1,3 differed between ketamine and fentanyl; concentration 2 differed between ketamine and fentanyl. No differences were found in mtDNA breakage.
Conclusions: Ketamine did not significantly affect cellular oxygen consumption at 2 h. All groups had variable effects on oxygen consumption, a sensitive marker for apoptosis. $\Delta\Psi$, an intermediate sign of cellular damage, was also altered in a variable manner. Finally, mtDNA, a later sign of cellular damage and apoptosis was not affected. Overall leukocytes did not appear to be affected by ketamine in a concentration or time-dependent manner. Isolation of leukocytes was bypassed to avoid additional chemical exposure; however, this may have diluted the results. Also, ketamine's effects may be due to a metabolite. Further *in vivo* evaluation is warranted.

KEYWORDS Ketamine; neurotoxicity; *in vitro*

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165. Morphine therapy leading to profound thrombocytopenia

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Background: Drug-induced thrombocytopenia is an immune-mediated phenomenon that is a relatively common complication of xenobiotic therapy attributable to an extensive list of drugs. Although there are many reports in the literature implicating numerous xenobiotics as causative agents of drug-induced thrombocytopenia, morphine-associated thrombocytopenia is exceedingly rare. We present a case of profound drug-induced thrombocytopenia, which developed secondary to morphine therapy.
Case report: A 47-year-old woman suffered approximately 40% TBSA burns to her back and arms, and after medical stabilization was discharged to physical rehabilitation. During her acute illness and throughout her rehabilitation stay, her platelet count remained normal. One month after her initial event, she was started on extended-release morphine sulfate for residual pain. Seven days after initiation of morphine therapy her platelet count began a steady decline from 396 K/uL to a nadir of 7 K/uL over the following 31 d, despite extensive repeated platelet transfusions. Heparin PF4 Platelet Antibody testing was negative and platelets did not improve after cessation of subcutaneous heparin therapy. The patient was not on any other medications routinely implicated in drug-induced thrombocytopenia. After morphine therapy was ceased, platelet count returned to normal range within 7 d with no further complications and normal platelet counts on subsequent follow up testing.
Case discussion: Temporal association of morphine therapy to platelet decline and cessation of therapy to rebound imply an association with morphine administration. The timeline of platelet decline and rebound are both consistent with an immunologic response, and an immune mechanism appropriately accounts for refractoriness to platelet transfusion. The workup for alternative causes of thrombocytopenia was negative.
Conclusion: While morphine has been associated with drug-induced immune thrombocytopenia, documented human cases are exceedingly rare. The patient in this case developed a profound thrombocytopenia, refractory to platelet therapy, and which only resolved once morphine therapy was discontinued. Because morphine therapy is commonly used drug in both inpatient and outpatient settings Clinicians should be aware that it can be associated with profound thrombocytopenia.

KEYWORDS Morphine; thrombocytopenia; immune

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166. Gadolinium aspiration following inadvertent endotracheal tube cuff injection in a pediatric patient

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Background: Gadolinium based contrast agents (GBCAs) are utilized during magnetic resonance imaging (MRI) as contrast agents. Recently, a growing number of adverse effects have been attributed to GBCAs. We report a case of inadvertent GBCA administration into the endotracheal tube of a pediatric patient resulting in pulmonary aspiration.
Case report: A 12-year-old female with a past medical history significant for mitochondrial disorder, bronchial asthma, autism, recurrent UTI, epilepsy, developmental delay, dysautonomia, and thrombocytopenia was scheduled for a contrast-enhanced MRI study. The patient was sedated and intubated in preparation for the study, during which 10 ml of Dotarem® (gadoterate meglumine) were inadvertently injected in the pilot line of the endotracheal tube instead of intravenously. This caused the endotracheal tube cuff to rupture, allowing the contrast material in to the patient's respiratory tract. The patient remained intubated and was admitted to the intensive care unit with close monitoring for signs of chemical pneumonitis. Chest radiograph was normal and she was successfully extubated around 24 h later with no complications. After one more day of observation on the floor she was discharged home without developing symptoms or signs of gadolinium toxicity.
Discussion: For years, GBCAs were considered excellent material for MRI contrast studies, posing minimal risk to patients being exposed to them with the exception of chronic renal failure patients, who were at risk for nephrogenic systemic fibrosis (NSF). NSF may result in fatal or debilitating systemic fibrosis affecting the skin muscles and internal organs. More recently, studies have shown that some GBCAs may be retained, undergo dechelation, and induce gadolinium deposition in different tissues, and reports of patients with normal renal functions developing symptoms attributed to parenteral exposure to the GBCA have been published. Symptoms included central torso pain, paresthesia, clouded mentation, pain in the hands and feet, difficulty

breathing, headache and skin changes. When injected intrathecally, GBCAs were reported to cause confusion, nausea, vomiting, ataxia nystagmus, hallucinations, blurred vision, and depressed mental status. Serum, hair, or urine gadolinium levels may have provided more insight on the absorption and distribution of gadolinium following respiratory exposure. Treatment of patients with gadolinium toxicity has not been fully elucidated and agents including N-acetyl cysteine, heavy metal chelators, and nanoparticles linked to chelators have been proposed.
Conclusion: We report what we believe to be the first case of pulmonary aspiration secondary to inadvertent GBCA injection. In this case, no clinical pulmonary toxicity developed, and the patient had an unremarkable hospital course.

KEYWORDS Gadolinium; aspiration; contrast

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167. Asymptomatic lipase elevation in a patient with proton pump inhibitor overdose

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Background: Omeprazole is a proton pump inhibitor (PPI) used in the treatment of gastritis and peptic ulcer disease. Multiple adverse effects have been attributed to its use, including clinically significant pancreatitis. Omeprazole-associated pancreatitis is typically reported in the setting of chronic omeprazole use. To our knowledge there have been no reports of omeprazole causing acute pancreatitis or pancreatic enzyme elevation in association with acute overdose of omeprazole. We present a case of elevated serum lipase concentration following ingestion of 200–300 mg omeprazole in a suicide attempt.
Case report: A 48-year-old African-American female presented to the Emergency Department (ED) from a homeless shelter approximately 4 h after attempting suicide by ingesting 10–15 20 mg omeprazole capsules. She had a past medical history of osteoarthritis, pulmonary embolism, cocaine and marijuana abuse, depression, and HIV/AIDS. Home medications included sulfamethoxazole-trimethoprim (TMP-SMX) for Pneumocystis pneumonia prophylaxis, and warfarin. The patient was asymptomatic on presentation, with an unremarkable physical examination. She also denied recent alcohol use. Her laboratory investigation revealed a lipase level of 665 IU/l (reference level 3–95 IU/l). The morning following her admission she had a brief episode of epigastric/substernal non-radiating chest pain that was reproducible on palpation with no exacerbating or relieving factors of note. She had no nausea, vomiting, fever, anorexia, diarrhea, blood in stool, shortness of breath or hemodynamic instability. On examination she had mild tenderness on epigastric palpation but with no guarding or rigidity. Serum lipase level was repeated on day two of her hospital stay and was elevated further to 1809 IU/l, but the patient was tolerating food and drink with resolution of the epigastric pain. On hospital day 3, the patient was discharged with outpatient follow up.
Case discussion: Pancreatitis in the setting of omeprazole use is typically reported in the setting of chronic therapeutic dosing rather than acute overdose. Whether treatment with omeprazole and other PPIs is associated with a statistically significant increased risk for acute pancreatitis is controversial. The mechanism by which pancreatitis may be associated with PPI use is unclear, but it has been suggested that it might be indirectly linked to an increase in the rate of gastrin production secondary to a suppression of acid secretion. In this case however, the likelihood of the ingested drug causing enough gastric acid suppression to increase gastrin and cause pancreatic inflammation over a several hour period is unlikely. Our patient was reported to be HIV positive and on TMP-SMX which are the only other risk factors that could have caused the patient's pancreatitis. Analysis using the Naranjo adverse drug reaction (ADR) probability scale, a score of 3 was calculated, indicating this was a 'possible' ADR due to the ingestion of omeprazole.
Conclusions: We report a case of serum lipase elevation following acute omeprazole overdose. Using the Naranjo scale this was a possible adverse drug reaction.

KEYWORDS Omeprazole; proton pump inhibitor; pancreatitis

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168. Keep calm and dialyze on: a case of lithium toxicity treated with continuous veno-venous hemodialysis and intermittent hemodialysis

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Introduction: Despite Lithium's narrow therapeutic index, its efficacy in mitigating the suicide rate in patients with bipolar disorder necessitates its continued use. Toxicity is managed best with supportive care, intravenous fluids and symptomatic control of its gastrointestinal and neurologic effects. Patients with severe toxicity are treated using hemodialysis. The use of continuous hemodialysis (CVVHD) over intermittent hemodialysis (HD) has been debated in the literature. We report a case of a 16-year-old female who presented with acute-on-chronic Lithium toxicity that was treated with continuous and intermittent hemodialysis.
Case reports: A 16-year-old girl with bipolar disorder on chronic Lithium therapy, goiter and frequent urinary tract infections presented to the emergency department (ED) for two weeks of worsening altered mental status and ataxia. Physical exam revealed normal vital signs, ataxia, clonus, lower extremity rigidity, confusion and slurred speech. Lab analyses were significant for a normocytic anemia (Hgb 8.1 g/dl, Hct 24.9%) and acute kidney injury with associated non-anion gap metabolic acidosis (pH 7.29, Na 133 mEq/l, K 5.8 mEq/l, HCO_3 19 mEq/l, BUN 77 mg/dl, Cr 6.01 mg/dl). Initial Lithium level was 4.25 mmol/l. EKG revealed a prolonged PR interval at 206 ms but was otherwise within normal limits. Urinalysis was remarkable for urinary tract infection. She was treated with 1 g of ceftriaxone, 2L of normal saline, and transferred to our tertiary pediatric center. Nephrology was consulted for HD, but due to their concern for the development of disequilibrium syndrome, CVVHD was initiated. Despite overnight treatment with CVVHD (10 h), her Lithium level rose to 5.79 mmoL/l and encephalopathy worsened with increasing agitation. Consequently, intermittent HD was performed which resulted in a decrease of her Lithium level to 0.34 mmol/l. The patient was evaluated for alternate causes of renal failure and was noted to have multiple cysts on bilateral kidneys that were drained by IR. She was also found to have a neurogenic bladder necessitating suprapubic catheter placement. Her hospital stay was complicated by diabetes insipidus treated with hydrochlorothiazide. She was discharged home on hospital day 28 with a creatinine of 1.5 mg/dl.

Case discussion: Lithium toxicity is primarily managed with supportive care and medication discontinuation. In the setting of renal failure or severe neurologic toxicity, HD is utilized for improved clearance. CVVHD has been discussed as a suitable alternative due to the concerns for a rebound level with intermittent HD, and the development of disequilibrium or SILENT syndromes. However, CVVHD is significantly less efficient than HD and can lead to prolonged toxicity and worse outcomes. Our patient showed minimal, if any clearance of her Lithium while on CVVHD, resulting in a rising level and worsening of her mental status. She was found to have large renal cysts but was also noted to have a neurogenic bladder. It is likely that her underlying neurogenic bladder was the source of her urinary infections and an underlying chronic renal insufficiency. Her acute urinary infection likely precipitated a worsening in her renal function and acute Lithium toxicity.
Conclusion: In patients with Lithium toxicity, CVVHD should only be utilized when patients are unable to tolerate intermittent HD.

KEYWORDS Lithium; hemodialysis; continuous veno-venous hemodialysis

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169. Complications associated with the administration of naloxone

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Background: United States (U.S.) drug overdose deaths have increased significantly over the past decade, in large part due to opioid overdose. Increasing access to naloxone, an opioid antagonist that rapidly reverses the effects of opioids, has been a key initiative in response to this crisis. Naloxone is touted as safe and effective in opioid overdose. However, data is lacking as to the adverse consequences associated with naloxone administration. The objective of this study is to evaluate potential adverse events associated with the administration of naloxone.
Methods: We conducted a retrospective chart review utilizing data from a regional Poison Center (PC) associated with a single tertiary university health system. ToxicallTM, a comprehensive case management software system used by 75% of U.S PCs, was queried for cases where naloxone was used as therapy from January 1, 15 to December 31, 16. Detailed case information was obtained by linking the PC exposures to the hospital records by utilizing the electronic medical record numbers. Cases were independently reviewed by two medical reviewers. Discrepancies were identified and resolved by a third reviewer.
Results: There were 132 cases of naloxone administration reported to the PC in the study period, with the majority in males (56.1%) between ages 20 and 39 years (41.7%). Of total naloxone administrations, 35/132 (26%) doses were administered to non-opioid exposures on final diagnosis, most commonly ethanol and benzodiazepine ingestions. Multiples substances were reported or determined by analytics as used in 59.1% of cases. Complications following naloxone administration included agitation (17.4%), agitation requiring the use medical sedation (10.6%), and vomiting (2.2%). Four patients (3.0%) experienced severe agitation after naloxone administration requiring both sedation and intubation with mechanical ventilation. One patient vomited following naloxone administration, developed an aspiration pneumonitis on chest radiography and was subsequently intubated for hypoxic respiratory failure. The median dose of naloxone given was 0.8 mg (mode –2 mg; range – 0.04 mg–4 mg). Of patients with agitation, the median dose of naloxone was 1 mg, with 78.1% of doses given intravenous (IV), 17.4% given intranasal (IN) and 1 dose given intramuscular (IM). For the four patients intubated and placed on mechanical ventilation, the doses and route of naloxone were 1 mg IV, 2 mg IV, 1 mg IV, and 2 mg IN followed by 2 mg IV, respectively. Patients were admitted to an intensive care unit (66%), admitted to a general medical floor (12.1%), or were treated and released (15.9%). A significant number of administrations (24.2%) were to patients with a documented respiratory rate $>$ 12/min just prior to administration. A pre-administration GCS $>$14 or an assessment noting the patient to be alert and oriented to person, place and time was noted in 4.0% of administrations.
Conclusions: Naloxone administration, when given at appropriate rate and at dose for appropriate indications, is hypothesized to be safe and effective. However, when given in doses that precipitate opioid withdrawal, administration can be complicated by vomiting, aspiration (especially if another coexisting sedative is present), or marked agitation. Agitation often requires sedation and intubation/mechanical ventilation.

KEYWORDS Naloxone; complications; opioids

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170. Teenage hydrocodone exposures reported to the U.S. Poison Centers

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Background: According to the Drug Enforcement Administration, over 136 million hydrocodone prescriptions were dispensed in 2013, with approximately 24.4 million people over the age of 12 years using it for non-medical purposes. The non-medical use of hydrocodone among teenagers is common, with the National Institute on Drug Abuse reporting the past year use of Vicodin (hydrocodone/acetaminophen) among this population being 1–5%. According to the Monitoring the Future survey, the annual prevalence rates of Vicodin use were 0.7%, 1.5%, and 2.0% for 8th, 10th and 12th graders respectively. This study examines the trends in hydrocodone exposures among teenagers reported to U.S. poison centers (PCs).
Methods: The National Poison Data System (NPDS) was queried for all hydrocodone exposures in patients between 13 and 19 years from 2011 to 2017. We descriptively assessed the demographic and clinical characteristics. Trends in hydrocodone frequencies and rates (per 100,000 teenage exposures) were analyzed using Poisson regression. Percent changes from the first year of the study were reported with the corresponding 95% confidence intervals (95% CI).
Results: There were 18,097 teenage exposures to hydrocodone reported to the PCs from 2011 to 2017, with the number of calls decreasing from 3051 to 2167 during the study period. Among the overall hydrocodone calls, the proportion of calls from acute care hospitals and EDs increased from 55.2% to 71.6% from 2011 to 2017. Multiple substance hydrocodone exposures accounted for 55.8% of the overall calls and 73% of the calls from acute care hospitals and EDs. Approximately 13.8% of the patients reporting hydrocodone exposures were admitted to the critical care unit, with 20% being admitted to a psychiatric facility. Residence was the most common site of exposure (93.6%) and 67% of cases were enroute to the hospital via EMS when the PC was notified. Females were more frequently exposed to hydrocodone (63.8% of cases). Suspected suicide (36.7%) was the most common reason for exposure, with intentional abuse accounting

for 12.1% of the cases. The proportion of suspected suicides (78.1%) was higher among cases reported by acute care hospitals and EDs, while abuse was less frequent (10.7%). Minor effects (34.1%) were the most prevalent among cases. There were 30 teenage deaths due to hydrocodone exposure, with 21 of them occurring in the hospital or ED setting. The most frequent co-occurring substances reported were benzodiazepines (12.3%), and Ibuprofen (10.4%). Tachycardia and vomiting were the most frequently demonstrated clinical effects. Naloxone was a reported therapy for 9.2% cases, with this therapy being performed prior to PC recommendation in most cases. Overall, teenage hydrocodone exposure calls decreased by 29% (95% CI: −32.8%, −24.9%; $p < .001$), while the rate of such exposures decreased by 34.1% (95% CI: −38.6%, −29.3%; $p < .001$).
Conclusions: PC data demonstrated a decreasing trend of hydrocodone exposures among teenagers, which may be attributed to the current decrease in opioid prescribing due to policy and practice changes. However, the increase in the proportion of calls from the acute-care hospitals and EDs indicates higher severity of such exposures, especially when multiple substances are involved.

KEYWORDS Hydrocodone; overdose; NPDS

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171. A physo unmasking of the opioid toxidrome

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Background: Physostigmine has been employed as an antidotal agent utilized for the reversal of the anticholinergic toxidrome. Physostigmine is a reversible acetylcholinesterase inhibitor that promotes rapid reversal of central nervous system (delirium) effects with a relatively effective and safe profile. The utilization of physostigmine over benzodiazepine in patients with anticholinergic toxicity has been shown to have a significantly lower rate of intubation and complications, while providing a shorter time to recovery. Polypharmacy ingestions can interact to increase, decrease, or cancel the effects of different drugs. The utilization of antidotes fosters the possibility of unmasking previously depressed toxic processes, placing the patient at risk for novel debilitating consequences. This case highlights how utilization of a physostigmine as an anticholinergic toxidrome antidote unmasked an underlying toxic opioid coingestion.
Case report: A 29-year-old male was found unresponsive by emergency medical services (EMS) in a parking lot unable to verbalize and minimally responsive to pain. At the scene, EMS noted hypotension and tachycardia. Upon presentation to the emergency department, the patient was afebrile and dry (not flushed) with persistent arterial hypertension (165/75 mm of mercury) and tachycardia (115 bpm). Xenobiotics identified at the scene were alprazolam, hydroxyzine, olanzapine, and phenazopyridine. At intake, a CT was performed and ruled out intracranial injury as a contributory factor to the patient's altered mental status, and a toxicology consult was requested. While at bedside, the toxicology team identified the patient as anticholinergic and administered physostigmine 1 mg/10 min. Physostigmine, the anticholinergic antidote, improved the patient's mentation and allowed him to provide his name and date of birth, follow simple commands, and report that he had also ingested methadone. Following a brief alert state, the patient's mental status and respirations quickly declined, unmasking an opioid toxidrome requiring the need for a naloxone infusion.
Conclusion: Physostigmine is suggested to be a possible safe and efficacious antidote for the anticholinergic toxidrome, which is associated with delirium, dry skin, hypertension, and tachycardia. Statistically, about half of overdose deaths are from combination drug ingestions. Providers responding to overdoses need to be cognizant of the potential for mixed ingestions and how to appropriately respond when the utilization of one antidote reveals an underlying toxicity.

KEYWORDS Physostigmine; opioid; antidote

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172. Neuropsychiatric changes associated with acute on chronic bromide toxicity from dextromethorphan abuse

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Background: Bromism is an unusual and infrequent occurrence, often discussed from a historical perspective. However, despite the rare use of bromides therapeutically, several medications continue to be available as bromide salts, such as dextromethorphan hydrobromide.
Case reports: A 27-year-old male with a history of hepatitis C presented 7 h after reporting a large ingestion of guaifenesin and a dextromethorphan co-formulated product in an attempt to achieve a recreational high. Upon further history, he also admitted to abusing this product several times a week over the preceding seven years, often intermixing with methamphetamine and acetaminophen for chronic back pain. He was noted to have a very unusual affect where he would stare into space and intermittently respond to questions. Physical exam was notable for bilateral lower extremity clonus, vertical nystagmus, and mild tachycardia. Initial laboratory work demonstrated a chloride of 111 meq/l, bicarbonate17 meq/l, anion gap of 8, alanine aminotransferase (ALT) 55 units/l, aspartate aminotransferase (AST) 68 units/l, and acetaminophen 70.5 mcg/ml. Renal function was normal. He was promptly treated with intravenous n-acetylcysteine and midazolam for acetaminophen toxicity and mild serotonin syndrome. Given hyperchloremia and a low anion gap acidosis, he was also aggressively treated with a sodium chloride 0.9% infusion following a liter bolus for suspected bromide toxicity. On hospital day two his tachycardia and clonus resolved yet his mentation and hepatic function remained unchanged. On hospital day three, his chloride normalized to 107 meq/l, bicarbonate 21 meq/l, and anion gap was 11. ALT and AST were 46 and 49 respectively and the patient was noted to be much more cognizant than upon arrival. A serum bromide level dispatched on day 3 was 7.3 mg/dl [reference 0.5–1.2].
Discussion: Toxicity from bromide salts results from accumulation of concentrations over time and lends to bromides' long half-lives. Bromide and chloride ions similarly cross membranes; however, it is postulated that bromide travels more rapidly and is more quickly reabsorbed. As a result of bromide's displacement of chloride and interference with chloride assays on laboratory analyzers, a falsely elevated serum chloride can be expected despite a true hypochloremia. Clinical manifestations center around neuropsychological symptoms, such as inappropriate behavior, apathy, headache, and irritability. While a paucity of

treatment recommendations exist, a small number of published cases discuss enhanced elimination of bromide through sodium chloride administration via fluid resuscitation or in tablet form and/or hemodialysis. This case is noteworthy given the patient's abrupt and unique behavior disturbances that persisted until his chloride and metabolic acidosis had resolved. Unfortunately, the patient's bromide concentration, while elevated, was drawn at hospital discharge once his metabolic disarray had resolved; his presenting bromide concentration remains unknown.
Conclusions: Neuropsychiatric symptoms coupled with a negative or low anion gap acidosis and elevated serum chloride in the presence of reported dextromethorphan should prompt the clinician to consider bromide toxicity. In this case, aggressive fluid resuscitation with sodium chloride improved the patient's clinical condition.

KEYWORDS Bromide; dextromethorphan; drugs of abuse

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173. Cranial dystonia as a complication of reversal of anticholinergic syndrome with physostigmine in a polysubstance overdose patient

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Background: Physostigmine is an acetylcholinesterase inhibitor derived from the Calabar bean. It is used diagnostically and therapeutically to reverse anticholinergic toxicity. Dystonia is a group of movement disorders characterized by involuntary muscle contractions that cause the body into abnormal movements or positions. Early neurologic data has shown that physostigmine can worsen dystonic reactions, while anticholinergics can improve the symptoms. We present a case of patient who presented with anticholinergic syndrome that was reversed with physostigmine who then suffered from cranial dystonia.
Case report: A 31-year-old female with history of bipolar disorder, diabetes, borderline personality disorder, and polysubstance abuse presented to the emergency department after being found by her sister with confusion. She was found by first responders to have empty pill bottles around her, including lithium, quetiapine, hydroxyzine, amitriptyline, alprazolam, and risperidone. Testing in the emergency department showed no detectable ethanol, salicylate, or acetaminophen. She had an unremarkable comprehensive metabolic panel with normal anion gap, creatinine of 1.14 mg/dl, and lithium level of 1.11 mmol/l (normal range 0.5–1.5). Her electrocardiogram (EKG) showed a normal sinus rhythm with a rate of 74, QRS 114 ms, and QTC 483 ms. Her urine enzyme multiplied immunoassay technique (EMIT) screen was positive for tricyclic antidepressants and qualitative urine gas chromatography/mass spectrometry (GC/MS) was positive for nicotine, ibuprofen, caffeine, diphenhydramine, metabolites of cyclobenzaprine or amitriptyline, topiramate, cyclobenzaprine, mirtazapine, buclizine, quetiapine metabolites, and noxiptyline metabolite.
Clinically, she had garbled speech, carphologia, and occasionally attempted to get out of bed. She was given a diagnostic dose of physostigmine 1 mg with mild effect and complete improvement after an additional 1 mg. However, she then became unable to control her tongue, close her jaw, and had fluttering eyelids despite maintaining her mental status. Her dystonia resolved with 1 mg lorazepam IV. Thirty minutes later her delirium recurred and persisted for an additional 3 d before resolving. Psychiatric evaluation revealed she had trialed several psychiatric medications and "abused her medications." She was transferred to a psychiatric facility without residual neurological sequelae.
Case discussion: Based on the patient's presentation, her constellation of symptoms and exposures were consistent with anticholinergic syndrome. However, her case was complicated as she had access to numerous possible medications and neuroleptics which likely contributed to her presentation. Many of the neuroleptics work via multiple mechanisms including potential anticholinergic properties and dopamine augmentation. Although physostigmine cleared her anticholinergic sensorium, the interaction with her neuroleptics likely induced a dystonic reaction. Normally, dystonia is treated with anticholinergics such as diphenhydramine. In this case, this would not be feasible, as this could worsen her potentially life threatening anticholinergic toxidrome. Benzodiazepine treatment is a reasonable alternative in this complicated situation, and has the advantage of also calming the patient with limited drug interactions that could worsen the patient's clinical status.
Conclusions: In polysubstance overdoses with neuroleptics, physostigmine may reverse the anticholinergic toxicity, but can potentially induce a dystonia. Symptoms in these rare cases can be ameliorated with benzodiazepines.

KEYWORDS Dystonia; physostigmine; reversal

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174. Hypertonic sodium bicarbonate in subacute flecainide toxicity

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Background: Flecainide is a class 1C antidysrhythmic, which acts by blocking fast sodium channels resulting in a decreased rate of phase 0 depolarization. Agents in this class typically slow cardiac conduction and decrease contractility. We present a case of subacute flecainide toxicity treated with hypertonic sodium bicarbonate.
Case report: A 76 year-old man with past medical history significant for atrial fibrillation status post ablation on anticoagulation and chronic kidney disease presented to an outside hospital with progressive dyspnea on exertion. He was transferred to a tertiary care center after an electrocardiogram (ECG) revealed a bizarre wide-complex tachydysrhythmia with QRS of 200 ms and QTC of 715 ms. His baseline ECG did have a right bundle branch block (RBBB) with QRS of 132 ms. Of note, his serum creatinine was found to be 2.1 mg/dl from a baseline of 1.3 mg/dl. Transthoracic echocardiogram revealed heart failure with a reduced ejection fraction (HFrEF) of 10–15%. He had normal ejection fraction on echocardiogram performed three months prior. A serum flecainide level returned at 1.47 mcg/ml (therapeutic 0.4–1.2 mcg/ml), available on post-hoc analysis. He was started on a hypertonic sodium bicarbonate drip with a total sodium concentration of 172 mEq/l (2 ampules of sodium

bicarbonate in 1L of half normal saline) at a rate of 125 ml/h, due to concerns for volume overload. Several attempts of discontinuing the infusion were made but subsequent widening of the QRS and morphological changes to the EKG promptedits restart. The infusion was subsequently discontinued after 60 h total, after which his serum creatinine had returned to baseline and ejection fraction had improved to 20–25%. Although his cardiac toxicity improved, his stay was complicated by a spontaneous intramuscular hematoma necessitating embolization by interventional radiology, and was subsequently discharged in good health.

Case Discussion: Flecainide is a class 1C antidysrhythmic acting via sodium channel and potassium channel blockade, manifesting as QRS widening and QT prolongation, respectively. This patient had a widened QRS at baseline due to a pre-existing RBBB. Although there was no overdose of flecainide, this patient likely developed toxicity due to acute on chronic renal failure. Furthermore due to this toxicity, his systolic ejection fraction decreased, which contributed to his renal failure propagating the drug's toxic effects in a vicious cycle. We chose a higher concentration than has been described in the literature due to concerns for potential fluid overload limiting the overall infusion rate and volume administered to this patient. This is the first known case of subacute flecainide toxicity treated with this concentration of sodium bicarbonate for a prolonged treatment period, 60 h in all. The drip's efficacy was demonstrated by the abrupt QRS widening and morphological changes that occurred in discontinuation during the toxic phase.

Conclusion: Sodium bicarbonate infusions with increased tonicity are effective in the treatment of flecainide toxicity and should be considered to decrease the volume administered in patients with HFrEF.

KEYWORDS Flecainide; hypertonic; bicarbonate

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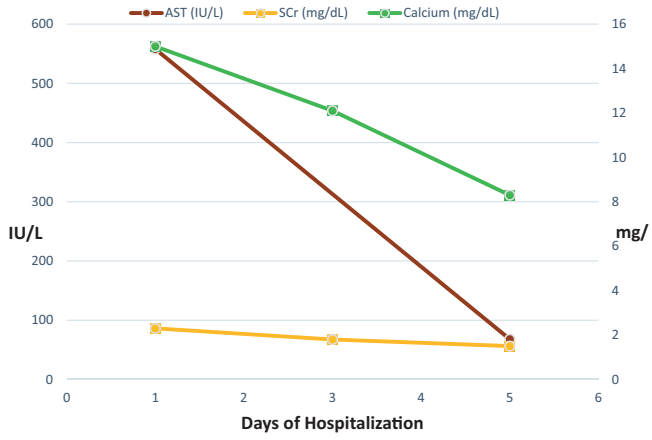
	3 H Post Ingestion	7 H Post Ingestion	Day 2	Day 3
apap (mcg/ml)	561	522	521	545.2
AST (IU/l)	25	wnl	47	13,776
ALT (IU/l)	17	wnl	167	8755
INR	1.2	wnl	1.6	6.9



	1	3	5
AST (IU/l)	558		68
SCr (mg/dl)	2.3	1.8	2
Calcium (mg/dl)	15	12.1	8

175. Is it better to look good than feel good? Chronic vitamin A toxicity

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Background: Vitamin A is a fat-soluble vitamin necessary for bone development, vision, and maintenance of epithelial tissue. It is commonly found in liver, fish, cheese, and milk as preformed vitamin A, whereas the vitamin A precursors, carotenoids, are found in fresh fruits and vegetables. The recommended allowance for vitamin A is between 2300 and 3000 IU for adults which typically is achieved in a daily diet. With potential effects on the skin, hair, bones, liver and brain, chronic vitamin A cases are rarely reported; here we report such a case.

Case report: A 23-year-old man presented to hospital after taking 50,000IU of vitamin A daily for the last six months for skin health, last dose was 3 d prior to admission. He reported having fatigue, weakness, headache, photophobia, blurry vision, body aches, polyuria, and a fever for weeks prior to hospitalization. Initial labs were concerning for hypercalcemia, acute renal failure, and hepatotoxicity, which are trended in Figure 1. Primary workup and treatment was for hypercalcemia in which intravenous fluids were started and patient was given a dose of zoledronic acid. Due to visual changes and headache, concern for idiopathic intracranial hypertension, in which lumbar puncture was performed and resulted with no growth in the cerebral spinal fluid. As symptoms were consistent with hypervitaminosis A, an initial vitamin A level was drawn which returned several days later supra-therapeutic at 1.84 mg/l (reference 0.3–1.2 mg/l). After 5 d of hospitalization, patient was discharged, the only symptom remaining was a headache which was expected to improve.

Discussion: A previous case report with a vitamin A level of 2.77 mg/l, the patient developed skin dryness, weakness, malaise, headache, muscle aches, and hypercalcemia; this case suggests similar symptoms may develop at a lower vitamin A concentration. It is thought that vitamin A directly stimulates bone resorption due to increased osteoclast formation and activity and also inhibits bone formation due to inhibition of osteoblast growth which leads to hypercalcemia. Common treatments include intravenous fluids, loop diuretics, and corticosteroids. In refractory cases, bisphosphonates can be considered. In this case, zoledronic acid was given despite a decreasing calcium level and likely was not a necessary treatment. The majority of hepatic vitamin A stores are the fat-storing cells in the liver, Ito cells, which are located in the area of the liver responsible for maintaining normal hepatic architecture. As vitamin A levels increase, these cells undergo hypertrophy and hyperplasia which can eventually lead to hepatocyte death, fibrosis, and cirrhosis with continued ingestion of vitamin A. The degree of hepatotoxicity is directly correlated with the length of time and dose of vitamin A. Renal dysfunction may develop in patients with hepatic failure from chronic vitamin A use.

Conclusion: Chronic vitamin A intake poses several significant health risks. Mainstay of treatment is to stop the offending agent. This case reiterates that doses of 50,000 IU/d for several months can lead to hepatotoxicity, hypercalcemia, and acute renal failure. With discontinuation of vitamin A and supportive care, most

symptoms of chronic vitamin A toxicity will resolve within one week.

KEYWORDS Vitamin A; chronic; hypervitaminosis A

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176. Five cases of accidental exposure to cloprostenol, a veterinary prostaglandin analog, in women

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Background: Cloprostenol (Estrumate®) is a prostaglandin analogue structurally related to prostaglandin F2α. It is used in cattle to manipulate estrus, to induce abortion and expel uterine contents. Estrumate® is provided as 250 mcg cloprostenol/1 ml. The recommended dose for cattle is 500 mcg. Per package insert, cloprostenol is readily dermally absorbed by human handlers, and may cause abortion and bronchospasm in humans. There is currently no entry for cloprostenol in standard databases such as Micromedex®. We report five cases of accidental cloprostenol exposure in women.

Case series:

Case 1. A 29-year-old woman contacted the Poison Center 30 min after inadvertently injecting herself with 0.5 ml of cloprostenol while attempting to inject a cow. She did not know her pregnancy status. She complained of vomiting, cramping and diarrhea. ED evaluation was recommended, but lacking insurance, she refused. Her symptoms resolved without treatment.

Case 2. A 20-year-old woman splashed approximately 0.5 ml of cloprostenol into her mouth, much of it landing on her cheek and not in her mouth. She rinsed her mouth immediately. She reported no symptoms. She was advised of a low likelihood of toxicity, but she became anxious after reading the package insert and presented to a local ED. The emergency physician determined that she was hyperventilating due to warnings in the product information. No further follow-up was available.

Case 3. A 31-year-old woman contacted Poison Control 5 min after accidental dermal exposure to a drop of cloprostenol. She did rinse immediately, but reported cramping, hot flashes, and a back labor feeling since exposure. Due to persistent symptoms, it was recommended that she see physician.

Case 4. A young woman called Poison Control 5 d after being injected with a small amount of cloprostenol. She reported no symptoms. Concerned that she might be pregnant, she was advised to see her physician. No further follow-up was available.

Case 5. A veterinarian called Poison Control on behalf of a 35-year-old woman 7 d after she was exposed to "a drop" of cloprostenol on her hand while injecting a horse. She reported a history of menstrual spotting in the interim.

Discussion: These cases – all small, inadvertent, occupational exposures to cloprostenol – were associated with mild, self-limited nausea, vomiting, diarrhea, and cramping. Prostaglandin F2 α analogues (e.g., dinoprost) have oxytocic, luteolytic, abortifacient, and vasocontractile properties. Potential complications of human exposure to cloprostenol thus include spontaneous abortion and bronchospasm in humans. Indeed, cloprostenol toxicity has been associated with cardiovascular collapse, with hypotension and pulmonary edema. While our cases suggest seemingly minimal toxicity, limited follow-up of a complex exposure fails to elucidate final post-exposure outcomes.

Conclusion: Five cases of accidental human exposure to cloprostenol developed apparent mild and self-limited adverse effects. While higher dose cloprostenol exposure may be more toxic, the limited exposure in these cases was not associated with significant morbidity. With limited guidance on how to properly handle these exposures, diligent follow-up should be performed to verify low likelihood of toxicity with small inadvertent exposures. It would be prudent to ascertain pregnancy status in exposed women.

KEYWORDS Cloprostenol; estrumate; veterinary prostaglandin analog

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177. Attitudes in a high risk population regarding a naloxone autoinjector capable of detecting acute overdose

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Background: Opioid overdose is the leading cause of mortality for individuals in the United States between the ages of 18 and 44. Opioid overdose is a major public health emergency, resulting in hundreds of thousands of deaths in the past 15 years. Current naloxone therapies require a bystander or first responder to administer the medication. Autoinjector technologies coupled with respiratory monitoring could enable a wearable naloxone delivery device that could automatically reverse an otherwise lethal overdose. It is not currently known whether individuals at risk for opioid overdose would be willing to wear such a device, and what design factors might make using such a device acceptable. Our primary aim is to determine the general acceptability of wearing a naloxone auto-injector and determine barriers to use in a population of subjects at risk for opioid overdose.

Methods: We conducted a prospective point-of-care survey of individuals presenting to a metropolitan emergency department at-risk for opioid overdose. Patients were deemed at-risk if they had a history of intravenous opioid use, presented to the emergency department for an opioid overdose, or were prescribed opioids for chronic pain management. Individuals were excluded if they were unable to consent, under the age of 18, pregnant, or a prisoner. The survey was presented orally to each participant. Survey questions explored willingness to wear a device with varying functionality and provided space to record any specific comments made by participants pertaining to each survey question. Additionally, space was provided to allow individuals to express any factors which might increase or decrease their interest in such a device. Study participants were given a $5.00 merchandise card which could be used at the hospital's coffee cart or gift shop.

Results: We surveyed 29 individuals; 12 (41%) were male and 17 (59%) female. Ages ranged from 19 to 64. Twenty-five (86%) participants indicated willingness to wear a device close to the skin and attached by a strap which would monitor their breathing while using opioids. Twenty-four (83%) respondents were willing to use a device containing an injectable dose of naloxone which would be administered if the respiratory monitor indicated an overdose. Eighteen (67%) of those surveyed believed that people would use the device if it were prescribed for all people who

saw a doctor for an opioid overdose. Fourteen (48%) were interested for the device to call emergency services and 23 (79%) were interested for the device to call a friend or family member. Qualitative analysis of free form comments indicated comfort, cost, and concealability of the device were major concerns.
Conclusion: Our survey suggests most people at risk for opioid overdose are willing to use a wearable autoinjector. Additional work is needed to develop and test an autoinjector.

KEYWORDS Naloxone; autoinjector; overdose

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178. Tramadol misuse and abuse: a six year retrospective cohort study assessing severity of exposure outcomes in relation to the rescheduling of hydrocodone in Texas

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Tramadol is often considered a safer alternative to other opioid analgesics with regard to abuse potential. In keeping with this perception, tramadol remains on the Schedule III list of the United States Controlled Substances Act. Data from the Texas Poison Center Network (TPCN) showed an increase in the number of tramadol prescriptions since hydrocodone was moved to Schedule II on October 6, 2014. The purpose of this study was to examine whether there has been an increase in severity of illness associated with tramadol misuse and abuse as reported to the TPCN since this rescheduling, as well as to investigate these trends over the last 17 years. This study was a six year retrospective cohort study investigating the severity of outcome and adverse events following exposure to tramadol as a single agent. Inclusion criteria were calls made to the TPCN for intentional single agent tramadol misuse or abuse by patients above age twelve. Cases where the outcome was not known, where the determined intent was self-harm, or where there was exposure to multiple agents were excluded. Outcomes were evaluated during the three years before and the three years after the reclassification of hydrocodone to Schedule II in October 2014. Data collected include patient demographics, date of call and exposure, and highest level of health care resources required. The primary outcome was severity of outcome as determined by level of healthcare resources utilized (home management, Emergency Department (ED) evaluation, hospital admission, Intensive Care Unit admission, or death). Secondary outcomes included changes in exposure frequency, and severity over time irrespective of scheduling of hydrocodone. A total of 454 cases met study criteria and were included for analysis during the period between October 6, 2011 and October 5, 2017. The total number of single-agent exposures to tramadol increased from 226 in the three years before to 238 in the three years after the rescheduling of hydrocodone. No overall difference in severity of post-exposure outcome was found when combined pre- and post-rescheduling data were compared. However, when cohorts from individual years were compared, exposures occurring between October 2016 and 2017 had significantly more severe outcomes and required higher levels of healthcare resources than two previous years ($p = .031$ for 2011–2012, $p = .01$ for 2013–2014), and approached significance for 2015–2016 ($p = .064$). Overall, the number of annual calls reporting tramadol exposure for abuse/misuse increased from 11 calls in 2000 to 78 calls in 2017. There was a concommittent increase in the level of health care resources required, particularly in the number needing evaluation in the ED, over this time. An increased frequency of and severity of tramadol exposure outcomes has been seen over the last 17 years. This pattern was re-demonstrated by comparing the cohorts before and after hydrocodone was rescheduled to Schedule II in Texas. Emergency care providers and toxicologists should be aware of both the growing frequency of tramadol misuse and abuse, as well as the increasing burden on health care resources.

KEYWORDS Tramadol; misuse; abuse

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179. Subacute methotrexate induced leukoencephalopathy presenting with stroke-like symptoms in two pediatric patients

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Background: Intrathecal (IT) methotrexate (MTX) is administered in patients with acute lymphoblastic leukemia (ALL) to reduce likelihood of isolated central nervous system relapse. MTX may cause acute (within hours), subacute (days–weeks), or delayed (months–years) neurotoxicity. The subacute toxicity of leukoencephalopathy may occur up to 2–14 d after the MTX and is associated with white matter changes on magnetic resonance imaging (MRI).
Case reports: Case 1: 14-year-old female with precursor B cell ALL presented to the emergency department (ED) after waking up with slurred speech, expressive aphasia and left facial droop. Her last dose of IT MTX was 12 d prior. She had received her vincristine and PEG-asparaginase the day prior. Her creatinine was normal. Brain MRI revealed acute restricted diffusion with in the bilateral centrum semiovale, slightly larger on the right. Electroencephalogram (EEG) was normal. Dextromethorphan was initiated at 1 mg/kg once a day and then twice a day. She improved over 5 d. Case 2: 9-year-old female with precursor B cell ALL presented to the ED with altered mental status and drooling. Her previous IT MTX was 10 d prior. Her creatinine was normal. Brain MRI demonstrated white matter changes in bilateral centrum semiovale and corona radiate on the diffusion weighted imaging (DWI). EEG was normal. Her symptoms resolved with overnight observation.
Case discussion: MTX induced leukoencephalopathy is a rare complication of MTX neurotoxicity and may present with stroke-like symptoms. MTX's mechanism of action depletes reduces folate in cells which diminishes the conversion of homocysteine to methionine. Elevated homocysteine levels in plasma and cerebrospinal fluid have been demonstrated in patients who received MTX. Homocysteine is a precursor to excitatory neurotransmitters which may stimulate inotropic glutamate receptors resulting in cellular injury. Increased adenosine in the cerebrospinal fluid has also been reported and may contribute to the toxicity. MRI findings include restrictive diffusion on DWI in cerebral white matter as DWI is sensitive to cytotoxic injury. Animal models have suggested that the use of dextromethorphan, an N-methyl-D aspartate receptor antagonist, may ameliorate the neurotoxicity.

Conclusion: We present two cases of pediatric patients who were treated with intrathecal methotrexate and presented with acute, focal stroke-like symptoms attributed to subacute methotrexate induced leukoencephalopathy.

KEYWORDS Methotrexate; leukoencephalopathy; pediatric

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180. A case of rattlesnake venom-induced platelet inhibition reversed by crotalidae polyvalent immune fab as demonstrated by thromboelastography

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Background: Approximately 5000 rattlesnake envenomations (RSE) are reported to US poison centers annually. Coagulopathy, thrombocytopenia, and hypofibrinogenemia are all known effects of venom and can be measured with specific laboratory assays. Rattlesnake venom is also known to inhibit platelet activation by adenosine diphosphate (ADP) which is not evaluated with routine assays. Thromboelastography (TEG) provides a global evaluation of clotting efficiency and includes a method for directly measuring platelet activation in response to arachidonic acid (AA) or ADP.
Case report: A 38-year-old woman with no past medical history sustained a RSE to the left lower leg while hiking. She self-administered a dose of ibuprofen 600 mg while waiting for medical care. She was air-evacuated directly to the regional toxicology referral center and arrived in the Emergency Department 3 h after the bite. Physical exam revealed two puncture marks to the anterior aspect of the left lower leg with edema extending distally past the ankle and ecchymosis to the dorsum of the foot. Laboratory evaluation revealed platelet count of 125,000/mm3, PT 12.8 s, aPTT 24.1 s, and fibrinogen of 238 mg/dl. Medical toxicology was contacted for admission and obtained a TEG® PlateletMapping® assay immediately prior to administering six vials of antivenom. The kaolin-activated sample (standard TEG) demonstrated normal clotting with reaction time (R) of 4.4 min (nl: 5–10), angle of 63.3 degrees (nl: 53.0–72.0) and maximum amplitude (MA) of 58.2 mm (nl: 50–70). However, platelet activation with both ADP and AA was inhibited (99% and 100% respectively). One hour after antivenom, repeat labs revealed platelet count of 424,000/mm3, PT 12.5 s, and fibrinogen 277 mg/dl. Standard TEG revealed R of 5.3 min and MA 47.2 mm. Platelet mapping revealed MA ADP of 53.0 mm and MA AA of 49.9 mm. Platelet inhibition was calculated at 0% for both. The patient received a total of 22 vials of antivenom and spent 7 d in hospital. On day 6, her labs demonstrated platelet count had decreased to 97,000/mm3 while a third thromboelastograph showed that platelet inhibition had not recurred.
Case discussion: This patient's thromboelastographs demonstrated inhibition of ADP-induced platelet activation that fully reversed after administration of crotalidae polyvalent immune Fab. The temporary AA inhibition was thought to be due to the self-administered ibuprofen as this has not been reported as a venom effect. Additionally, her platelet mapping on the day prior to discharge suggests that platelet inhibition is independent of platelet count as she had normal MA's and minimal inhibition despite concurrent thrombocytopenia.
Conclusion: This case demonstrates that platelet activation can be inhibited by rattlesnake venom *in vivo* and that crotalidae polyvalent immune Fab can reverse this platelet inhibition. Additionally, platelet inhibition may occur independently of thrombocytopenia. Thromboelastography can be used to measure this venom effect but the clinical implications merit further study.

KEYWORDS Rattlesnake envenomation; platelet inhibition; thromboelastography

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181. The first reported case of systemic toxicity from a western hognose (*Heteron nasicus*) bite

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Background: The Western Hognose snake (*Heterdon nasicus*) is a rear-fanged Colubridae popular in the North American pet trade. Its natural distribution ranges from southern Canada to Northern Mexico. *H. nasicus* has rear fangs that secrete venom from the Duvernoy glands by capillary action to help immobilize prey. Bites to humans previously have been reported to cause local effects including pain, swelling, and blistering at or near the bite site. Systemic toxicity has not been previously reported.
Case report: A 20 year-old woman with a past medical history of iron deficiency anemia was bit on the web between the 3rd and 4th digits while transferring her Western Hognose snake for feeding. Just prior to transferring, she handled a thawed mouse. The snake latched for approximately 2 min, then spontaneously released. The patient immediately noted pain and edema at the bite site that progressed proximally from her hand to her upper arm over several hours. She then developed numerous large fluid-filled blisters on her forearm and upper arm. With no improvement of symptoms by day 3 after the bite, the patient sought medical care. She was found to have her baseline anemia (hemoglobin 10.7 g/dl) and a new thrombocytopenia (platelet count 90×109/l). Previous platelet counts 1 and 2 years prior showed platelet counts of 315×109/l and 373×109/l respectively. She showed no signs of bleeding or other systemic effects. She was discharged after consultation with the Rocky Mountain Poison and Drug Center and followed by her primary care doctor. The bullae resolved over 14 d and the ecchymosis resolved over 30 d. Unfortunately, the patient was lost to follow up for several months. A platelet count obtained 4 months after the bite showed a rebound of her platelet count to 315×109/l. At the time of her 4 month labs, she continued to have slowly resolving hyperpigmented dermatitis at the sites of bullae and ecchymosis without pain.
Case discussion: *H. nasicus* possess two large grooved teeth just posterior to mid-mouth designed to deliver secretions from the Duvernoy glands by capillary action allowing quick incapacitation of prey. This mechanism of venom delivery is slower with less venom injected than elapidae or viperdae, which have hollow front fangs and dedicated stores of venom in glands. Previously reported cases of *H. nasicus* envenomation consistently involve prolonged bites of several minutes causing local symptoms. Our patient also had a prolonged bite in an

area of thinner skin which may have led to more venom exposure. A previous venomic study of *H. nasicus* reported moderate to high protease activity with low phosphodiesterase activity and no PLA2 activity while another venomic study found high levels of PLA2 activity and no protease activity. The medical significance of these findings remains unclear.

Conclusions: Systemic toxicity due to *H. nasicus* envenomation has not previously been reported. Healthcare providers should be aware for the potential of clinically significant dermatologic and now hematologic effects. Captive specimens should be handled with precaution, especially during feeding.

KEYWORDS Envenomation; thrombocytopenia; dermatitis

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182. Where there is smoke there is not always cyanide: Evaluation of prehospital hydroxocobalamin use

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Background: The indications for using prehospital hydroxocobalamin (OHCob) are not well defined. Our aim was to evaluate prehospital signs and symptoms in patients who received OHCob to improve future use. We also wanted to analyze in-hospital clinical, laboratory and outcome data to more accurately characterize probable cyanide exposures with others that were not.

Methods: In this retrospective study, all patients at our tertiary care burn center who received prehospital OHCob from December 2012 to March 2018 were reviewed. Age, gender, characteristics of the exposure, prehospital symptoms, hospital clinical and laboratory findings, additional doses of OHCob and outcomes were extracted. Each case was evaluated for evidence of suspected cyanide toxicity: hypotension, syncope, dysrhythmia, altered mentation, seizures, respiratory or cardiac arrest. A determination was made whether or not OHCob was indicated.

Results: In this study, EMS providers administered OHCob to 42 patients between December 2012 and March 2018. The average age was 46 years ($SD = 19$), and 55% were males. Table 1 summarizes demographic and prehospital characteristics of the patients. The majority (71%) of suspected cyanide exposures were from house fires. The most common prehospital finding were coma or depressed CNS (36%), followed by hypotension (16%) and cardiac arrest (12%). The overall majority of patients (60%), treated with OHCob had none of the seven clinical indicators of potential cyanide toxicity. There was little consideration of whether the exposure type could be a source of cyanide. Six of these patients were smoking cigarettes while on supplemental oxygen, which caused ignition. Four fell asleep with a burning flame that caught the bed or chair on fire. Four others were cooking and caused a grease fire. Four were exposed to carbon monoxide only or hydrogen sulfide only. One patient overdosed on pharmaceuticals and was exposed to gas, and two were burning trash outside. Carboxyhemoglobin, serum lactate and pH were significantly different in patients with an indication for OHCob (Table 2). These hospital findings support the seven clinical indicators as accurate predictors of possible cyanide exposure.

Conclusions: Prehospital OHCob is often used with unclear indications. Greater clarity of prehospital protocols, focusing on source of exposure as well as clinical indications, could reduce unnecessary use of OHCob.

Table 1. Demographic, exposure and prehospital characteristics by hydroxocobalamin indication.

			Hydroxocobalamin				
	Total $N = 42$		Non-indicated $N = 25$		Indicated $N = 17$		
Characteristics	*n*	%	*n*	%	*n*	%	*p*-Value[a]
Age (mean, sd)	46.1	18.8	49.1	16.9	41.6	20.9	0.170
Male[b]	23	54.8	16	64	7	41.2	0.253
Smoker	17	60.7	11	64.7	6	54.5	0.701
Exposure characteristics							
EMS mode[b]							0.604
Ground	29	69.0	16	64.0	13	76.5	
Air	13	31.0	9	36.0	4	23.5	
Nature of exposure							0.296
Housefire	29	70.7	15	62.5	14	82.4	
Other	12	29.3	9	37.5	3	17.6	
Closed Space	41	97.6	24	96.0	17	100.0	>.999
Prehospital findings							
HR (mean, sd)	96.4	40.6	108.9	24.4	77.6	52.3	.118
RR (mean, sd)	18.1	9.3	21.1	7.0	12.6	10.7	.024
SpO_2 (mean, sd)	87.6	27.0	96.7	4.7	70.9	40.9	.006
SBP (mean, sd)	118.1	52.6	136.1	34.6	90.5	64.0	.052
DBP (mean, sd)	71.0	34.2	83.1	22.8	52.4	40.9	.031
MAP (mean, sd)	87.1	40.1	100.8	25.5	64.8	49.8	.034
Hypotension	6	15.8	1	4.3	5	33.3	.027
Respiratory arrest	5	11.9	0	0.0	5	29.4	.007
Cardiac arrest	5	12.2	0	0.0	5	31.2	.006
Syncope	4	9.5	1	4.0	3	17.6	.286
Seizure	0	0.0	0	0.0	0	0.0	
Coma or depressed CNS	15	35.7	1	4.0	14	82.4	<.001
Prehospital GCS (mean, sd)	11.0	5.3	14.1	2.8	6.5	4.7	<.001

Fisher's exact test or Wilcoxon signed-rank test. [b]Chi-squared test.

Table 2. In-hospital clinical characteristics by hydroxocobalamin indication.

	Total N = 42		Hydroxocobalamin Non-indicated N = 25		Hydroxocobalamin Indicated N = 17		
Characteristics	Mean	SD	Mean	SD	Mean	SD	p-Value[a]
SBP	145.7	40.4	153.3	29.4	133.8	52.2	0.087
DBP	93.7	25.7	99.6	20.7	84.4	30.4	0.141
HR	91.6	26.9	93.5	19.2	88.8	36.4	0.894
HTN or Bradycardia (n, %)	29	70.7	19	76.0	10	62.5	0.485
ED findings							
Lactate	5.6	5.0	3.8	2.7	8.2	6.3	**0.024**
COHb%	12.2	14.3	5.7	6.1	22.8	17.6	**0.002**
MetHb	0.8	0.2	0.8	0.0	0.7	0.3	>0.999
pH	7.3	0.2	7.3	0.1	7.2	0.2	**0.002**
VBG (n ,%)	38	92.7	25	100.0	13	81.2	0.053
ED GCS	10.4	5.7	13.2	4.4	6.3	5.0	**0.001**
Outcomes							
Acute lung injury (n, %)	2	5.4	0	0.0	2	15.4	0.117
Mechanical ventilation (n, %)	33	80.5	17	68.0	16	100.0	**0.014**
Days of mechanical ventilation	5.3	6.4	6.5	7.5	4.0	5.1	0.081
Days of hospitalization	12.0	23.1	15.4	29.2	6.8	6.1	0.667
Days of ICU	8.0	13.9	9.9	17.5	5.3	5.3	0.852
Death (n, %)	10	24.4	1	4.2	9.0	52.9	**0.001**

[a]Fisher's exact test or Wilcoxon signed-rank test.

KEYWORDS Hydroxocobalamin; cyanide; prehospital
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183. Tetramethylammonium hydroxide occupational exposure cases reported to a poison center

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Background: Tetramethylammonium hydroxide (TMAH) is a water soluble, alkaline corrosive chemical used in etching of computer chips and in fracking hydrocarbons. Recent cases from non-U.S. countries report severe toxicity after occupational exposure to TMAH. This poison center (PC) reports on 5 occupational exposures to TMAH over the last 12 years from our state, 4 from the same city.

Case series: (see Table) The PC was called 12 years ago about 32-years-old male with 4 d of cough following inhalation of TMAH from a leaking sprayer. He was treated with albuterol as advised by the PC. A clinic 3 years later reported that a 24-years-old female chemistry student splashed TMAH on her arm, rinsed immediately and complained of finger numbness without signs of burn. Six years later the PC received report of a 22-years-old male sprayed with 25% TMAH while cleaning computer chips. Irrigation was prompt, but 45 min later he had superficial head and chest burns including a large partial thickness area. Concern was escalated upon finding reference to potential systemic toxicity. Reassuringly, none was seen and the patient was discharged after overnight observation. The PC was contacted last year about a 39-years-old male worker sprayed for 20 s from a broken pipe containing TMAH. The patient rushed to a shower, collapsed during the decontamination and suffered a witnessed cardiac arrest. He received 5 min of CPR with return of spontaneous circulation. ECG showed inferior ischemia and chest X-ray showed "fluffy" pulmonary congestion. Vital signs and labs were otherwise normal and a hypothermia protocol was initiated. Superficial burns and petechiae were noted on his upper chest without partial thickness burns. Sedation was weaned on day 3 but the patient showed unresponsiveness, spastic movements, followed by seizures, suggestive of anoxic brain injury. A rapid demise ensued while on comfort care 12 d post-exposure. Finally, the PC got report (same city, cases 1,3 & 4) of a 28-years-old male exposed to TMAH by inhalation and by dermal exposure to head and neck. The patient was discharged after resolution of facial flushing, headache and hypokalemia. Treatment consisting of prompt, on-scene irrigation.

Discussion: Dermal burns from TMAH are likely from the hydroxide anion while systemic toxicity results from the tetramethylammonium cation. Excessive depolarization followed by inhibition of autonomic ganglion/neuromuscular junctions, among other

Table. Case series of occupational tetramethylammonium hydroxide (TMAH) exposure.

Gender (Years)	TMAH %	Route	Time to Irrigation	Clinical Effects	Treatment	Outcome
M (32)	Unknown	Inhalation	Unknown	Respiratory irritation, cough	Albuterol	survived
F (24)	Unknown	Dermal < 5% BSA	<1 min	Numbness in fingers	Irrigation	survived
M (22)	25%	Dermal < 5%	<1 min	Mostly superficial, area of 2nd degree burns	Irrigation, ibuprofen, silvadene	survived
M (39)	Unknown	Dermal 16% BSA	prompt	Cardiac arrest, apnea, seizures, anoxic encephalopathy, petechiae	Irrigation, ACLS, therapeutic hypothermia, ventilation	died
M (28)	25%	Dermal < 5% BSA Inhalation	Unknown	Rosacea-like, flushing of face & neck, headache, Potassium 3.4	Irrigation	survived

effects, may lead to respiratory paralysis, hypotension and bradycardia. The systemic sequelae without significant burns seen in case 4 highlight the potency of TMAH. Cases 2 and 5 exhibited subtle systemic signs with little or no dermal injury, yet a significant burn in case 3 had no systemic signs. Most disturbing of all, 4 out of 5 cases happened in the same city, with 2 confirmed at the same manufacturing plant.
Conclusion: The occupational danger of TMAH is documented through this series of case reports. Employers, poison centers, and emergency care providers should be aware that severe, rapid respiratory and cardiovascular toxicity is possible even without severe dermal burns or large surface area exposure.

KEYWORDS Tetramethylammonium hydroxide; systemic toxicity; occupational accidents
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184. Seizure after inhalation of decafluoropentane

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Background: Decafluoropentane is a specialty hydrofluorocarbon fluid solvent used for cleaning and vapor degreasing at an industrial level. It was developed to replace the ozone-depleting perfluorocarbons (PFCs) and hydrochlorofluorocarbons (HCFCs). We describe the first reported case of human toxicity following an occupational inhalation exposure.
Case reports: A 27-year-old male with past medical history of asthma was brought by ambulance to the ED from his workplace at NASA's Jet Propulsion Laboratory. He was cleaning aeronautics parts using Vertrel XF degreaser (DuPont Vertrel XF specialty fluid, 1,1,1,2,2,3,4,5,5,5,-Decafluoropentane). He reached into a large bucket of the degreaser to retrieve a dropped item, and immediately upon standing felt eye irritation, lost consciousness, and was witnessed by co-workers to have a full-body convulsive episode lasting 1 min with tongue biting. Upon EMS arrival pt was disoriented and confused, with return to normal mental within several minutes. In the ED, pt was afebrile with normal vitals and a normal neurologic exam. Ocular exam was normal. Laboratory analysis was within normal limits, with the exception of initial bicarbonate of 17 and WBC 11. Ethanol, acetaminophen and salicylates were undetectable. Head CT was normal. The patient was discharged with instructions to follow up with his primary care provider.
Discussion: Vertrel XF specialty fluid (1,1,1,2,2,3,4,5,5,5,-Decafluoropentane) is a high-density, low-viscosity, fluorocarbon liquid used as a solvent, particulate remover, cleaning, and rinsing agent in high-tech industrial environments such as aerospace development. To our knowledge, no case reports of human exposure and toxicity have been previously reported. Neurotoxicity, including seizures, have been described in rats following high-level decafluoropentane exposure. This patient with no prior seizure history experienced conjunctival irritation and a self-limited seizure immediately following a brief inhalational exposure to decafluoropentane.
Conclusion: Occupational exposure to decafluoropentane may cause seizure, in addition to mucous membrane irritation.

KEYWORDS Decafluropentane; vertrel; seizure
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185. Biochemical and histotopographical alterations in the brain of rats exposed to low doses of deltamethrin: striatum apoptosis assessment

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Human is exposed to different xenobiotics that can affect his health and his environment. Among these substances, pesticides are agents widely used in agriculture and which can be found in our food. Only 1% of the quantities of pesticides used reach the target, while the rest is distributed in the environment. Deltamethrin is an insecticide of the pyrethrinoid family, it is considered to have excellent activity against insects, which can cause blocking effects for Canaesic and Potassium, resulting in excitation, abnormal paralysis and death of pests. (the insects). However, the question today is whether the problem of chronic toxicity of this new pesticide has been eliminated? In this study, we investigated the neurotoxicity of Deltamethrin (DM) at a dose of 0.32 mg/kg/day for 90 d in Wistar rats. Our experiment is divided into three areas of study; study of cellular apoptotic parameters, assessment of neurotransmitter levels and histological study of brain topography in the striatum. The majority of assay techniques used in this study are colorimetric techniques. Our results show a neuroneurological disturbance by the pesticide used (DM), through the increase of stress, the disruption of neurotransmitters and the degeneration of brain cells. From the analysis of apoptosis results, it is observed that the treatment with DM increases the activity of caspase-3 and the cytochrome-c rate; this increase little causes a state of organized cell death in the striatum. In addition, the evaluation of neurotransmitters shows a very clear disturbance in rats exposed to the pesticide. The topographic study of the brain (striatum region) shows structural changes in the brain shape and special structure of the striatum with black spots that may be the remains of tissue destruction by DM. Finally, that Deltamethrin induced at a dose of 0.32 mg/kg for 90 d; neurodegenerative effects in striatum cells of Wistar rats.

KEYWORDS Neurotoxicity; deltamethrin; rats
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186. Survival following novel interventions to treat severe acute toxic inhalational injury in a steel foundry worker

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Background: Steel foundry worker exposure to blast furnace gas is a means of potential acute toxic inhalational injury. The gas

composition is mixed and variable. Oxygen supplementation and supportive measures are the mainstay of treatment even if involvement of specific toxins such as irritants, carbon monoxide, carbon dioxide, or corrosives are identified.
Case report: A 54-year-old male steel foundry worker with type 2 diabetes was injured from an explosion when he mixed blast furnace iron and steel furnace slag. He sustained 8% total body surface area thermal burns to his head, face, and hands. He had no respiratory changes but before transfer to a burn center, was intubated for reported oropharyngeal soot and concern for smoke inhalation injury. Burn service evaluation was negative for typical findings associated with smoke inhalation injury; carboxyhemoglobin was 0.4% and there were no carbonaceous secretions upon burn center presentation. The patient was extubated at 8 h post event after tolerating pressure support ventilation with acceptable weaning parameters. He was awake, alert, and clinically stable until 17–18 h post event when he developed acute and profound hypoxia refractory to progressive interventions including oxygen supplementation (FiO_2 100%, PEEP 15), reintubation by 29 h post event, and epoprostenol. No airway changes were identified during reintubation. Chest x-ray identified bibasilar atelectasis. The patient developed hemodynamic instability requiring multiple inotropic agents for mean arterial pressure support, in addition to a severe metabolic acidosis. Administration of hydroxocobalamin did not improve his condition. Extracorporeal membrane oxygenation (ECMO) was instituted shortly thereafter (40 h post event). Additional measures included administration of IV hydrocortisone and IV N-acetylcysteine. Bronchoscopy (80 h post event) findings included moderate thin secretions (not proteinaceous; pH 7.5), mild mucosal edema and hyperemia, no carbonaceous soot, and no tissue necrosis. Aggressive measures were continued. The patient had a subsequent period with copious, thin secretions requiring frequent suctioning and respiratory tubing changes. He improved and tolerated ECMO decannulation by 10 d post event, epoprostenol discontinuation by 11 d post event, N-acetylcysteine discontinuation by 12 d post event, and extubation by 13 d post event. He had eventual return to apparent baseline respiratory status at discharge 32 d post event and follow up 52 d post event.
Discussion: This patient's course was notable for delayed-onset severe hypoxia that was not explained by a smoke inhalation injury. Delayed onset, absence of eosinophils, and lack of significant response to steroid therapy made a hypersensitivity reaction unlikely. Different toxic exposures were considered. Delayed onset is consistent with toxicity of low water solubility irritant gases such as nitrogen oxides. The hypoxia was refractory to standard supportive measures. Aggressive novel interventions including ECMO, inhaled epoprostenol (for reduction of mean pulmonary arterial pressure, through vasodilation, to assist oxygenation), and N-acetylcysteine (as an oxygen free radical scavenger), were utilized in this patient who survived without apparent residual respiratory injury.
Conclusion: Further investigation is needed on novel interventions including ECMO, epoprostenol, and N-acetylcysteine in the management of irritant gas and other toxic inhalational injuries.

KEYWORDS Inhalational toxin; N-acetylcysteine; epoprostenol

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187. Persisted cortical blindness after carbon monoxide poisoning

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Background: Carbon monoxide poisoning can cause severe neurological injuries, including varied degrees of persisted and delayed neurological sequels. Cortical blindness resulted from carbon monoxide poisoning was rare. Here, we report a case of cortical blindness after carbon monoxide poisoning, and proved by functional magnetic resonance imaging (MRI).
Case reports: A 26-years-old female with depressed history was found unconsciousness in a closed balcony with burn down charcoal after 6 h of being missing. Her blood carboxyhemoglobin level was 15%, and brain computerized tomographic (CT) scan showed minimal change over left globus pallidus. She received oxygen therapy with non-rebreathing mask and other supportive treatment due to her parents' opposition of aggressive management. Her conscious level got improved progressively, and blurred vision and decreased visual acuity were complained a few days later. Normal visual evoked potential (VEP) was reported. Brain MRI showed increased signal intensities over bilateral occipital lobes and hippocampus on the mode of diffusion-weighted image (DWI) on the 5th day. Further functional MRI examination confirmed that her visual function was severely damaged. No other delayed neurological sequels were found. Minimal improvement of visual acuity was noted after 4 years of follow-up.
Discussion and conclusion: Carbon monoxide poisoning could injury visual cortex and presents cortical blindness with other minor neurological deficits. Function MRI or MRI, instead of VEP might be the better way to confirm the impairment of visual function.

KEYWORDS Carbon monoxide; cortical blindness; MRI

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188. Atrial flutter and respiratory distress following exposure to palytoxin

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Background: Palytoxin and its analogues are among the most potent toxins known to man. They affect multiple organ systems via oral, dermal, and inhalational routes. While palytoxin has previously been associated with cardiac dysfunction and electrocardiogram (EKG) changes, we report what we believe to be the first case of atrial flutter caused by exposure to palytoxin.
Case report: A 43-year-old male with no significant past medical history presented with shortness of breath, palpitations, and diaphoresis. He reports aggressively scrubbing his fish tank, 3 d prior to presentation, which contained 'Green Button Polyp' coral. Resulting particles were aerosolized, inhaled, and there was significant dermal exposure through the arms. Symptoms progressed to metallic taste in his mouth, frequent sneezing, chills, dizziness, nausea, and cough productive of maroon–colored sputum. He sought medical attention after the symptoms proved persistent and progressive. Vital signs on arrival were a temperature of 36.8 °C, a heart rate of 180–200, a respiratory rate of 54, and oxygen saturation of 88% on room air. Abnormalities on the

physical examination included anxiety, diaphoresis,mild intercostal retractions, scattered expiratory wheezing, crackles, and a pruritic erythematous macular rash on trunk and extremities. Blood investigations were significant for an elevated procalcitonin 6.24 ng/ml, leukocytosis of 29.9 with 31.1% bandemia, and hyponatremia to 132 mEq/l. EKG revealed narrow complex tachycardia, when temporarily slowed by adenosine revealed 2:1 atrial flutter. Administration of a digoxin dose of 500 mcg, and a total diltiazem dose of 50 mg followed by a 15 mg/h infusion had no effect on the patient's tachyarrythmia. Only after receiving metoprolol 5 mg intravenously did the rhythm revert to sinus with a rate of around 80. Computed tomography of the chest showed bilateral panlobular ground-glass patchy opacities with intralobular septal thickening. Respiratory support initially required the use of non-invasive positive pressure ventilation in the form of BiPAP set at pressures of 16/10 cm H2O at 70% FiO_2 which was weaned over the course of 3 d.

Discussion: Palytoxin and palytoxin analogues have been shown to be present in dinoflagellates of the genus Ostreopsis, which are widely distributed marine environments. The main mechanism of action by which it exerts its effects is by converting the Na/K-ATPase pump into an ionic channel leading to uncontrolled membrane depolarization. Mortality has only been reported after exposure through the oral route, but myriad symptoms have been described following other forms of exposure. Despite being exposed through non-oral routes, this case, however, describes a critically ill patient whose course of illness could have been more complicated had he not presented to care, resulting in further morbidity and even death.

Conclusion: Palytoxin is cardiotoxic and has been reported to have caused many ECG changes. We describe the first case of atrial flutter caused by palytoxin. The mechanisms of toxicity of palytoxin are not entirely understood and management is supportive. Continued research into the subject and updated risk assessment studies appear to be warranted.

KEYWORDS Palytoxin; green button polyp; atrial flutter

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189. A case of reversible cardiomyopathy associated with elevated cobalt and chromium levels

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Background: The association between cobalt (Co) and cardiomyopathy is debatable, with most case series confounded by concomitant alcoholism and malnutrition. It is more widely accepted that cobalt-associated cardiomyopathy is a multifactorial pathology, with malnutrition and vitamin deficiencies acting as strong contributors to its causation. The role of elevated chromium (Cr) levels in cardiac toxicity is even more tenuous, without any clear association. We present a case of reversible cardiomyopathy in a patient with elevated Co/Cr levels due to joint arthroplasty failure.

Case reports: A 60 year-old male with a medical history of obesity, hypertension, and early-onset osteoarthritis, began to experience a global decline in aerobic function, dyspnea, and poor memory between 2008 and 2010. He was a nonsmoker, did not abuse drugs, and there was no family history of cardiac disease. His surgical history was significant for bilateral total knee arthroplasty (1998 and 1999), and right metal-on-metal total hip arthroplasty (2008). Prior to his orthopedic procedures, the patient had undergone pre-operative cardiac stress testing, which was unremarkable for any significant disease. In 2010, workup of his symptoms culminated in coronary angiography and transthoracic echocardiogram, which revealed normal coronary anatomy but an ejection fraction (EF) of 40–45%. CBC, electrolytes, cardiac enzymes, renal, thyroid, and liver function testing were unremarkable. At that time he was diagnosed with idiopathic cardiomyopathy and started on carvedilol. It was not until 2014 that heavy metal screening revealed significantly elevated serum Co & Cr levels of 208 ng/ml & 45.5 ng/ml, respectively (ref: $<$ 3.0 ng/ml for both Co/Cr). Subsequent orthopedic re-evaluations with multiple MRIs did not suggest a clear site of joint failure or pseudoabscess formation. A revision of his right hip in 2014 did not significantly augment the Co/Cr levels. However, left knee arthroscopy in 2016 revealed a damaged plastic insert and blackened synovial fluid. The polyethylene insert was promptly revised, and less than 6 months afterwards, his Co & Cr levels had dropped to 3.6 ng/ml and 14.5 ng/ml, respectively, with an overall subjective improved quality of life. Objectively, repeat echocardiograms and stress testing have demonstrated a trend towards normal cardiac function, most recently with an EF of 60% (2017).

Discussion: It is safe to assume that the patient's orthopedic hardware was the source of his significantly elevated Co/Cr levels. There is no alternative exposure, and the fact that his Co/Cr levels plummeted after revision of his damaged components strongly support this notion. While there is no test sensitive nor specific to cobalt-induced cardiomyopathy, there are two compelling aspects of this case that point towards an association between cobalt, chromium, and his transient cardiomyopathy. First, the lack of an alternative etiology (e.g., ischemic, endocrine, arrhythmogenic, etc.) to explain his symptoms, and second, the temporal relationships between his Co/Cr exposure, abatement, and cardiac recovery. The implication of cobalt more so than chromium in the pathogenesis of his condition, or vice versa, is ultimately unclear. Regardless, Co/Cr screening seems appropriate in the workup of a patient with idiopathic cardiomyopathy and a history of total joint replacement.

KEYWORDS Cobalt; cardiomyopathy; chromium

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190. Massive elemental mercury ingestion; addicted to glitter

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Background: Elemental mercury ingestions are rare and present challenges in decontamination, waste containment, HAZMAT involvement and therapy. We present a case of massive ingestion with persistence in the intestines for 17 d following aggressive gastrointestinal decontamination, and hospital monitoring of ambient mercury concentrations.

Case report: A 30-year-old female with ingested 60–700 ml elemental mercury because she was "addicted to glitter" and thought the mercury was beautiful. Collateral was later obtained from a male acquaintance, later seen in the Emergency Department with other complaints, who stated "my girlfriend is upstairs, the one who drank mercury." He revealed that the mercury must

have belonged to previous owners, since she had found it on a shelf in the garage. On initial presentation, the patient was exhibiting bizarre behavior, hallucinating that "terminators were dancing on [my] skin". Abdominal x-ray showed numerous radiopaque bowel material, covering a 15 × 15 cm area. Whole bowel irrigation was initiated via nasogastric tube and continued through day 10. High fiber diet and bulk forming and stimulant laxatives were utilized in addition to frequent turning of the body for gravitational assistance with clearance. Fecal waste was immediately bagged and disposed of in a covered HAZMAT waste container. With frequent stooling and continuous 1:1 sitter in the room, there was concern for safety. Using a Jerome meter, air mercury concentrations were undetectable inside the patient's room and above the bedpan containing recent waste. The waste contents were 9.6 mcg/m^3 in a small waste container and 2.2 mcg/m^3 in a larger waste container. On day 2, mercury was visualized in the appendix, rectum and large intestine. A rectal tube was placed to avoid transfer of contaminated waste. The polyethylene glycol -electrolyte solution dose was suboptimal (250–400 ml/h) due to abdominal pain. Colonoscopy was performed on day 9; repeat x-ray showed reduced mercury content but mercury still present in the colon, cecum, with evidence of intestinal lumen leakage. At that time, the patient had pancytopenia, acute neuropathy and pruritus. Blood mercury was 114 mcg/l on day 1, 121 mcg/l on day 3, and 115 mcg/l on day 9. Succimer 500 mg three times per day was initiated on day 11 and continued through day 25. X-ray on day 18 showed only mercury in the appendix. The patient was discharged to a mental health center where she eloped on day 25. Blood mercury four months after ingestion was undetectable. The exposure site residence was condemned prior to ingestion, tested positive for mercury using a Jerome meter at 16 mcg/m3 after exposure, and remains condemned.

Conclusion: This case demonstrates difficulties in gastrointestinal decontamination after very large elemental mercury ingestion and issues of environmental contamination with potential for caregiver exposure. Whole bowel irrigation was not completely effective in removing mercury from the gastrointestinal tract and could not be given at the optimal rate. Coordination among the hospital emergency management team, medical toxicology and health department was critical in attaining success.

KEYWORDS Mercury; air monitoring; HAZMAT

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191. Dose-dependent pulmonary injury following Kinepak exposure

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Background: Ammonium nitrate/nitromethane (ANNM) is a powerful explosive used in both terrorist attacks and commercial demolition. Nitrogen oxides, including nitrogen dioxide, are byproducts of these explosions. Nitrogen dioxide exposure may result in dose-dependent pulmonary injury including fatal acute respiratory distress syndrome (ARDS), with a delayed onset of up to several hours. We present a series of three patients with dose-dependent pulmonary injury after[DP1] likely nitrogen dioxide exposure following the use of Kinepak®, a commercially available ANNM binary explosive device.

Case reports: Three patients presented to the emergency department (ED) 12–24 h after a spelunking expedition where they crawled 1.5 miles, partially submerged in water, and detonated a Kinepak® to clear debris. They denied any shockwave or symptoms of blast injury following the detonation, however, a large gaseous cloud was produced. Patient #1(P1) was closest to the explosion and exited through the area of explosion after some panic. Patient #2(P2) had a brief exposure to the gaseous cloud and #3(P3) was furthest from the cloud. Patients #1 and 2 both crawled out after the gas dissipated. All three had no signs of trauma and normal methemoglobin levels on presentation to the ED. P1 was a 47-year-old male that presented 12 h post incident with progressively worsening dyspnea. On exam, the patient's vital signs were: BP 112/52, HR 91, RR 31, SpO_2 71%. He was in visible respiratory distress with crackles in all lung fields. X-ray and CT both showed evidence of ARDS. Despite BiPAP, he continued to be hypoxic, so he was intubated and sedated. Post-intubation he required norepinephrine due to hypotension. After 5 d, vasopressors were discontinued and he was extubated. P2 was a 30-year-old male that presented 14 h post incident. He was initially feeling well, but noted dyspnea while visiting P1 in the ICU. On exam, the patient's vital signs were: BP 141/74, HR 104, RR 18, SpO_2 83%, no apparent distress, clear breath sounds. An X-ray and CT showed evidence of ARDS. He was placed on non-rebreather mask at 10L with improvement in SpO_2 to 96%. Over time, his oxygen requirements decreased and he was discharged on day 3. P3 was a 22-year-old female that presented 28 h post incident with dizziness and mild dyspnea. On exam: BP 127/67, HR 110, RR 20, SpO_2 100%, X-ray showed subtle ground glass opacities. Her symptoms improved the following day and she was discharged.

Case discussion: Nitrogen dioxide is a known source of delayed pulmonary edema. It is well described in both silo filler's disease, where anaerobic metabolism combines nitrites and organic acids to produce nitrogen oxides, and as an explosive byproduct. Nitrogen oxides have limited water solubility, allowing for deeper inhalation into the lungs. They then react with water in the respiratory tract to slowly form nitric and nitrous acid resulting in delayed pulmonary irritation and inflammation, as was evident in a dose-dependent manner in these patients.

Conclusion: The use of commercially available ANNM explosives can create nitrogen oxides, including nitrogen dioxide than can result in delayed pulmonary injury.

KEYWORDS Nitrogen dioxide; pulmonary; spelunking

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192. Photographical documentation of facial hyperpigmentation related to use of facial whitening cream and elevated mercury levels

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Background: Mercury is a naturally occurring metal and exists in several forms. Exposure to mercury can cause toxicity to multiple organ systems. Inorganic mercury is a common ingredient found in skin whitening products.

Case report: This is a single patient chart review. A 47-year-old female initially from Burma was found to have elevated mercury levels as part of a community-screening project for immigrants to the United States. High mercury levels in both blood and urine indicate an exposure to inorganic mercury. She used a whitening cream imported from Thailand which she had been applying to her face for about 2 years from 2015 to 2016. She reported onset of hyperpigmentation to her face when she began using the cream.The rest of her skin and exam was normal. She denied tremor, weakness, gait disturbance, paresthesias and visual changes. In December 2015, her urine mercury level was 109 mcg/l (reference range 0–19 mcg/l) with a blood level of 24.4 mcg/l (reference range 0–14.9 mcg/l). As she was otherwise asymptomatic, it was decided to trend her levels and chelation was not performed. She stopped using the cream in December 2016. A repeat blood level in January 2017 was 40 mcg/l. Blood lead and arsenic levels were within normal range. In March 2017, her mercury levels decreased to a blood level of 36.1 mcg/l and urine level of 28 mcg/l. Her serum creatinine was 0.8 mg/dl. Additional testing and monitoring could not be done due to loss of follow-up.
Case discussion: Topical mercury compounds can be absorbed across the skin and potentially cause systemic toxicity including renal, gastrointestinal and nervous system. Deposition of mercury in the dermis has been reported to cause skin discoloration. Our case demonstrates elevated mercury levels as well as skin discoloration after prolonged use of whitening creams. Other sources of inorganic mercury exposure were not found; however,our study is limited by an inability to obtain and investigate a sample of the product.
Conclusion: This is a case report of facial hyperpigmentation associated with elevated mercury levels likely due to prolonged exposure to inorganic mercury in a whitening cream.

KEYWORDS Mercury; hyperpigmentation; whitening cream

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193. Comparison of 5 and 10 mg doses of intravenous vitamin K in warfarin-related INR reversal

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Background: Warfarin reversal is indicated for patients with supratherapeutic international normalized ratios (INR), clinical signs of bleeding, or due to need for invasive procedures. Strategies for reversal of INR including fresh frozen plasma (FFP), four factor activated prothrombin complex concentrate (4-factor PCC), and vitamin K administration. While FFP and PCC acutely supplement clotting factors, endogenous clotting factor production comes from the use of vitamin K. Few studies evaluating different intravenous (IV) doses of vitamin K exist. The difference between 5 mg and 10 mg are not clear and may impact outcomes beyond the initial reversal, including the duration of INR reversal.
Objective: To characterize INR reversal in patients with asymptomatic INR elevation, non-life threatening bleeds, or a planned procedure in patients receiving 5 mg or 10 mg IV vitamin K without FFP or PCC.
Methods: This was a retrospective study conducted from January 1, 2016 to December 31, 2016. Included patients were 18 years of age and older on warfarin who received 5 mg or 10 mg IV vitamin K once for INR reversal. Patients were excluded if no INR values were collected within 24 h of vitamin K administration or co-administration with 4-factor PCC or FFP. Outcomes evaluated were reversal within 24 h, duration of anticoagulation reversal, and time needed for the INR to become therapeutic after warfarin was re-initiated.

Table 1. Time to therapeutic INR after warfarin resumption.

	5 mg ($n = 5$)	10 mg ($n = 9$)	p-Value
Duration, hours			$p = .1$
Median [IQR]	35.6 (31.4 60.3)	106.3 (38.5–107.3)	
Mean (± SD)	47.3 (± 25)	85.2 (± 44.4)	

Results: In total 56 patients were included, 34 of whom received 5 mg of vitamin K and 22 received 10 mg of vitamin K. The median pre-reversal INR in the 5 mg and 10 mg cohorts were 4 (IQR, 2.7–4.6) and 7 (IQR, 2.6–6.4) ($p = .43$), respectively. Three patients in both groups had an initial pre-reversal INR > 10. The median post-reversal INR in the 5 mg and 10 mg cohorts were 1.5 (IQR, 1.4–1.7) and 1.6 (IQR, 1.4–1.6) ($p = .44$), respectively. An INR < 2 within 24 h was reached in 32 of 34 (94%) patients in the 5 mg group, and 17 of 22 (77%) in the 10 mg group ($p = .06$). Therapeutic INR was reached an average of 47.3 ± 25 h after warfarin resumption in the vitamin K 5 mg group, and 85.2 ± 44.4 h in the 10 mg group ($p = .1$).
Conclusions: Both 5 mg and 10 mg IV doses corrected INR to <2 within 24 h, though numerically 5 mg had a higher percentage <2 within 24 h. This may have been due to higher median pre reversal INR in the 10 mg group. When anticoagulation was resumed, time to therapeutic INR was shorter and approached statistical significance for the lower dose vitamin K group. Study limitations include small sample size and retrospective nature, limiting control of confounding variables.

KEYWORDS Vitamin K; warfarin; reversal

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194. Straight to psych: healthcare facility calls: increasing complexity of Poison Center patient triage

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Background: Over the past decade there has been an overall increase in the number of cases reported to U.S Poison centers (PC) by healthcare facilities (HCF). There has been concern about increasing acuity of calls due to increasing HCF exposures taking up more PC staff time. This study was undertaken to examine disposition of HCF cases reported to US PCs.
Methods: Using NPDS data, a 10 year period from January 1, 2008 to December 31, 2017 was examined for the total number and percentage of: total exposures managed in a HCF, those treated and released, admitted to a medical unit (ICU and non-ICU), admitted to a psychiatric facility, and lost to follow up.
Results: The total number of patients managed in a HCF has increased by 10% over the past 10 years (total increase of 57,569 exposures). The number of patients admitted directly to a psychiatric unit increased by 67%, patients admitted to a medical unit increased by 20%, and patients treated and released directly from an ED increased 4%. The only decrease occurred in patients lost to follow-up (decrease of 19.2%).

Table 1. Net case volume change.

	2008	2017	Volume change	Percent change
Total HCF Cases	598,048	655,617	57,569	9.60%
Treated and Released	295,834	309,125	13,291	4.50%
Admitted to Medical Unit	148,974	178,546	29, 572	19.90%
Admitted to Psychiatric Facility	51,338	85,613	34,275	66.80%
Lost to FU/AMA	101,902	82,333	−19,569	−19.20%

Table 2. Percent disposition to volume.

	% to Total (2008)	% to Total (2017)	% Difference	% Change in % Difference
Treated and Released	49.47%	47.15%	−2.32%	−4.70%
Admitted to Medical Unit	24.91%	27.23%	2.32%	9.30%
Admitted to Psychiatric Facility	8.58%	13.06%	4.47%	52.10%
Lost to FU/AMA	17.04%	12.56%	−4.48%	−26.30%

Conclusion: Nationally, there has been a 10% increase in the number of poisoning/overdose cases over the last 10 years reported to poison centers. There has been a significantly higher percentage admitted directly to psychiatric facilities from emergency departments. Medical clearance from the emergency department is a complex decision-making process and may involve multiple follow-ups by a PC. The relatively small increase in medical admissions seems to indicate that the acuity of patients is not increasing as rapidly. However, the complexity of the triage decision-making that PC staff must perform has increased significantly.

KEYWORDS Disposition; psychiatric admissions; call volume

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195. Using Emergency Department discharge data to evaluate pediatric opiate related encounters: do ICD-9 codes provide accurate data?

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Background: Over 64,000 Americans lost their lives to an overdose in 2016. Most of these deaths, which have increased by more than 300% since 2000, are opioid-related. Numerous nonfatal opiate exposures and events occur annually, causing high levels of morbidity as well as billions of dollars in health care expenditures and other costs. Effective tracking and evaluation of opiate overdose morbidity and mortality is necessary for identification of trends and appropriate intervention. Use of International Classification of Disease (ICD) diagnosis codes for analysis of overdose events has been shown to be fairly specific but insensitive in general Emergency Department (ED) settings. The positive predictive value of ICD codes has not been previously evaluated in a pediatric population.
Objective: To evaluate the positive predictive value of ED diagnosis codes in correctly identifying opiate overdoses and related events in a pediatric population
Design/methods: A retrospective chart review of patients 0–18 years seen in 16 EDs across one regional healthcare system from October, 2013 to September, 2015. Patients were initially identified by ICD-9 discharge codes (304, 304.01, 304.02, 304.03, 304.7, 304.71, 304.72, 304, 73, 305.5, 305.51, 305.52, 305.53, 965, 965.01, 965.02, 965.09, 965.69, 965.7, 965.8, 965.9) followed by manual chart review.
Results: Three hundred and twenty-five patients were identified by an ICD code indicating opioid overdose or exposure, opioid withdrawal and/or for opiate detoxification/treatment needs. Of these, manual chart review determined that 125 (38%) did not have clinical presentation consistent with the coded event. ICD-9 codes were more effective at identifying opiate events in the younger population (0–5 years). Image 1 shows the number of cases broken down by age and by opiate exposure identified after chart review.
Conclusions: Accurately identifying patients who have experienced an opiate overdose or opiate related event is crucial in monitoring the impact of the current epidemic on the pediatric population. This review of one health system found large discrepancies between ICD codes indicated in discharge data and actual overdose events identified by independent chart review. Utilizing only ICD-9 codes to quantify opiate exposures and events has unexpectedly low positive predictive value. Given the necessity of accurate information to track and appropriately respond to this continuing crisis, changes in coding practices and in diagnosis code clarity are urgently needed.

KEYWORDS Opiate overdose; ICD coding; pediatric

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196. Development of national consensus recommendations for the management of colchicine poisoning by Poisons Information Centers

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Background: Prompt risk assessment and initiation of management in colchicine poisoning can improve outcomes. Of the available resources, specific thresholds for medical review and treatment are not commonly provided and do not take into account risk factors, such as drug interactions and co-morbidities. We developed national consensus recommendations for the management of colchicine exposures.
Methods: A small focus group performed a systematic review of the literature and developed draft recommendations that considered information on the dose-response, pharmacokinetics, toxicokinetics, effect of renal and liver disease, other drug exposures (notably inhibitors of P-glycoprotein and cytochrome P450 3A4) and the relationship between clinical features and laboratory tests on outcomes. Feedback was obtained from toxicologists and specialists in poisons information at each poisons information center across the country, then the final proposed recommendations were presented at a local toxicology meeting for further discussion and debate.
Results: (1) patients with symptoms potentially due to any acute or chronic colchicine exposure should be admitted and given single dose of activated charcoal (SDAC) and consideration of multiple-doses of activated charcoal (MDAC); (2) acute exposures <0.1 mg/kg and no risk factors is low risk so no intervention is needed but the patient should be admitted if symptoms develop; (3) 0.05–0.1 mg/kg and any risk factor is at risk of severe

toxicity so should be admitted and given SDAC; (4) 0.1–0.5 mg/kg and no risk factors are at risk of severe toxicity so should be admitted and given SDAC; (5) 0.1–0.5 mg/kg and any risk factor are at risk of severe toxicity so should be admitted and given SDAC and MDAC; (6) 0.5–0.8 mg/kg is at risk of severe toxicity and 10% mortality so should be admitted and given SDAC and MDAC; (7) > 0.8 mg/kg has a high risk of severe toxicity including multiorgan dysfunction and death so should be admitted and receive continuous cardiac monitoring, SDAC and MDAC (consider intubation to facilitate treatment in high risk cases). Referral to a clinical toxicologist is indicated if the patient is symptomatic or specialist in poisons information is otherwise concerned. The quantification of dosages includes the amount of colchicine taken within a 24 h period. Hospital admissions should be for a minimum of 24 h (during which supportive care is provided and blood tests are checked every 4–6 h in symptomatic patients). Risk factors are any of a drug-drug interaction (DDIs), renal impairment or liver impairment. Important DDIs were amiodarone, azithromycin, azole antifungals, clarithromycin, diltiazem, ciclosporin, erythromycin, isoniazid, protease inhibitors, quinidine, verapamil. Patients who are asymptomatic with normal blood tests 24 h post-ingestion do not require further monitoring or interventions.

Conclusion: A conservative approach to the management of colchicine poisonings is proposed, and the risk assessment requires consideration of multiple factors. An audit of adherence to these recommendations is underway.

KEYWORDS Colchicine; poisoning; guidelines

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Table 1. Demographics.

	Patients with single poisoning ($n = 40,802$) Mean, (SD) or %	Patients with repeat poisonings ($n = 3430$) Mean, (SD) or %
Female	61.3%	57.4%
Age [years]	33.1 (16.1)	32.9 (14.5)
Substances		
Prescription drugs	49.6%	52.4%
Over-The-Counter drugs	27.1%	23.1%
Non-medication substances	23.3%	24.5

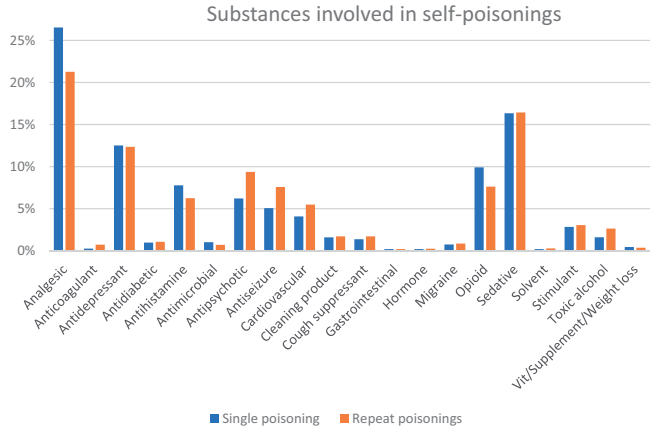

Figure 1. Substances involved in self-poisonings.

197. Patterns of repeat self-poisoning based on a novel poison center database

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Background: Poisoning is a common method of self-harm. It has been previously described that patients attempting self-harm are at increased risk for recurrence of self-harm attempts. Prior literature examining incidence and timing of repeat self-poisoning has generally not used patient level data such as substances involved to characterize these attempts. Anecdotally, the prescription drug on which a patient overdoses is often continued, potentially increasing the risk the patient may overdose again with the same drug. Though a 2014 study demonstrated that total pills prescribed tend to actually increase after a deliberate self-harm attempt, the patterns of substances involved in repeat self-poisonings is generally unknown. The purpose of this study was to characterize patterns of repeat self-poisoning using poison center data, for the purpose of developing strategies to reduce the incidence of repeat overdose, such as by restricting access to certain drugs.

Methods: This was a retrospective study of self-harm attempts reported to a regional poison center. Data were obtained for potential self-harm or suicide attempts by poisoning from October 1, 2008 to December 31, 2017. Patients were considered to have repeat self-poisoning if <1 call to the poison center was listed, based on identical first name, last name, and state, and ages consistent with a single person (eg calls two years apart should have an age difference of 2 years). Data such as demographic information, dates and number of self-harm attempts, and substances involved were abstracted and analyzed. Primary substances involved or suspected were classified by category.

Results: There were 40,802 patients with single attempt self-poisonings, and 3430 patients with repeat self-poisonings (with a total of 8002 cases) over the study period. Women comprised the majority of both the single poisonings group ($n = 25,026$, 61%) and the repeat poisonings group ($n = 1969$, 57%). The proportion of substances that were prescription medications, over-the-counter, or non-medication were relatively similar between groups (Table 1). The majority of substances used for self-poisoning were classified as "Other." Of substances classified, the proportions of specific classes appear similar between the two groups (Figure 1). The most common primary substances in single versus repeat overdoses included non-opioid analgesics (27 versus 21%), sedatives (16% in each), antidepressants (12% in each), opioids (10 versus 8%), antipsychotics (6 versus 9%), and antiseizure drugs (5 versus 8%), respectively. Among patients with repeat self-poisonings, the mean number of attempts was 2.4 (SD 0.98; range 2–20). Of 8002 cases of repeat self-poisoning, 10.5% ($n = 840$) involved the same substance as a prior attempt, and more specifically, 4.1% ($n = 329$) involved a prescription medication the patient had previously overdosed on.

Conclusions: Previous reports using hospital records or large registries have investigated incidence and timing of repeat self-poisoning. This study is unique in that it utilizes poison center records as a novel data source to examine this subject, and it describes substance patterns in repeat overdose that were previously unknown. Given the global scale of self-harm by poisoning, the finding that 4.1% of repeat overdoses involve the same prescriptions previously used in overdose represents a potential avenue for intervention.

KEYWORDS Repeat; recurrent; overdose

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198. Garlic burn: a pediatric case of uncovered garlic causing partial thickness burns

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Background: Chemical burns due to garlic are seldom described in the literature. Case reports have documented contact dermatitis and rare chemical burns resulting from topical application of crushed garlic under an occlusive dressing. We report a case of a partial thickness burn secondary to raw, uncrushed garlic without an occlusive dressing. This unique case broadens understanding of chemical garlic burns.
Case report: A 2-year-old female with no past medical history or known allergies was brought to the Emergency Department by her parents for a skin reaction. The night prior, due to abdominal discomfort, her parents used a traditional remedy from their home country of wrapping a raw garlic wreath around her abdomen. It was left in place for approximately 9 h. There was no trauma, thermal injury, or other potential chemical exposure. On examination, the patient had periumbilical skin erythema and sloughing, with small additional areas over the bilateral iliac crests. The chemical burn was characterized as 2nd degree partial thickness with 2% TBSA (Image 1). It was debrided under intranasal fentanyl (Image 2), and a foam dressing was applied. Follow up occurred in the Burn Clinic 8 d later, and the patient had near complete wound resolution at that time.
Case discussion: Garlic (Allium sativum) has antimicrobial and additional properties that have been used for medicinal benefits since 3000 BCE. It continues to be used by naturopathic doctors and as a traditional topical remedy in many cultures. Topical garlic has been associated with not only contact dermatitis but also chemical burn. Rafaat et al. reported a case of a 3-month-old female who sustained partial thickness burns from overnight application of crushed garlic wrapped in bandages. Another case report described skin blistering in a 17-month-old who had garlic petroleum jelly applied to her feet. In 2004, a case report described a 60-year-old male with diabetic neuropathy who required admission to a Burn Unit for partial thickness burns to the feet after applying crushed garlic with an occlusive dressing. Previous reports have attributed garlic's acantholytic effect to diallyl disulfide. When garlic is cut or crushed, the enzyme alliinase hydrolyzes aliin to form allyl sulfenic acid. Two molecules of allyl sulfenic acid combine to form one molecule of allicin, a defense molecule responsible for garlic's pungent odor. Allicin then decomposes to diallyl disulfide, an irritant and allergen associated with contact dermatitis. This case is unique in that the garlic was not cut or crushed, so there would have been minimal diallyl disulfide present, and this is the first report of a garlic chemical burn without an occlusive dressing.
Conclusion: While garlic's potential medicinal properties continue to be studied, its adverse effects must also be appreciated, and clinicians should recognize the potential for significant chemical burn secondary to topical garlic. Patients and families should be counseled on this potential adverse effect.

KEYWORDS Garlic; chemical burn; pediatric

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199. Ocular exposures reported to United States poison control centers

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Purpose: To investigate the epidemiology of ocular exposures reported to poison control centers in the United States.
Methods: A retrospective analysis of ocular exposures from 2000 to 2016 was conducted using data from the National Poison Data System.
Results: Poison control centers received 1,436,683 reports of ocular exposures during 2000–2016, averaging 7043 exposures per month. The annual frequency of exposures declined significantly by 37.2% from 2006 to 2016. The exposures rate per 10,000 US residents was highest among children <6 years (10.7 exposures), especially among 2-year-old (20.5 exposures), and was lowest among adults ≥20 years (1.9 exposures). The majority of the exposures resulted in minor (51.4%) or no effect (4.7%). Among those exposed, 67% were managed on-site (non-HCF), 23.0% were treated and released and 0.3% were admitted to a HCF. Household cleaning products (22.2%), cosmetics/personal care products (15.7%), and pesticides (7.4%) were the most common substance categories associated with the exposures, but exposure to building and construction products (17.6%), industrial cleaners (14.5%), and chemicals (13.6%) resulted in higher percent of moderate effect. In addition, exposures to substances containing alkali tend to resulted in higher percent of moderate effect. Major effects occurred in 1880 patients (0.13%) and occurred most commonly in alkalies: including drain cleaners, oven cleaners, hair relaxers and industrial alkali cleaners. Of the major product categories comprising greater than or equal to one percent of all cases, industrial cleaners, chemicals, and swimming pool/aquarium products were associated with the highest proportion of serious medical outcomes. Adults (>19 years) had the greatest proportion (9% of age group) reporting serious effects compared with 3% for children <6 and children 6–12 years. The annual frequency of exposures declined significantly by 37.2% from 2006 to 2016. This decrease was driven by the decline in the number of exposures among many of substance categories, including household cleaning products, cosmetics/personal care products, pesticides, and eye/ear/nose/throat preparations (Figure 1).
Conclusion: To our knowledge, this is the first multi-year study of ocular exposures among individuals of all ages reported to US poison control centers. Although the annual frequency of exposures has declined during the last ten years, the number remains high, especially among young children, and represents an important preventable source of morbidity. The substance categories commonly associated with ocular exposures offer opportunities for targeted prevention efforts.

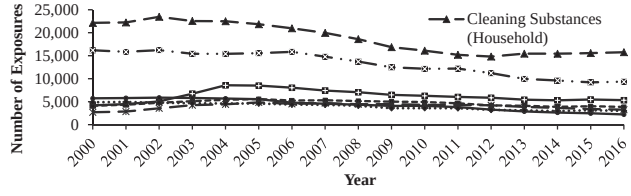

Figure 1. Annual number of ocular exposures for the top seven substance categories, National Poison Data System (NPDS) 2000–2016.

KEYWORDS Ocular injury; poison center; alkalai

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200. Modified high? adult modified release stimulant exposures reported to the NPDS

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Background: Modified release stimulants (MRS) are commonly used in the treatment of attention-deficit/hyperactivity disorder (ADHD). The numbers of these products have increased over the last decade and due to their modified release properties may be associated with significant toxicity. We sought to characterize adult single agent exposures to MRS to report to the National Poison Data System (NPDS).
Methods: The modified release stimulant product codes for this dataset were gathered through an analysis of Micromedex product codes that fall under the amphetamines and related compounds and methylphenidate generic codes. Using the identified set of product codes, SQL queries were written to extract data from the NPDS database for cases from December 1, 2007 to December 31, 2017. The result set was validated by two separate data analysts – one external to the AAPCC Central Office and one within the Central Office. Case involving a single agent exposure to an MRS in a patient 19 years of age or greater were selected. All data entered into NPDS was collected and analyzed using Microsoft Excel (Microsoft Corp., Redmond, Washington, 2010).
Results: A total of 7123 cases were identified. The average age was 35.0 years (range 19–97, SD 11.4) and 58% of cases were female ($n = 4129$). The highest number of cases were reported in 2011 ($n = 880$) followed by 842 in 2009. In all, intentional exposure, including misuse, abuse, and suspected suicide accounted for 42% ($n = 2973$) of exposures. Ingestion of the MRS was reported in 6964 (98%) exposure but there were 107 cases (1.5%) of inhalation/nasal route. Adderall (amphetamine/dextroamphetamine) XR 30 mg was the most common single agent involved in exposures. In all Adderall XR products accounted for 58% ($n = 4129$) of all exposures. Table 1 lists the top five products involved in exposures. Ninety-three percent ($N = 6644$) of exposures occurred at the caller's residence and 59% ($n = 4234$) of calls originated from a own residence. Forty-nine percent ($n = 3471$) of cases were either referred to or managed in a HCF. Of symptoms documented as being related, tachycardia ($N = 1150$) was the most common. Agitation was documented as related in 713 cases while paradoxically drowsiness/lethargy was documented as related in 392 cases. The most common disposition for those referred/treated at a HCF was treated and release ($n = 1229$). Seven-hundred fifty-three cases were admitted to either a noncritical care unit ($n = 337$) or critical care unit ($n = 416$). Of the 3391 cases that were followed to a known medical outcome there was 1 death, 63 major effect, 1333 moderate effect and 1190 minor effect documented. The one death involved intentional ingestion of Adderall XR 20 mg.
Conclusions: Adult single agent MRS exposures most commonly involve Adderall (amphetamine/dextroamphetamine) XR products and are not typically associated with major effects or death.

Table 1. Top five most common modified release stimulants products reported to NPDS for adult exposures.

MRS Product	# of Exposures Reported
Adderall XR – 30 Mg Capsule	1509
Adderall XR – 20 Mg Capsule	1293
Ritalin LA	1266
Focalin XR	1035
Adderall XR – 25 Mg Capsule	498

KEYWORDS Stimulant; modified release; amphetamine
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201. Boost poison center data accuracy with staff driven tools

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Background/objective: Poison centers collect data to track patient treatments and outcomes, identify trends and emerging threats, and supplement existing surveillance systems. Reliable data is necessary to mitigate poison or disaster-related morbidity and mortality with evidence-based, cost-effective management and treatment decisions, provide demographics for funding, and help inform public health during threats to public safety. Exception reports, searches identifying data that fall outside specified criteria, are an indispensable tool for increasing the accuracy of data and protection against potential errors.
Method: Common coding errors were identified during regular call handling, poison center Quality Assurance activities, random data reviews, or when processing deliverables for contracts. Coding requirements and guidelines were reviewed with staff; however, errors remained and correcting this data was an ongoing burden to management. Exception searches were created in toxiCALL™ for the situations described below and monthly emails were sent to remind to staff retrieve their own cases for correction. Cases were corrected as staff had downtime between calls during normal shift hours.

- Reason coded abuse with a substance containing caffeine
- Inconsistencies between caller relationship and caller site
- Free Area 1 not flagged for toxicologist consult
- Coded "no therapy provided", case not followed
- Worksite calls not coded as Unintentional-Occupational
- Eye exposure, route coded as ingestion only
- Adult exposures coded as Unintentional-General
- No scenario coded per PC guidelines

Staff identified that in some charts the coding was accurate, therefore all cases that were reviewed and not changed were assigned to a fictional SPI named "$$done." This eliminated the chart from returning on future searches and assured staff that it had been reviewed for coding.
Results: Review of data from 1999 to 2017 showed improvement after the exception searches were instituted for each data point being reviewed. Reason coded abuse with a substance containing caffeine showed 80.0% improvement. Inconsistencies between caller relationship and caller site showed 87.8% improvement. Free Area 1 flagged for toxicologist consult showed 25.9% improvement. No therapy provided coded, case not followed showed 87.6% improvement. Worksite calls not coded as Unintentional-Occupational showed 87.2% improvement. Eye exposure, route coded as ingestion only showed

Table 1. Yearly averages before and after exception reports were instituted.

Before	After	Improvement	
5.0	1.0	80.00%	Reason coded abuse with caffeine product
258.8	31.7	87.76%	Inconsistencies between caller relationship and caller site.
9.0	6.7	25.93%	Free Area 1 flagged for toxicologist consult
4281.9	533.1	87.55%	No therapy provided coded, case not followed
253.6	32.5	87.19%	Worksite calls not coded as Unintentional-Occupational
304.6	35.6	88.31%	Eye exposure, route coded as ingestion only
6845.8	1363.5	80.08%	Adult exposures coded as Unintentional-General.
46,128.8	27,370.0	40.67%	No scenario coded per PC guidelines

88.3% improvement. Adult exposures coded as Unintentional-General showed 80.1% improvement. No scenario coded per PC guidelines showed 40.7% improvement.
Conclusion: Staff performed Exception Searches dramatically improve data with minimal supervision or impact on work flow. Additionally, an unexpected benefit was identified, staff overall coding improved as they became more aware of coding errors.

KEYWORDS Data; quality improvement; coding

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202. Homicide with intramuscular cyanide

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Background: Cyanide poisoning most commonly occurs from smoke inhalation, less commonly by oral ingestion for suicide or homicide. There are rare cases of intravenous or subcutaneous parenteral cyanide used for homicide. We report a case of intramuscular cyanide used as a homicidal agent.
Case report: A 35-year-old female was trying to enter her home when an assailant jumped out of nearby bushes and injected her left buttock using a syringe. She was awake and talking when emergency medical services arrived on the scene. On arrival to the emergency department, she was unresponsive and flaccid. She was immediately intubated and mechanically ventilated. Initial assessment revealed a BP 130/83 mmHg and HR 102 bpm, which rapidly deteriorated to SBP 72 mmHg and HR in the 40's. Initial serum pH was 6.95 and serum lactate was 7.7 mmol/l. An epinephrine infusion was started to treat shock. Three hours after the injection, with no significant clinical improvement, consultation with a medical toxicologist raised the suspicion of cyanide. Hydroxocobalamin 5 g and sodium thiosulfate 12.5 g were administered intravenously, with subsequent serum pH of 7.37. The patient required norepinephrine at 20 mcg/min and vasopressin at 0.4 units/min IV to maintain adequate blood pressure. The following day the patient remained unresponsive and was declared brain dead after documenting no cerebral perfusion. Post-mortem exam revealed hypoxic encephalopathy and cerebral edema with bilateral uncal herniation. Plasma cyanide levels drawn approximately 1 and 4 h post-exposure were 3.4 and 4.1 mg/l, respectively. Only caffeine was detected in addition to cyanide. Further testing was negative for dimethylsulfoxide, acetone, ethanol, isopropanol, methanol, barbiturates, cannabinoids, salicylates, amphetamines, anticonvulsants, antidepressants, antihistamines, antipsychotic agents, benzodiazepines, CNS stimulants, cocaine and metabolites, hallucinogens, sedatives, hypoglycemics, muscle relaxants, nonsteroidal anti-inflammatory agents, opiates and opioids.
Case discussion: Homicide by poisoning has occurred since ancient times. Cyanide is among several prototypical poisons used for homicidal purposes. Cyanide exists as a gas or salt in nature. Inhalation of hydrogen cyanide gas is the most common and lethal form of poisoning. Ingestion of cyanide salts results in a more insidious onset of symptoms, with early GI effects progressing to systemic toxicity. Injection of solubilized cyanide appears to be very rare with fatalities reported following intravenous and subcutaneous exposures. Our case demonstrates that intramuscular injection can also result in fatal cyanide poisoning.
Conclusion: Fatal cyanide poisoning can occur from multiple routes of exposure. Intramuscular injection of cyanide resulted in rapid absorption and severe toxicity. Serial serum cyanide levels demonstrated continuing absorption at 4 h post injection.

KEYWORDS Cyanide; parenteral; homicide

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203. Characterizing the use of extracorporeal membrane oxygenation in cases reported to a Regional Poison Control Center

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Context: Antidotes are available to treat some specific poisonings; however, mainstay of treatment for the poisoned patient remains general supportive care measures. Extracorporeal membrane oxygenation (ECMO), also known as Extracorporeal Life Support (ECLS), is an invasive supportive measure that can be effective for a patient with cardiac or pulmonary failure, or both. ECMO is often reserved for severe toxicities causing cardiac or pulmonary failure. Cases reported to poison centers have become progressively complex, and ECMO is increasingly used as a treatment.
Objective: The purpose of this study is to characterize the use of ECMO in cases reported to a regional poison control center (PCC).
Methods: This retrospective review queried the PCC database from January 1997to August 2017 for the American Association of Poison Control Centers therapy code for ECMO, as well as "ECMO" and "ECLS" free-text searches. Cases were included if ECMO was initiated. Collected data includes year of exposure, age, gender, reason for exposure, substances involved, route of exposure, symptoms reported to PCC by the health care facility, treatments performed, duration of ECMO, and medical outcome.
Results: Of 147 cases initially identified, 122 cases were excluded because ECMO was never initiated, leaving 25 cases where ECMO was performed. Only 11 (44%) cases were properly coded with ECMO as a therapy. The first case of EMCO being used as treatment was reported to the PCC in 1998. From 1998 to 2009, the average number of cases reported per year was 1.7. The average increased to 2.25 cases per year from 2010 to 2017; with three cases reported in years 2012–2014 and 2016. Mean age was 25.6 years, and ranged from 1 month to 67 years, with 16 cases (64%) involving patients under 18 years. Sixteen cases involved a known toxin; five involved multiple substances (Table 1). Eight cases (32%) involved a cardiovascular agent, 2 each (8%) a hydrocarbon, opioid or stimulant drug of abuse, and 1 each (4%) colchicine, ethanol, arsenic, white phosphorus or an unknown Chinese herbal supplement. Most common adverse clinical effects experienced were hypotension (76%), asystole (56%) and acidosis (40%). Most common treatments provided were ECMO (100%), intubation and mechanical ventilation (88%) and the use of a vasopressor (72%). Eleven cases had ECMO initiated due to cardiovascular failure (44%), 7 cases (28%) due to pulmonary failure and 7 cases (28%) due to both cardiovascular and pulmonary failure. In-hospital mortality was 28%; 15 cases (60%) survived, and 3 cases (12%) were lost to follow-up. Average time to start of ECMO from time of presentation to the emergency room was

Table 1. Case information.

Year	Age	Gender	Reason for exposure	Substances	Route	Symptoms	Treatment	Outcome
1998	1 year	Male	Unintentional General	Hydrocarbon Furniture Polish	Oral	Acidosis Aspiration Pneumothorax	Intubation ECMO	Major Recovered
2000	14 years	Female	Unintentional General	Medical Hantavirus	Inhalation	Cyanosis Asystole	Intubation ECMO	Death
2001	1 month	Male	Unitentional Therapeutic Error	Digoxin	Intraveneous	Vtach/Vfib Asystole	Digibind Cardioconversion CPR ECMO	Death
2001	9 years	Male	Unintentional General	Medical Unknown	Non-applicable	Hypotension Vfib	Pacer Vasopressors ECMO	Major Recovered
2002	6 months	Female	Adverse Effect Drug	Chinese Herb	Oral	Hypotension Acidosis Asystole	Vasopressors Intubation CPR ECMO	Major Recovered
2007	14 years	Male	Unintentional General	Medical Streptococcal Toxic Shock	Non-applicable	Hypotension Acidosis Renal failure Coma Asystole	Vasopressors Hemodialysis Intubation ECMO	Death
2009	2 years	Male	Unintentional General	Digoxin Flecainide	Oral	Hypotension Bradycardia Vtach/Vfib Seizures Asystole	Digibind Vasopressors Intubation ECMO	Major Recovered
2010	17 years	Male	Intentional Suspected Suicide	Atenolol Amlodipine Cochicine	Oral	Hypotension Pulmonary Edema Renal failure Asystole	Calcium Glucagon Vasopressors ECMO	Death
2010	10 years	Male	Unintentional General	Medical Unknown	Non-applicable	Hypotension Coma Asystole	Vasopressors Intubation CPR ECMO	Major Recovered
2011	24 years	Female	Unintentional General	Medical Antiphospholipid Syndrome	Non-applicable	Hypotension Pulmonary Edema Acidosis Cyanosis Coma	Hemodialysis Intubation ECMO	Major Recovered
2011	45 years	Male	Unintentional Occupational	White Phosphorous Arsenic	Dermal Inhalation	Hypotension Vtach Cyanosis	Vasopressors Hemodialysis Intubation ECMO	Major Recovered
2012	22 years	Male	Intentional Abuse	Ecstasy	Oral	Hyperthermia Acidosis Ast &/or Alt >1000 Renal failure Rhabdomyolysis Multiple seizures Coma	Vasopressors Hemodialysis Intubation ECMO	Major Recovered
2012	54 years	Female	Intentional Suspected Suicide	Diltazem	Oral	Hypotension Bradycardia	Calcium Glucagon Vasopressors HDI Intralipid Intubation ECMO	Major Recovered
2012	13 years	Male	Unintentional General	Medical Septic Shock	Non-applicable	Hypotension Acidosis Renal failure Respiratory arrest Asystole	Vasopressors Hemodialysis Intubation ECMO	Death
2013	7 months	Male	Unintentional Therapeutic Error	Flecanide	Oral	Vtach/Vfib Asystole	Vasopressors Intralipid Intubation CPR ECMO	Major Recovered
2013	26 years	Male	Intentional Suspected Suicide	Diltiazem	Oral	Hypotension Bradycardia Coma Asystole	Glucagon Vasopressors HDI Intralipid Pacemaker Intubation ECMO	Major Recovered

(*continued*)

Table 1. Continued.

Year	Age	Gender	Reason for exposure	Substances	Route	Symptoms	Treatment	Outcome
2013	11 years	Male	Unintentional General	Unknown	Non-applicable	Hypotension Acidosis Renal failure Respiratory arrest	Intubation ECMO	Unknown
2014	14 years	Male	Unknown Reason	Medical Unknown	Non-applicable	Hypotension Bradycardia Acidosis	Glucagon Vasopressors Intubation ECMO	Unknown
2014	17 years	Male	Intentional Suspected Suicide	Amlodipine	Oral	Hypotension Respiratory arrest Asystole	Vasopressors Intubation ECMO	Major Recovered
2014	1 year	Female	Unintentional General	Pine Sol	Oral	Hypotension Aspiration Asystole	Vasopressors Intubation CPR ECMO	Death
2015	67 years	Female	Intentional Abuse	Oxycodone	Oral	Hypotension Respiratory arrest	Vasopressors Hemodialysis Intubation ECMO	Unknown
2015	27 years	Male	Intentional Abuse	Cocaine Ethanol	Oral Inhalation	Hypotension Respiratory arrest Coma	Vasopressors Intubation ECMO	Major Recovered
2016	17 years	Female	Unintentional Therapeutic Error	Diltiazem Metoprolol	Intraveneous	Hypotension Asystole	Glucagon Calcium Vasopressors Intubation CPR ECMO	Major Recovered
2016	38 years	Female	Unintentional General	Unknown	Non-applicable	Hypotension Acidosis Renal failure Asystole	Hemodialysis Intubation ECMO	Death
2016	24 years	Male	Contamination Tampering	Fentanyl	Oral	Acidosis Respiratory arrest	Intubation ECMO	Major Recovered

1.3 d (<1 d–3 d). Average duration of ECMO therapy was 6.3 d (<1 d–42 d).
Conclusion: The number of cases reported to the PCC using ECMO over the study period was small, but a steady increase in reported cases over the time period was seen. ECMO is a potentially life-saving treatment for the acutely poisoned patient. This study shows the use of ECMO in poisoned patients is increasing. Poison center specialists should be educated on this increasingly utilized treatment.

KEYWORDS Extracorporeal membrane oxygenation; extracorporeal life support; poisoning

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204. Outcomes of amiodarone exposures reported to US Poison Centers

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Objective: Amiodarone is used therapeutically for ventricular and supraventricular tachydysrhythmias in adult and pediatric patients. It inhibits alpha and beta receptors and antagonizes sodium, potassium, and calcium channels. Although commonly used, more needs to be understood about potential dangerous outcomes associated with this drug. Our objective was to describe outcomes of patients exposed to amiodarone utilizing U.S. poison center data.
Methods: This retrospective study utilized data from the National Poison Data System (NPDS). Inclusion criteria were single substance exposure to amiodarone between July 1, 2009 and December 31, 16. Variables of interest were collected and descriptive statistics were performed. IRB approval was obtained.
Results: Out of 2073 patients, 1011 (49%) met inclusion criteria. Ages ranged from 5 d to 97 years, 334 (31.5%) patients were 17 and younger and 5 (0.5%) patients were of unknown age. Five hundred forty-eight (51%) patients were female and 5 (0.5%) were unknown gender. Five hundred fifty-five (52.2%) exposures were coded as therapeutic errors, 72 (6.8%) adverse drug reactions, and 49 (4.6%) were suspected suicides. Major effects were reported in 13 (1.8%) adult patients. Sixteen (4.8%) pediatric patients had moderate effects, the most common being bradycardia and hypotension. One (0.3%) pediatric exposure was due to an adverse drug reaction. Five hundred fifty-seven (76%) adult patients and 317 (95%) pediatric patients had minor or no effects, respectively. Death was reported in nine adult cases and in one pediatric case. Review of fatality abstracts revealed that the pediatric case was attributed undoubtedly to amiodarone. Among the nine adult deaths, one was coded as probably responsible and one was considered contributory. All other deaths were unknown as to the relative contribution to fatality. None of the deaths were deemed to be suicides.
Conclusion: This is the largest known study of amiodarone exposures using NPDS data. While most patients had minimal or no effects, 10 deaths were reported. Limitations include the use of retrospective data, passive reporting, reliance on caller accuracy and nearly half of cases were not followed to a known outcome. Further investigations into amiodarone overdose are needed to

clarify range of acute toxicity, clinical effects, and optimal treatment regimens.

KEYWORDS Amiodarone; exposures; poison centers

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205. Impact of healthcare resources on intentional and unintentional toxic exposures in urban and rural communities

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Background: There are misconceptions about toxic exposures in urban and rural populations. This research seeks to identify differences in medical outcomes of intentional and unintentional toxic exposures in both urban and rural communities. Additionally, it compares the medical outcomes of toxic exposures across communities with different healthcare resources.

Methods: The researchers reviewed a poison center database from 2002 to 2017 from the rural Eastern shore and two urban counties of the Western Shore. Using caller zip codes, the data was characterized according to the motivation of toxic exposures and the severity of medical outcomes. The data was also analyzed for patterns of toxic substances resulting in major outcomes or death. The Rural Health Information Hub Tool, which is supported by Health Resources and Services Administration (HRSA), was used to categorize each zip code according to primary care provider (PCP) coverage, availability of mental health (MH) services, and status as a medically underserved area (MUA). HRSA defines PCP/MH shortage as clinicians and MUA a shortage of services. Unadjusted odds ratios (ORs) and their 95% confidence intervals (95% CIs) were estimated in order to quantify the association between intentional or unintentional exposures and medical outcomes, community type, and healthcare resources. Statistical analyses were performed in SAS 9.4 (SAS Institute, Cary, NC).

Results: For the years 2002–2017, there were 79,121 recorded exposures to a toxin. Of these, 17% were intentional and 83% were unintentional. The odds of an intentional exposure were higher in communities with PCP or MH shortage, whereas the odds were lower in medically underserved areas and urban areas (Table 1). For both intentional and unintentional exposures, the odds of major effect or death after the exposure were higher in communities with PCP and/or MH shortages (Tables 2 and 3). In the rural population, major effects were most commonly due to intentional exposure to sedative-hypnotics (13 exposures), or unintentional exposure to antihistamines (2 exposures). Deaths were most commonly due to intentional exposure from antihypertensives (3 exposures), or unintentional exposure to chemicals (1 exposure). In the urban population, major effects were most commonly due to intentional exposure to sedative-hypnotics (239 exposures), or unintentional exposure to antihypertensives (28 exposures). Deaths were most commonly due to intentional exposure to sedative-hypnotics (19 exposures), or unintentional exposure to hydrocarbons (4 exposures).

Conclusions: The data suggests the types of toxic exposures and outcomes may be associated with healthcare disparities and population density. These data may help guide future allocation of clinician resources.

Table 1. Association between types of communities and intentional toxic exposure.

Community type	Odds ratio	95% CI	p
PCP shortage	1.67	(1.61, 1.74)	<.001
MH shortage	2.00	(1.93, 2.08)	<.001
MUA	0.85	(0.82, 0.89)	<.001
Urban	0.82	(0.78, 0.86)	<.001

Table 2. Association between types of communities and medical outcomes after intentional toxic exposure.

Community type	Outcome	Odds ratio	95% CI	p
PCP shortage	Major effect	1.05	(0.91, 1.20)	.522
	Death	1.11	(0.60, 2.03)	.740
	Major effect or death	1.05	(0.92, 1.20)	.484
MH shortage	Major effect	1.21	(1.05, 1.39)	.008
	Death	2.74	(1.35, 5.56)	.005
	Major effect or death	1.25	(1.09, 1.44)	.001
MUA	Major effect	0.61	(0.51, 0.74)	<.001
	Death	0.61	(0.27, 1.38)	.238
	Major effect or death	0.61	(0.51, 0.73)	<.001
Urban	Major effect	1.29	(1.07, 1.55)	.007
	Death	1.27	(0.56, 2.85)	.569
	Major effect or death	1.29	(1.08, 1.55)	.006

Table 3. Association between types of communities and medical outcomes after unintentional toxic exposure.

Community type	Outcome	Odds ratio	95% CI	p
PCP shortage	Major effect	3.15	(2.29, 4.35)	<.001
	Death	6.01	(1.56, 23.26)	.009
	Major effect or death	3.28	(2.40, 4.48)	<.001
MH shortage	Major effect	2.89	(2.08, 4.03)	<.001
	Death	3.86	(1.00, 14.93)	.050
	Major effect or death	2.95	(2.13, 4.07)	<.001
MUA	Major effect	0.64	(0.43, 0.96)	.031
	Death	0.30	(0.04, 2.37)	.253
	Major effect or death	0.62	(0.42, 0.92)	.017
Urban	Major effect	1.01	(0.66, 1.56)	.949
	Death	1.81	(0.23, 14.29)	.573
	Major effect or death	1.05	(0.69, 1.59)	.838

KEYWORDS Urban; rural; resources

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206. Utilizing a poison center electronic medical record to facilitate real-time studies

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Background: Data collection for poison center (PC) studies has traditionally relied on retrospective data analysis or prospective use of paper forms or ancillary systems, necessitating inefficient double data entry. PC electronic medical record systems (EMR) can provide the opportunity to utilize real-time data collection, prompting SPIs to obtain additional information only when preselected criteria identify an appropriate case.

Objectives: To build, configure, and test a PC EMR to use specified criteria to prompt SPIs to offer PC callers the opportunity to participate in a study and then collect study data within the patient's case record, in real time.

Methods: This EMR was augmented and configured to compare case data to specified study parameters while the patient data was being entered in real time. If the rules were met, the system would prompt the specialist in poison information (SPI) that the current call met the criteria for inclusion. The SPI was then provided the ability to enroll the caller in the study and was presented with the appropriate questions utilizing branching logic. Identical criteria, utilizing computer-based rules, were embedded into the PC EMR of each collaborating center, contributing to study uniformity. Research data was merged into a central data set by each center's export of appropriate case data into Microsoft Excel 2016 (Redmond, WA). Analyzed variables included substance class(es), patient age, intended recipient of medication(s), and storage of medication at time of ingestion. Success of enrollment and data completeness were analyzed in aggregate per center.
Results: Five participating PCs utilizing this EMR collected 4523 cases (mean of 62.1% of eligible callers, range 55.3%–70.9%) over 8 months. More than 90% of cases have complete data sets.
Conclusions: Inclusion of rule-based prompts and embedded data collection tools into a PC EMR facilitated study enrollment, enabled efficient real-time study data collection, and eliminated the need for double data entry. The use of identical case selection rules in each participating PC enhanced consistency of data collection. Further development of this concept across EMRs may reduce barriers to PC study participation and improve study completion.

KEYWORDS Informatics; study design; poison center operations

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207. Potline: a pilot of a poison-center based Marijuana health and safety hotline

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Introduction: Legal use and commercial sale of recreational marijuana was approved by voter ballot in our state in 2012. Retail dispensaries opened their doors on January 1, 2014. After legalization, we recognized the information gap that existed among marijuana users regarding health-related issues. Legalization of marijuana resulted in a need by consumers for accurate and evidence-based information surrounding the health and safety aspects of marijuana. In 2017, our regional poison center (RPC) collaborated with city and county officials to establish a pilot program to provide a dedicated hotline for visitors and residents to use for all health-related questions about marijuana and its various related products.
Methods: This study is a retrospective chart review of all calls received through the Marijuana Health & Safety Line (MHSL) from May 10, 2017 to March 31, 2018. IRB approval was received. A proposal for a 90-day pilot for a dedicated hotline for questions regarding the health and safety of marijuana use was drafted by our RPC and submitted to city and county officials. Funds received were spent on advertising and consultant fees. Staffing was adjusted based on actual and projected call volume. Cases were reviewed daily for response accuracy and additional follow up was scheduled if indicated. Customized data was analyzed and sent to city and county designees as well as cases identified as having public health significance. At the end of the pilot, each case was categorized and analyzed by 3 clinical and medical toxicologists. Call types were determined by consensus, and some calls met criteria for more than one category. Descriptive statistics were calculated for each call type.
Results: The MHSL pilot ran from May 10 to July 10, 2017. A total of 48 calls were received during the pilot period. At the end of the 90 d, service on the line was maintained. Calls were stratified ([n = number during pilot, n = total number from May 10, 2017 to March 31, 2018]) to mutually agreed upon categories during analysis: questions regarding additives/contaminants [5, 9], drug-disease interactions [1, 3], drug-drug interactions [3, 17], drug testing [4, 10], pharmacokinetics [0, 5], legal matters [5, 13], questions regarding specific marijuana products [5, 9], medical marijuana registry questions [2, 8], report an adverse event (AE) [9, 30], questions on a theoretical AE [5, 11], general safety questions [2, 8], therapeutic use/efficacy of marijuana [5, 12], and other [2, 11]. A total of 140 calls were received by March 31, 2018 with 146 unique inquiries. A majority of the calls (79%, $n = 110$) were informational. Twenty-six percent of calls originated within the proposed city and county boundaries.
Conclusions: The preliminary findings from the MHSL hotline indicate the need for accurate and reliable health and safety information regarding marijuana. The most common types of calls were reports of drug adverse events and questions about drug-drug interactions. Local and state health departments should partner with their local poison center to serve as a vital 24-h resource for individuals who have a spectrum of questions surrounding marijuana.

KEYWORDS Marijuana; poison center management; hotline

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208. Novel educational initiative for specialists in poison information

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Background: Specialists in Poison Information (SPIs) are an integral part to an efficient and functioning poison center. The majority of SPIs are either registered nurses (RNs) or pharmacists. To become a Certified-SPI (CSPI), one must take 2000 poison center calls and pass the American Association of Poison Control Centers (AAPCC)-sponsored certification examination. To maintain CSPI certification, one must pass a recertification examination every seven years. An optional examination review course is offered, however beyond that, there are no specific educational requirements. States have varying continuing education requirements, however the quality and subject matter of continuing educational content is highly variable and usually does not include concepts related to toxicologic exposures. SPI education is under-developed in its current state and has opportunity for expansion.
Methods: Beginning in February, 2017, we instituted a SPI-driven educational platform to enhance SPI learning and education. Our poison center has between 9 and 10 SPIs (depending on the month related to new hires). Each month, one SPI was designated to create a learning activity on a toxicology topic of their choosing as well as a 5 question post-activity quiz. The educational content and quiz questions and answers were reviewed by a Medical Toxicology faculty member prior to distribution. The educational content along with a link to quiz questions was sent via email to all poison center staff and faculty. On months where there was no SPI-assigned content, other content such as SPI webinars was encouraged, and the Medical Toxicologist created

a quiz on this content. Quiz data were collected via SurveyMonkey (San Mateo, CA).
Results: From February 2017 to January 2018 there were a total of 12 educational offerings: 10 SPI presentations and 2 webinars. The average percent participation was 75% overall, with a 78% participation rate for the SPI-based content and 60% participation for the webinars.
Conclusions: We present a novel educational offering aimed at SPI education. In the first year, our aim was to encourage participation in a new initiative. We would consider a 75% participation rate successful for a new program, especially considering response rates for online surveys are often approximately 35%. Although the numbers are small, our data suggest that engagement with peer-created content engaged more SPIs than instructions to watch a webinar. In addition to the toxicology content, many SPIs also learned other valuable skills, such as how to use Power Point, how to access content on the AAPCC website, as well as publishing their content in the SPI newsletter for national distribution. We have continued this initiative and in the future are hoping to be able to obtain state-approved continuing education credits for the SPIs through this monthly education.

KEYWORDS Poison center; education; CSPI

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209. Novel program development and cross-disciplinary collaboration including the poison center in targeting collegiate alcohol misuse

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Background: Consumption of alcoholic beverages and binge drinking is commonplace on United States (U.S.) college campuses. BASICS (Brief Alcohol Screening and Intervention for College Students) is a confidential, evidence-based program that consists of an online survey followed by a motivational interview with a trained facilitator. There are multiple studies that have demonstrated the efficacy of BASICS in reducing alcohol consumption and alcohol-related consequences in college students. Our initiative is the first to implement a collaborative referral program to a Student Health-based BASICS program from the Emergency Department (ED), utilizing the Poison Center (PC) to provide and track referrals.
Methods: On August 18, 2017, a BASICS referral program was implemented from a University-based ED with approximately 64,000 yearly visits. This program was structured to be compliant with the U.S. Federal laws protecting privacy, including the Family Educational Rights and Privacy Act (FERPA) and the Health Insurance Portability and Accountability Act (HIPAA). The BASICS program resides within Student Health under the University's Division of Student Affairs, a unit that must abide by FERPA laws. However, the program was strategically administered under the direction of the Health System's Department of Psychiatry, thereby assuring that associated personnel were confidential reporters (not "mandatory" reporters) per the Clery Act and Title IX laws, while also assuring the program was compliant with not only FERPA laws, but also HIPAA laws. Patients presenting to the ED who were identified as students at the affiliated university and who were given an alcohol related diagnosis as contributing to their presentation were given a physician prescription and a specific flier referring them to BASICS upon discharge. Since the Student Health Center and the ED have distinct electronic health record programs that do not communicate in part due to the Federal laws noted above, the ED providers partnered with the local PC, a confidential entity, to report each case presentation and to help track the case to assure the appropriate referral occurred.
Results: Between August 18, 2017 and March 31, 2018, a total of 169 students were referred to BASICS using the ED collaborative initiative. Among the referrals, 40.2% were males and 59.8% were females. The age breakdown is shown in Table 1. A breakdown of cases by the day of the week indicated that the majority of cases presented on Saturdays (44.3%) or Fridays (21.3%). Prior to this program's development, there was no direct referral plan from the ED for college students presenting with alcohol related diagnoses.
Conclusions: We present a unique referral guideline for college students presenting to the ED with an alcohol-related diagnosis that enables coordination of care between ED, Poison Center, Student Health, and Psychiatric personnel and that is compliant with all U.S. Federal privacy laws. This model allows the PC to play a pivotal role in coordinating subsequent care related to alcohol misuse among college students. The created system also enables an enhanced confidential tracking of student alcohol

Table 1. Association between types of communities and intentional toxic exposure.

Community type	Odds Ratio	95% CI	*p*
PCP shortage	1.67	(1.61, 1.74)	<.001
MH shortage	2.00	(1.93, 2.08)	<.001
MUA	0.85	(0.82, 0.89)	<.001
Urban	0.82	(0.78, 0.86)	<.001

Table 2. Association between types of communities and medical outcomes after intentional toxic exposure.

Community type	Outcome	Odds Ratio	95% CI	*p*
PCP shortage	Major effect	1.05	(0.91, 1.20)	.522
	Death	1.11	(0.60, 2.03)	.740
	Major effect or death	1.05	(0.92, 1.20)	.484
MH shortage	Major effect	1.21	(1.05, 1.39)	.008
	Death	2.74	(1.35, 5.56)	.005
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MUA	Major effect	0.61	(0.51, 0.74)	<.001
	Death	0.61	(0.27, 1.38)	.238
	Major effect or death	0.61	(0.51, 0.73)	<.001
Urban	Major effect	1.29	(1.07, 1.55)	.007
	Death	1.27	(0.56, 2.85)	.569
	Major effect or death	1.29	(1.08, 1.55)	.006

Table 3. Association between types of communities and medical outcomes after unintentional toxic exposure.

Community type	Outcome	Odds Ratio	95% CI	*p*
PCP shortage	Major effect	3.15	(2.29, 4.35)	<.001
	Death	6.01	(1.56, 23.26)	.009
	Major effect or death	3.28	(2.40, 4.48)	<.001
MH shortage	Major effect	2.89	(2.08, 4.03)	<.001
	Death	3.86	(1.00, 14.93)	.050
	Major effect or death	2.95	(2.13, 4.07)	<.001
MUA	Major effect	0.64	(0.43, 0.96)	.031
	Death	0.30	(0.04, 2.37)	.253
	Major effect or death	0.62	(0.42, 0.92)	.017
Urban	Major effect	1.01	(0.66, 1.56)	.949
	Death	1.81	(0.23, 14.29)	.573
	Major effect or death	1.05	(0.69, 1.59)	.838

misuse for future studies and determination of the impact of various prevention programs.

KEYWORDS Alcohol misuse followup; college drinking; poison center

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210. Dangerousness of liquid laundry detergent pods perceived by reference adults: analysis of the results obtained from the questionnaire used directly in emergency by an Italian Poison Control Center

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Background: An Italian Poison Control Center (PCC) observed an increase of 20% of the pediatric exposure to liquid laundry detergent pods (LLDPs) during the year 2017 compared to 2016 and thought it useful to analyze the perception that parents have of the dangerousness of LLDPs.
Methods: A questionnaire was distributed to parents present pediatric department (PD) and in pediatric emergency department (PED) from January 12, 2018 to February 16, 2018. The questionnaire consists of 33 items, of which 23 are multiple choice and 10 are open, divided into four topics: "General" in which the characteristics of the family unit are identified (parents and children age, number of children, nationality); "LLDP" which investigates presence of the product at home, storage and accessibility to children; "In case of ingestion": in which it is described the first intervention carried out by parents and caregivers following accidental ingestion; "For the parent": dedicated to the comments of those who fill in the questionnaire.
Results: During the study period, 150 questionnaires were distributed and 112 were collected ($n = 99$; 88.4% in PED and $n = 13$; 11.6% in PD). The age groups distribution was: less than 24 years ($n = 8$; 7.1%), 25–35 years ($n = 44$; 39.3%), 35–45 years ($n = 29$; 25.9%) and more than 45 years ($n = 31$; 27.7%). Eighty-five% of the participants ($n = 95$;) are Italian; most families, ($n = 50$; 44.6%,), have just one child ($n = 79$; 70.5%, age group 2–5 years) and only in the age group >45 years most children aged >5 years ($n = 41$; 36.6%). Eighty-four partecipants (75%) have the LLDPs at home; of which 69 (82%) usually stored the LLDP in an accessible place for children. Of all the partecipants, only 20 are parents who belong to the age group >45 years. It is to be noted that all of them (100%) inappropriately, do not keep LLDP out of reach of their children. Twenty-one partecipants (25%) has declared to cut the pods and 20 (95%) to put the remaining part in the package. Only 47% of the participants, believe that the LLDPs are dangerous, while most of them, especially in the age group 25–45 years, consider the ingestion be a route of exposure difficult to occur (68%). Unfortunately almost all participants (82%) mistakenly believe it is correct to induce emesis in this event and 40% believe it is correct to give water (23%), milk (15%) or both (2%). The majority of participants ($n = 59$; 53%) considered it appropriate to take the child to the hospital in case of exposure, while only 13 participants (12%), of which $n = 8$ of age> 45, considered to be more correct to contact a PCC.
Conclusions: From the data analysis it is clear that the perception of the dangerousness represented by the LLDPs is extremely underestimated. This study showed the lack of knowledge of the opportunity and/or possibility of calling a PCC and a poor knowledge about what it is to be done in case of exposure. Therefore it emerges that the continuous information of reference adults to contain this risk is extremely useful.

KEYWORDS Liquid laundry detergent pods; prevention; questionnaire to reference adults in emergency

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211. The 'tide PODs challenge' social media phenomenon

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Background: In late 2017, videos featuring teens biting into liquid laundry detergent packs (LLDPs) surfaced on popular internet sites and social media platforms. This phenomenon, coined the 'Tide Pods Challenge' (TPC), involved a dare to eat Tide PODs and post about the experience. The TPC gained widespread attention when picked up by the media. This is an evaluation of LLDP 'Challenge' cases from 11 U.S. poison centers (PCs) participating in an ongoing prospective study (serving 24% of the US population) and cases reported directly to Procter & Gamble (P&G), the manufacturer of Tide Pods and Gain Flings.
Methods: Exposure cases were extracted from the PC study database and P&G post-marketing surveillance database for the TPC period (November 2017–January 2018) and baseline comparison period (November 2016–January 2017). Inclusion criteria for the PC dataset included all LLDP exposures coded as 'Intentional' involving a teen or young adult (age 12–24 years, age category 'teen' or '20s'). The P&G dataset included any US LLDP adverse event (AE) case coded with at least one intentional product misuse term. Due to the unstructured nature of social media reporting, the P&G dataset was not filtered by patient age.
Results: During TPC period, 104 intentional exposures involving teens and young adults were reported to PC study sites. This represented an increase of 97 cases (1386%) from the baseline period ($N = 7$). Of these, 94 cases (90%) met criteria as 'Intentional Misuse' and 10 (10%) included suspicion of suicidal ideation. Tide Pods accounted for 94% of cases with a known product ($N = 98$). The primary route of exposure was ingestion (93%), ocular (6%) and rectal (1%). Among ingestions that were initially triaged by the PC ($N = 78$), 18% were referred to a healthcare facility. There were no major outcomes reported. During the TPC period, P&G identified 1425 LLDP adverse event (AE) cases involving product misuse, representing an 8806% increase from the baseline period ($N = 16$). The majority of AE cases were received via P&G-sponsored social media pages (71%), followed by email (15%) and phone (14%), which was significantly disproportionate from the baseline period for social media (71% versus 12%). Twenty AE cases were assessed as 'serious' during the TPC period; however, none could be medically verified. Follow-up information for social media cases was generally not available due to a lack of consumer contact information. The major route of exposure was ingestion (reported in 70% of all AE cases), and no symptoms were reported in the majority of these cases.
Conclusions: Post-marketing surveillance data from both the PC study and P&G provided insights into the scale of the TPC

phenomenon. Cases reported via P&G-sponsored social media pages provided limited verifiable information due to a lack of direct contact with the consumer, and many were suspected hoaxes. In contrast, PC exposure cases provided a more robust understanding of verified exposures and related patient outcomes.

KEYWORDS Tide pods challenge; social media; intentional misuse

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212. Study of caregivers regarding pediatric poisoning

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Objectives: The objectives of this study were to: (1) categorize the initial action taken by caregivers of pediatric patients when a potential poison occurs, (2) determine the caregiver's awareness of poison control center services, and (3) identify potential barriers for utilizing poison control center (PCC) services.
Methods: This study prospectively surveyed caregivers of pediatric patients who presented to a local children's hospital for potential poisoning between August 2016 and August 2017. The study received an IRB exemption determination. Survey respondents were prospectively identified by trained research assistants on presentation to the emergency department (ED).The survey collected demographic information and was comprised of 12 questions on knowledge, attitudes, and behaviors of caregivers related to managing pediatric poisonings. Care givers were included if the age of the child was 14 years or younger, the exposure was unintentional, and the child had one of the following chief complaints: poisoning, exposure, ingestion, [fuzzy, agitated, or irritable], lethargic,foreign body, bug bite or sting, snakebite, carbon monoxide or other asphyxiant, allergic reaction, or medicine reaction. Caregivers were excluded from the survey if the child had a designated high acuity level.
Results: There were 371 surveys completed in a 12 month period. The majority of caregivers were female (77%), married (69%), Caucasian (69%), with more than a high school education (75%). The majority of patients (62%) had private insurance and 32% had government coverage. The most common reasons for the ED visit were: foreign body (28%), hives or allergic reaction (23%), swallowed medicine or overdose (17%), bite or sting (10%), adverse medicine reaction(2%), and other (18%). The majority (92% of respondents had heard of the PCC,but only 52% had the number readily available. When stratified by race,97% of Caucasians compared to 81% Hispanics had heard of the PCC. Caregivers who sought information after the poisoning most commonly searched the internet(24%) and only 6% called the PCC. Less than half of respondents (46%) thought that paid healthcare professionals answer PCC calls. Nearly half (48%)think the PCC reports child poisoning calls to other authorities. When stratified by race, 42% of Caucasians compared to 66% of Hispanics thinks the PCC reports to other authorities.
Conclusions: While use of an ED my seem justified from the caregiver's perspective, our results suggest that further outreach education efforts related to capabilities andqualifications of PCC staff are needed to reduce barriers to utilizing the PCC.

KEYWORDS Poison exposure; pediatric; survey

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213. Parental poison prevention education after unintentional opioid exposure

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Background: With increasing use of opioids in adults, a corresponding increase in exposures have occurred in children. NPDS data from 2014 to 2015 revealed a 73% increase in opioid exposures in children <6-years-old. The aim of this study was to determine if poison prevention education was provided to parents after a child's unintentional exposure to an opioid. A secondary objective was to provide poison prevention instructions and assess compliance.
Methods: A regional poison center database was queried for nonfatal unintentional opioid exposures in children <6-years-old from January 1, 2015 to August 31, 16. Two surveys were attempted. First the parents or guardians were contacted by phone and verbally consented to a survey regarding whether they received any poison prevention education before or after the exposure. If poison prevention was not provided, it was verbally discussed and emailed or mailed to their address. A follow-up survey was performed at least 1 month later to assess for preventative actions taken.
Results: There were 78 cases identified during this 20 month period. Forty-eight cases were excluded due to lack of contact information ($n = 12$), refusal to participate ($n = 5$), or inability to make contact ($n = 31$). Data collection from the initial call was completed for the 30 eligible participants, and 20 participants completed the follow-up survey. Seventy percent of participants had not received information on poison prevention before the child's exposure. Fifty-eight percent did not receive any education after the exposure occurred. Seventeen percent of respondents recalled receiving education during the initial call to the poison center. Preventative actions initiated following the exposure were: Up out of reach; Advised friend or family member; locked medicines; increased awareness; changed storage; talked to child about medications; Poison center magnet. In some cases multiple actions were employed. Upon conclusion of the first survey, 80% of respondents felt they did not need further education on medication safety and exposure prevention, but all agreed to receive a follow up call. At follow up, 35% had made further changes to prevent medication exposure and 45% felt that the calls were helpful.
Conclusions: These results suggest that parents and guardians often don't receive but are receptive to poison prevention education after unintentional exposures. Despite small sample size in an opioid model, these data likely are applicable to other pediatric exposures and should influence educational efforts by poison centers.

KEYWORDS Unintentional; pediatric; prevention

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214. Naloxone administration by Montgomery County, Pennsylvania Law Enforcement Agencies

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Table 1. Opioid reversal with naloxone January 2016–December 2017 in Montgomery County, Pennsylvania.

Opioid Reversal with IN Naloxone	2016	2017
Yes	164 (91%)	338 (92.10%)
No	17 (9%)	29 (7.90%)
	$N = 181$	$N = 367$

Table 2. Demographics of individuals receiving naloxone January 2016–December 2017 in Montgomery County, Pennsylvania.

	2016	2017
Gender		
Male	71%	75%
Female	29%	25%
Age (Years)		
18–30	52%	43.6%
31–45	38%	43.5%
46–60	9%	10.35%
61+	1%	2.18%

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Background: In 2017, there were 64,070 reported opioid overdose deaths in the United States, surpassing the number of deaths from motor vehicle accidents that year and greater than the death toll during the Vietnam War. All 50 states, except for Alaska and Hawaii, allow the administration of naloxone by law enforcement officials (LEOs). The Commonwealth of Pennsylvania passed the Opioid Overdose Reversal Act in September, 2014, providing first-responders and LEOs access to naloxone. Formal training in the use of naloxone was provided to LEOs under the auspices of the Pennsylvania Law Enforcement Opioid Antidote Program. Studies performed evaluating the LEO opioid reversal with intranasal (IN) naloxone in several states with similar programs, including Massachusetts, Indiana, Ohio, New York, California and North Carolina show a success rate ranging from 65.1% to 97%.
Objectives: The purpose of this study is to describe the experience regarding prehospital IN naloxone administration, by LEOs in Montgomery County, Pennsylvania, from January 2016 to December 2017.
Methods: This is a descriptive study of data collected by the Montgomery County Department of Public Safety with regard to LEO prehospital administration of IN naloxone. Each LEO who administered IN naloxone in response to a reported or suspected opioid overdose completed a mandatory "Narcan Administration Form." The first dataset was collected from January 1, 2016 to December 31, 2016 and the second from January 1, 2017 to December 31, 2017. Events, defined as administration of naloxone by LEOs in response to a reported or suspected opioid overdose were assessed. Comparisons of opioid reversal by year were evaluated using the Fisher exact, binomial proportion statistical test.
Results: The difference in opioid reversal between 2016 and 2017 was only 1.1%, showing that success rates were similar ($p = .66$). Opioid overdoses occurred on streets, highways, in vehicles, at public access restrooms, 24-h operated facilities, and hotels. Remaining data are summarized in Tables 1 and 2.
Conclusions: These data demonstrate that from January 2016 to December 2017 successful opioid reversal by LEO IN naloxone administration in Montgomery County, Pennsylvania, ranged from 91 to 92.1%. Results we report compare favorably to similar programs throughout the United States and demonstrates that this is an effective use of IN naloxone by prehospital LEOs. These data demonstrate that LEO administration of naloxone can be life-saving. LEOs should be encouraged to undergo formal training regarding the pre-hospital and the outcomes of their administration should be monitored.

KEYWORDS Naloxone; opioid overdose; law enforcement officials

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215. Long acting anticoagulant rodenticide poisoning – treatments and monitoring

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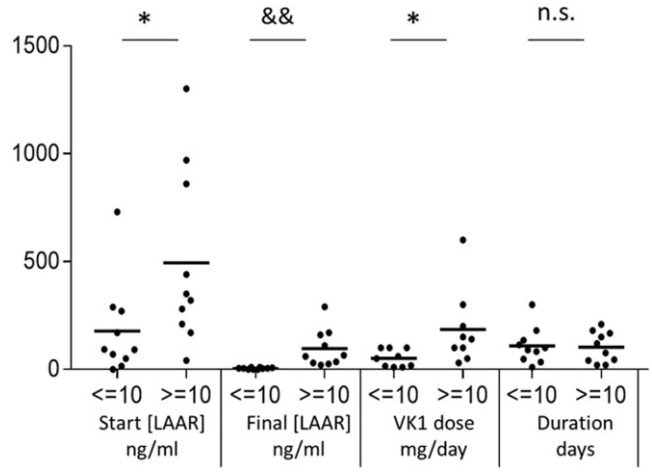
Background: Long lasting anti-coagulant rodenticides (LAARs) are used to eliminate warfarin-resistant rodents; however, their wide spread use has led to increased incidents of unintentional and intentional poisonings. The potential for a widespread event is suggested by the recent outbreak of LAAR poisoning in the Midwest which affected over 150 patients in Illinois alone, due to inhalation of synthetic cannabinoids found to be contaminated with the LAAR brodifacoum (BDF). The current recommended treatment for LAAR poisoning includes providing blood products followed by high-dose, long-term (extending over months) oral vitamin K (VK1) therapy. The high cost and long duration of VK1 raise concerns about access to care and adherence to therapy. The response to VK1 is monitored by measurement of INR. However, discontinuing VK1 based on INR poses risk since significant levels of LAARs may persist which can lead to recurrence of bleeding as well as other secondary types of pathology.
Methods: To estimate the duration of treatment needed to reduce LAAR levels to safe levels (<10 ng/l), we carried out a retrospective analysis of 20 case reports where levels were quantified before and after VK1 treatment.
Results: In the entire cohort of patients, the initial serum LAAR levels were 336 ± 80 ng/ml. The patients were treated with oral VK1 for 106 ± 17 d with 118 ± 33 mg daily dose; and at discharge their LAAR levels were reduced by 82%. In 10 patients final LAAR levels were 10 ng/ml or less; however levels in the other patients



Values for indicated parameters in patients whose serum LAAR levels at admission were <= 10 ng/ml ($n = 10$) or >= 10 ng/ml ($n = 10$). After testing for normality, groups were compared by parametric unpaired *t*-test (*) or Mann Whitney non-parametric test (&). *, $p < .05$; &, $p < .050$; &&, $p < .005$. Bars indicate means.

was 97 ± 28 ng/ml. In the cohort discharged with acceptable levels, the initial LAAR levels were 178 ± 69 ng/ml and they were treated with 51 ± 13 mg/d VK1 for 109 ± 26 d. In contrast, the cohort discharged with high LAAR levels had initial levels of 494 ± 129 ng/ml and were treated with 186 ± 55 mg/d for 103 ± 22 d. Thus, despite similar duration and significantly higher VK1 dosing, treatment in the latter cohort was insufficient to reduce LAAR to acceptable levels.
Conclusions: Treatment of LAAR poisoning with VK1 should be continued until serum LAAR levels fall below safe limits. Following discharge from hospital, patients may need to be monitored for blood LAAR levels and clinical outcomes for prolonged periods of time. Methods to accelerate LAAR clearance need to be developed to reduce the duration of VK1 treatment, and minimize subsequent symptom recurrence.

KEYWORDS Brodifacoum; rodenticide; vitamin K

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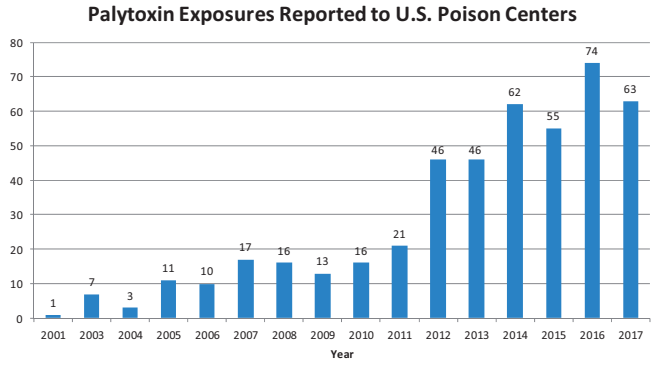

Figure 1. Values for indicated parameters in patients whose serum LAAR levels at admission were < = 10 ng/ml ($n = 10$) or > = 10 ng/ml ($n = 10$). After testing for normality, groups were compared by parametric unpaired *t*-test (*) or Mann Whitney non-parametric test (&). *, $p < .05$; &, $p < .050$; &&, $p < .005$. Bars indicate means.

216. Increase in palytoxin exposures reported to US Poison Centers

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Background: Palytoxin is an extremely potent toxin isolated from zoanthid coral species as well as some dinoflagellate and cyanobacteria. It functions by converting Na+/K+ ATPase pumps into passive diffusion channels, destroying the ion concentration gradients that are necessary for life. Palytoxin exposure may occur if exposed to sea water during blooms of palytoxin producing dinoflagellates, eating marine animals which have ingested palytoxin, or through routine maintenance of home aquariums containing zoanthid coral. Internal data at our poison center suggested an increased incidence of poison center calls related to palytoxin. National data was then queried to evaluate if this trend is occurring nationwide.
Objective: To characterize palytoxin exposures reported to U.S. poison centers over time.
Methods: This retrospective observational study examined data from the National Poison Data System (NPDS) derived from U.S. poison center cases. Inclusion criteria were all human patients with exposure to palytoxin from January 1, 2000 to December 31, 2017.
Results: There were 461 reported palytoxin exposures between 2000 and 2017. Annual exposure increased every 5 years since 2000, with only a single exposure reported in 2001, 63 exposures reported in 2017, and a peak of 74 exposures in 2016 (Figure 1). Three hundred and forty six (75%) exposures occurred within the most recent five years of the data set (2012–2017). Two hundred and thirty four (50.7%) of the exposures were from dermal contact, 130 (28.1%) were inhalational, 64 (13.9%) were ocular, and 50 (8.9%) were ingestions. Of the 461 exposures, 128 (27.7%) were managed on site, 78 (16.9%) were referred into a healthcare facility, and 247 (53.5%) were already in a healthcare facility care at the time of poison center contact. A total of 325 (70.9%) of the exposures had healthcare evaluation and treatment. Only six exposures reported major effects, one via dermal exposure, four from inhalational, and one from ocular exposure. Common major clinical effects included fever (5/6), dyspnea (4/6), chest pain (3/6), tachycardia (3/6), tremor (2/6), cough (2/6), and headache (2/6). Common moderate effects included fever, dyspnea, nausea, tachycardia, and dermal irritation.
Conclusions: Palytoxin exposures reported to U.S. poison centers have increased in recent years. It is unknown if this is due to an increase in human cohabitation with zoanthid coral species harboring this toxin, or if there is an increase in awareness of this toxin causing the exposed to seek care. The majority of exposures received healthcare facility treatment, and thus have a higher cost per exposure, however only 16.9% were referred to a healthcare facility by a poison center. Inhalational exposures made up the majority of major effects. Despite the potency of this toxin, few major effects were seen in exposed patients and no deaths occurred in this data series. Increased familiarity with these exposures may aid in optimizing triage consideration for U.S. poison centers. Healthcare facilities and poison centers should be aware of this possible toxin and suspect it when symptoms are reported after home aquarium exposure.

KEYWORDS Palytoxin; zoanthid coral; epidemeology

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217. Characterization of drug abuse information questions submitted to an online forum

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Background: Real time information regarding emerging trends in public drug use is difficult to obtain but can be a valuable resource for public health and medical professionals. Reddit is an online news aggregator and discussion forum where members can post content such as links to news articles or original text. Anyone with an email address can become a member; membership is required to add content (post) but not necessary to view content. Multiple areas of interest are represented and categorized into content-focused 'Subreddits'. Members can comment on original posts and comments can be 'up-voted' or 'down-voted' by other members. Posts with the highest number of up-votes (minus the number of down-votes) are generally regarded

as being of the highest quality. The Subreddit 'AskDrugs' is a forum where members seek information regarding recreational drug use. As of Jan 2017, Reddit had 234 million subscribers, with over 12,000 AskDrugs subscribers. By Dec 2017, AskDrugs had over 16,000 subscribers. Medical professionals might hesitate to give advice regarding drug abuse for legal and/or ethical reasons. Therefore, people often turn to their peers in the relative anonymity afforded by Internet message boards. The current study seeks to characterize the types of questions being asked online.

Methods: A Google script called 'Reddit Scraper' was modified to save posts from the AskDrugs Subreddit. The modified script ran from January 1, 2017 to December 31, 2017 extracting the post's title, description, posting date, and top three comments, which were saved to an online spreadsheet. Substances prompting questions were categorized as to the type of question, type of substance, whether fact or opinion was solicited, whether the question was asked pre- or post-exposure, and whether the question was regarding legitimate medical use. If more than 2 substances were mentioned in a post, then no substances were individually categorized and the substance type was categorized 'more than 2 substances.' If multiple questions were asked, a reason for question was not assigned and was categorized as 'multiple questions.' If a question was unintelligible, no data was collected.

Results: In total, 1353 questions were asked during the study period and are characterized as follows:

- Opinion or fact: 54.7% opinion versus 45.3% factual
- Pre/post exposure: Pre-exposure 65% versus 35% post-exposure
- Single question: 85% of posts asked a single question.
- Substance type: Controlled prescription medications were the substances most commonly asked about, followed by non-pharmaceutical illicit substances, natural products, and prescription/legend drugs.
- Substance details: Opioids prompted the most questions, followed by benzodiazepines, LSD, marijuana, amphetamines, and MDMA. More than 2 substances: 90.9% of questions were regarding one or two substances.
- Medical Use: 6.6% of questions were regarding medical use.
- Reason for Question: The most common reason posting was to ask about adverse effects, followed by clinical/desired effects, drug-drug interactions, multiple questions, seeking suggested drugs for abuse, and drug testing information.

Conclusion: This surveillance method could provide public health professionals with better insight into emerging drug trends and help target education efforts. Further analysis of the data to evaluate the quality of responses is necessary.

KEYWORDS Reddit; drug abuse; information

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218. Revisiting pill and capsule ingestions by children: when, where, how

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Poison center calls for solid dose medication exposures in children aged <6 years, by containers from which medications were accessed, February 1, 2017–September 2017

Container type	Medication classes with high potential for harm		Other medication classes	
	n	%	*n*	%
Original bottle or container	326	31.4	2134	61.3
Blister pack/unit dose packaging	11	1.1	330	9.5
The medicine was not in any container	378	36.4	636	18.3
In another kind of container or bottle	242	23.3	245	7.0
Different container types	1	0.1	3	0.1
Unknown/missing	81	7.8	136	3.9
Total	1039	100.0	3484	100.0

Background: Annually, > 60,000 children less than 6-years-old are evaluated in EDs for unintentional (unsupervised) medication ingestions; solid dose medications, such as pills, tablets, and capsules (SDMs), comprise 70% of these. However, little is known about the circumstances permitting ingestion of these SDMs, hindering development of further prevention efforts.

Objectives: We sought to characterize circumstances and characteristics of unsupervised SDM ingestions.

Methods: This was a cross-sectional study of exposure calls to 5 poison centers (PCs) serving about 40 million people in three states from February 1, 2017 to September 30, 2017. Calls involving children less than 6-years-old in which an ingestion of a human SDM was reported were analyzed. Such a call automatically triggered an electronic medical record real-time alert notification, instructing the PC staff member to offer enrollment into the study. Participants were presented with up to five additional contextually appropriate questions. Outcome variables include use of original containers, unit-dose packaging, alternative containers, and intended recipient of medication. "Medications with high potential for harm" were considered as belonging to one of the following classes: Opioid Analgesics, Sedative/Hypnotic Agents, ADHD Medications, Cardiovascular Agents, Oral Hypoglycemic Agents, Antidepressants, Antipsychotic Agents, or Anticonvulsants.

Results: There were 7280 eligible calls during the study period, of which 4523 (62.1%) calls involving 5101 substances were enrolled. Callers from a residence were more likely to participate compared to those from healthcare (66% versus 44%, $\chi^2 = 163$, df = 1, $p < .0001$). Most exposures involved a single substance (92.3%) and occurred in the child's residence (94.0%). Only 1.5% of participants experienced a moderate or major effect. Parents were the most common intended recipient of the SDM ($n = 2011$; 47.5%), followed by grandparents in 677 cases (16.0%). Cases were also analyzed by medication class. Medications with high potential for harm were transferred to alternate containers in 64% of calls, more often than other medications ($\chi^2 = 485$, df = 1, $p < .0001$).

Conclusions: In this study, most unsupervised SDM exposures in young children occurred from original packaging. However, for high harm potential medications, most unsupervised SDM exposures occurred from alternate containers. Improvements in child-safety packaging of SDMs are needed and likely to further restrict child access. Packaging changes to decrease the frequency of adult choice to take SDMs out of original containers may help to reduce these exposures with particularly high harm potential.

KEYWORDS Unintentional; pediatrics; prevention

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219. The impact of opioid CME and PDMP mandates on provider referrals to behavioral health services

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Background: In 2016–2017, WI mandated that physicians prescribing controlled substances receive 2 h of continuing education (CME) on responsible opioid prescribing and use the Prescription Drug Monitoring Program (PDMP). Some healthcare systems tailored the required CME to their system and provided it to providers free of charge. The trainings intended to improve identification and treatment of individuals with potential substance use disorders. This study characterizes provider attitudes and opinions towards those healthcare system changes and evaluates if those changes led to increased referral of patients to Behavioral Health treatment services (BH).
Methods: Prior to the April 2017 PDMP mandate, prescribing providers at an entire community healthcare system in Wisconsin ($N = 800$; $n = 154$; 19% response) were surveyed to regarding their referral behavior, and knowledge of opioid use disorder resources and the PDMP mandate. Reports of daily patient volume and the number of referrals to BH between July 1, 2016 and June 30, 2017 were generated, including 958,469 patient visits and 4976 referrals over the study period. A baseline (Time 1; T1) was established as the time prior to implementation of the first mandatory provider CME trainings (July 1, 2016–October 12, 2016). T2 was the time that occurred between the CME session 1 and session 2 (October 13, 2016–February 2016). T3 occurred after CME session 2 but before the PDMP mandate (February 17, 2017–March 31, 2017). Finally, T4 occurred after the PDMP mandate was in place (April 1, 2017–June 29, 2017). Total referrals and daily referral rates per 1000 patient visits were calculated and Z tests for population proportions and a one way ANOVA compared referral rates across time periods.
Results: 80.4% of providers responding to the survey reported confidence in their ability to locate local opioid use disorder resources. Among those who made referrals for BH treatment in the past, 70.3% reported making on average less than one each week. 65.3% of providers believed the PDMP mandate would not increase the number referrals they make. Referral rates were: 1250/265,213 (T1); 1185/342,739 (T2); 608/116,873 (T3); and 1303/233,644 (T4). There was a significant differences between T1 and T2 ($Z = -3.18$, $p < .001$) and between T1 and T4 ($Z = -4.27$, $p = < .001$). The ANOVA was not significant $F(3, 363) = 1.884$, $p = .13$.
Conclusion: The time after the first CME session included a significantly higher proportion of referrals than what was seen during the baseline period. Referral proportions were also significantly higher after the PDMP mandate (T4), compared with the baseline period. The increases in proportions of the time periods suggest a potential upward trend/cumulative impact of the three efforts over time—a notion that is reinforced by the insignificant ANOVA and paired tests between (T2 & T3) and (T3 & T4). Multiple approaches may be required to change provider behavior in a significant way over time. As the majority of providers reported confidence in finding and using opioid use disorder resources, future education or changes could focus on increasing referral utilization and BH referral rates. It is interesting that referral rates significantly increased in T4, compared to T1 despite most providers reporting that the PDMP will not likely influence their referral behavior – however, again, this may be due to cumulative impact of multiple efforts.

KEYWORDS PDMP; opioid; referral

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220. Falsely elevated serum salicylate concentration secondary to hyperlipidemia

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Background: Some qualitative and quantitative drug tests are known to cross-react with other substances and produce false positive results. However, common quantitative measurements for salicylates are generally accepted as correct. This case report describes a patient with hypertriglyceridemia and had a falsely elevated salicylate concentration that resulted in unnecessary hospitalization.
Case report: A 46-year-old male truck driver with a history of type 2 diabetes, hyperlipidemia, peripheral neuropathy, gout and GERD taking allopurinol, atorvastatin, canagliflozin, gabapentin, gemfibrozil, glimepiride, lisinopril/hydrochlorothiazide, metformin, omeprazole, propranolol, and an investigational drug made from hepatocyte growth factors presented to the emergency department after a motor vehicle crash [BC1] resulting in minor injuries including lacerations needing sutures. He requested toxicology testing to document that he was not chemically impaired at the time of the crash. His serum salicylate concentration was >100 mg/dl which triggered further labs and workup for salicylate intoxication. The patient denied taking any source of salicylates. He had no tachypnea, tinnitus, nausea or vomiting, altered mental status, or any other symptoms outside of his physical injuries sustained in the motor vehicle crash. A venous blood gas noted pH 7.41, pCO_2 37 mmHg, HCO_3 23 mmol/l. The salicylate concentration was repeated four times, all resulting with salicylate >100 mg/dl. The blood analyzer, a Seimens Advia 1800 that uses the enzymatic method, was tested to ensure it was not an equipment error. He was admitted for observation while the high salicylate concentration was investigated. However, no alkalinization or dialysis was performed since his clinical appearance did not indicate salicylate toxicity. While investigating possible laboratory interferences it was discovered that hyperlipidemia has caused interference with spectrophotometric quantification, the common method used to quantify salicylate concentrations. Our patient was known to have hyperlipidemia and his lipids the day of the crash were: total cholesterol 200 mg/dl, triglycerides 1888 mg/dl, HDL 17 mg/dl, LDL 14 mg/dl. A lipid clearing reagent (LipoClear®) was used to remove the interference caused by the light absorptive properties of lipids in the serum. After clearing his blood sample of the triglycerides the repeat salicylate concentration was <5 mg/dl.
Case discussion: This patients underlying hyperlipidemia likely produced a falsely elevated serum salicylate concentration. Prior to this patient, the facilities documentation for the salicylate assay noted lipemia causes no significant interferences, which is consistent with information published when the enzymatic method was developed. Two similar cases have been published where patients with triglycerides of 6390 mg/dl and 7650 mg/dl had false salicylate concentrations. One case specified using the enzymatic method as well.
Conclusion: Elevated serum lipids may interfere with quantitative serum salicylate assays. Clinicians should be aware of this interaction and rule out this interference in patients with elevated serum salicylate concentrations who do not demonstrate clinical signs of salicylate poisoning.

KEYWORDS Salicylate; hyperlipidemia; laboratory

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221. The elusive phytonadione – a bloody mess

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Background: Synthetic cannabinoids are mind-altering chemicals sold as herbal remedies. These products may be smoked or vaporized in e-cigarettes and other devices. Individuals who use synthetic cannabinoids in our state recently began experiencing bleeding and elevated international normalized ratios (INR). It was determined that the synthetic cannabinoids were tainted with long acting anticoagulants. We present the dilemmas associated with providing antidotal therapy for a large number of patients poisoned with long acting anticoagulants in a recent outbreak in our state.
Case report: The sentinel case was treated March 10, 2018. In the ensuing days many more patients have presented to area hospitals with abnormal bleeding associated with synthetic cannabinoid use. Patients were treated with vitamin K1 either intravenously (IV) or orally depending on the severity of bleeding. Vitamin K1 is available as 5 mg tablets and 10 mg/ml 1 ml vials. Supplies of oral vitamin K1 tablets and IV injection were tenuous and quickly became unavailable in many area hospital pharmacies. Alternative treatment modalities were needed.
Discussion: We recommended vitamin K1 50 mg orally every 8 h (30 tablets daily) once patients' bleeding was controlled and INR normalized. Several problems soon became apparent with oral vitamin K1 treatment. Hospital pharmacy supplies of vitamin K1 oral tablets were quickly depleted because of the large numbers of patients requiring large quantities of tablets. Hospital supply vendors soon reported that vitamin K1 tablets were unavailable. Community pharmacies do not typically stock vitamin K1 products. Over the counter formulations of vitamin K1 found at health food stores are only available in 100 mcg strength or as vitamin K2 which will not normalize coagulopathy resulting from oral anticoagulants. Additionally the cost to the patient for oral vitamin K1 tablets was found to be $68 per tablet ($12,240 for a 6 d supply, at a dose of 50 mg 3 times daily) at a local university hospital outpatient pharmacy. It is unrealistic that patients will be able to afford this antidotal therapy for weeks to months. Hospital pharmacists resorted to administering the undiluted IV vitamin K1 preparation orally. Undiluted IV vitamin K1 is s table for 30 d at both room and refrigerated temperatures. A filtered needle may be considered for vitamin K1 withdrawal from the vial. This product is light sensitive and must be stored in amber bottles or syringes. Orange juice can be used to mask its unpleasant taste.
Conclusion: Adequate antidotal supplies are critical in managing outbreaks. Pharmacists are integral in finding novel modalities when shortages arise. Governmental agencies should be proactive in securing antidotes and other treatment modalities to manage affected patients in isolated outbreaks and to minimize morbidity and mortality. Antidotal therapies must be made affordable to all patients.

KEYWORDS Vitamin k1; synthetic cannabinoid outbreak; long acting anticoagulant

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222. Acetylcysteine for acetaminophen repeated supratherapeutic ingestion: how much is needed?

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Background: There is extensive literature on acute acetaminophen (APAP) overdose, but fewer publications to guide the management of repeated supratherapeutic ingestion (RSTI). The purpose of this study was to survey U.S. poison center leadership in order to determine the degree of consistency between centers in their recommendations for managing APAP RSTI.
Methods: Using the American Association of Poison Control Centers' listserv, an electronic survey link was sent to managing/medical/associate/assistant directors ($n = 379$) at all 55 U.S. poison centers (PCs). This study was approved by our university's institutional review board. The survey asked PC directors about their approach to RSTI in contrast to acute overdose patients, as well as factors influencing their treatment recommendations.
Results: We received 41 responses from 32 of 55 U.S. PCs, yielding a response rate of 10.8% for individuals and 58.2% for PCs. Twenty-seven of forty-one (65.8%) respondents reported having a guideline that specifically addresses APAP RSTI. When asked about the proportion of APAP cases they estimate to be RSTI-related, respondents' responses ranged from 5% to 64% with a mean of 23%. With regard to their minimum treatment recommendations in the absence of liver injury, 8 of 41 (19.5%) respondents indicated that 12 h would be acceptable, while 18 of 41 (43.9%) chose 20 or 21 h, and the remainder (36.6%) indicated that cessation of treatment would depend on repeat lab results. When asked the proportion of RSTI patients consulted on through their center that develop hepatotoxicity (ALT $>$ 1000 IU/l), respondents gave estimates ranging from 1% to 75% with a mean of 19%. Of the 40 respondents who answered the question on their role at the PC, 75% were physician toxicologists.
Discussion: Because APAP RSTI is a spectrum condition with some patients initially presenting in hepatic failure and others never demonstrating evidence of liver injury, it's not surprising that there is variability in treatment recommendations between PC directors. Most recommend some form of patient-tailored treatment with continuation of N-acetylcysteine (NAC) until APAP is undetectable or $<$10 mcg/ml, and aminotransferases and coagulation parameters are either improving or below specific thresholds. However, there may be less consensus regarding the minimum treatment needed in the absence of liver injury, with nearly 20% of respondents indicating that 12 h of antidote would be acceptable in this situation, while a larger proportion would recommend a standard 20–21 h course of NAC.
Conclusions: Most U.S. poison center directors follow a patient-tailored approach to treatment of APAP RSTI, with NAC therapy guided by clearance of APAP and improving aminotransferases. Among a sizable minority, there appears to be interest in shorter (12 h) treatment for patients without evidence of liver injury, and further study may be warranted in appropriate patients.

KEYWORDS Acetaminophen; repeated supratuerapeutic ingestion; poison centers

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223. Use of an Immersive, Simulated Learning Game to Teach Pharmacy Students Clinical Concepts of Toxicology

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Background/objectives: Management of a poisoned patient is a critical part of any health care professional's education. A new, innovative teaching platform has been developed allowing students to try to "break out" of various kits, locks, and scrambled codes and build collaboration, problem-solving, and critical thinking skills – similar to the recently popular "escape room" experiences. To our knowledge, there are no articles that researched such a learning game in health care professional education. One article analyzed the activity in a collegiate writing class found that students had "increased commitment and energy," and it "[r]evealed the rewards of perseverance" and fostered collaboration. The purpose of this study is to illustrate how such a learning game can be utilized in pharmacy education to teach and apply clinical knowledge, as well as to evaluate its effectiveness on student confidence and competency in recommending treatment for a patient with a toxicologic emergency.
Methods: Students participated in the learning game, as part of an acute care elective, in two separate cases. The activity was developed by subject matter experts for third-year PharmD professional students, which included concepts of: clinically-relevant drug interactions and lithium toxicity (case 1) and acetaminophen toxicity and serotonin syndrome (case 2). They worked within groups of 3–4 students to complete the simulation. Students were given the same test pre- and post-game for each case to assess changes in toxicology knowledge after simulation. Each test included five multiple-choice questions, covering the domains of: clinical presentation, treatment options, pharmacokinetics, therapeutic drug monitoring, and proper dose calculations. Students were administered a survey about the learning game and their confidence in managing toxidromes after completion of the activity.
Results: Twenty-two students participated in this learning activity. For case 1, 4/22 students (18%) got a passing grade (>70%) on the pre-test and 18/22 (82%) got a passing grade on the post test. One question on the quiz for case 2 was eliminated because students interpreted it as misleading. For case 2, 0/22 students (0%) got a passing grade on the pre-test and 15/22 (68%) got a passing score on the post-test. The mean improvement in quiz scores for cases 1 and 2 were 1.64 and 2.09, respectively. On a Likert scale of 1 (least confident) to 5 (most confident), all students ranked their confidence in managing a toxicology case at or below a 2. After the learning game, 21/22 students reported a score at or above 3. When asked to rate how the activity strengthened their toxicology knowledge on a Likert scale of 1 (strongly disagree) to 5 (strongly agree), 21/22 students responded with a 4 or 5. On the same scale, 21/22 students were overall satisfied with the activity, and 20/22 agreed it should be incorporated into future pharmacy learning.
Conclusions: The learning game was an effective and satisfying educational tool to understand and apply medical toxicology principles for pharmacy students. Additional implementation of this game would be preferred by most students and may aid in the educational of other health care professionals, including interprofessional collaboration.

KEYWORDS Education; simulation; pharmacy student

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224. The KRATOMic Bomb: Dangers arise behind America's newest street drug

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Background: Kratom has risen in popularity among America's recreational drugs for its opioid-like and some stimulant-like properties. Derived from the Mitragyna speciosa plant which is native to Thailand, Malaysia, Indonesia, and Papua New Guinea, kratom has drawn much controversy – not only because of its health risks including respiratory depression, liver injury, and seizures, but also because of its risk for misuse and addiction. Since 2014, the FDA has played an active role in discouraging the use of Kratom. Recently, Kratom has also been linked to salmonella infections. Here, we discuss a patient who presents with seizure and found to have bandemia secondary to salmonella infection.
Case report: A 30-year-old male with a history of seizure disorder, anxiety, hypertension, and hyperlipidemia presented to the emergency room after a witnessed reported generalized tonic-clonic seizure. When investigating for cause of this seizure episode, likely etiologies including medication noncompliance, breakthrough seizures, infection, or drug use were considered. He revealed he had run out of his levetiracetam 4 d prior to admission and he denied recurrent seizures once initiated on levetiracetam therapy of 2000 g daily 3 months prior. He denied any fevers or chills, recent sick contacts, and infectious symptoms including cough, rhinorrhea, nausea, vomiting, diarrhea, or dysuria. He denied history of tobacco, alcohol, or illicit drug use, but did report using Kratom for treatment of pain and anxiety. Brought in by EMS, his initial presentation was significant for fever of 101 °F and tachycardia, as well as diaphoresis and facial flushing. Cardiopulmonary, abdominal, and neurologic exams were otherwise unremarkable. Laboratory values were notable for a normal white blood cell count of $8.4 \times 1000/\mu L$, however with 24% bands. His levetiracetam level returned at <2.0 μg/ml. His urine drug screen returned negative for amphetamines, cocaine, cannabinoids, and opiates and positive for methadone, which he denied using. Research into his use of Kratom as a contributing etiology to his seizure revealed multiple accounts of Salmonella infection linked to Kratom use as reported by the CDC. Stool samples were obtained from our patient and pathogens detected by PCR revealed salmonella species, which later speciated to Salmonella O, Type D.
Discussion: This case reflects the popularity of kratom use for both its mood and pain relieving effects. We suspect that his seizure, while likely multifactorial and largely due to subtherapeutic antiepileptic therapy, may have also been triggered by salmonella infection from contamination of the Kratom he purchased online. Infection is known to lower the seizure threshold, and his fever and bandemia suggest a clinically significant infection from the Salmonella exposure. The CDC's published and ongoing monitoring of salmonella-contaminated Kratom captures an ongoing public health threat and was key to the appropriate diagnosis in this patient.
Conclusion: As its popularity rises, Kratom has found to be associated with respiratory depression, liver injury, seizures, and other medical comorbidities and has potential for misuse and addiction. Most recently, this drug has also been associated with salmonella infections.

KEYWORDS Kratom; salmonella; public health

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225. Coding of hurricane Harvey-related calls by statewide poison center network

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Background: Hurricane Harvey, tied with Hurricane Katrina as the costliest tropical cyclone on record, made landfall in Texas on August 25, 2017. Our statewide poison center (PC) network has a standard procedure for documentation of calls related to public health events, such as tropical storms, so that the calls may be identified. On August 24, 2017, the PC network managing directors were instructed to implement a procedure for documenting calls related to Hurricane Harvey. If PC staff received a Hurricane Harvey-related call, they were to (1) add the public health emergency code to the Free Area 1 field and (2) mention Hurricane Harvey in the Notes field of Toxicall. On August 25, 2017, the American Association of Poison Control Centers (AAPCC) instructed U.S. poison centers to use a new (3) PoisIndex Product Code with all Hurricane Harvey-related calls. This report describes the utilization of these three different documentation methods by the PC network.
Methods: All PC network calls received during August 25–October 31, 2017 and related to Hurricane Harvey were identified. For each record, it was determined whether each of the three documentation methods was used. (For the Notes documentation, mention of "hurricane," "Harvey," or "flood" was considered proper documentation.) The distribution of the documentation methods was determined.
Results: Of 246 calls considered to be Hurricane Harvey-related, 84.6% were assigned the Free Area 1 code, 54.1% documented the storm in the Notes, 50.8% were assigned the PoisIndex Code, and 0.4% ($n = 1$) were not documented by any of these three methods but identified another way. All three of the methods were used in 23.2% of the calls, two methods in 43.5%, and one method in 32.9%. The Free Area 1 code alone was used in 19.1% of the calls, the Notes documentation alone in 13.4%, and the PoisIndex code alone in 0.4% ($n = 1$).
Discussion: Documentation by all three methods occurred in only a fraction of the calls; however, only one call was identified not using any of the methods. The most effective documentation methods were the Free Area 1 code, followed by mention of the storm in the Notes. Use of the PoisIndex Code was least effective and identified only one call missed by the other two methods. One problem encountered was confusion over what calls should be considered Hurricane Harvey-related. Poison centers may need to ensure that staff is aware of proper documentation of calls of public health events and the importance of doing so. Having multiple methods for documenting such calls ensures that a higher number is identified during public health events for PC preparedness.

KEYWORDS Hurricane; coding; preparedness

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226. Toxicology education in pediatric residency programs – is tox outside the box?

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Background and objective: Childhood poisoning is a significant public health problem in the United States (U.S.). Pediatric residents must learn how to properly evaluate and manage poisoned patients and provide important education to patients and their families regarding medication safety. Pediatric residents also benefit from exposure to the public health and community outreach aspects of toxicology, as well as learning about the field as a potential career path. A survey study published in 2000 describing the educational experience of pediatric residents in emergency care found that 53% of programs had no available toxicology rotation and only 4% had a required rotation. We believe that most board certified pediatricians have neither received formal toxicology education during residency nor have they had the opportunity to be exposed to the field of medical toxicology. We aim to characterize the toxicology curricula and educational opportunities currently incorporated into pediatric residency programs throughout the U.S.
Methods: To determine the extent of toxicology education in pediatric residencies in the United States, an online review of American College of Graduate Medical Education (ACGME)-certified categorical pediatric residency programs was performed. Residency programs were assessed for explicit mention of "toxicology" in their curriculum and identified though FREIDA Online®, the American Medical Association Residency & Fellowship Database®. Program demographics were collected from the database and the presence of any toxicology curriculum was determined by a thorough review of each program's website, including all published education and curriculum sections. Three researchers performed the review, with one person (RL, a current post-graduate year level III pediatric resident) performing the initial search, a second person (CF, a current post-graduate year level II pediatric resident) performing the same search separately and finally, a third person (MR, a current fellow level I in Medical Toxicology) to adjudicate any discrepancies.
Results: Two hundred and six pediatric residency programs were identified. All programs had functioning websites during August–September 2017 and/or February 2018 when the researchers performed their separate reviews. However, 50/206 (24.3%) had limited information on their program websites and/or did not list their electives. The initial reviewer (RL) identified 16/206 programs as having toxicology as part of their curriculum. The second reviewer (CF) identified 19/206 programs (Cohen's Kappa = 0.73). Adjudication by a third member of the team (MR) determined that in total 20/206 (9.7%) programs had a toxicology component to their residency training. Of these 20 programs, 19 offered toxicology as an optional elective. Only one program described a formal Poison Control Center rotation as part of its emergency department rotation.
Conclusions: There is a paucity of formal toxicology curricula across pediatric residency programs in the U.S., highlighting a possible deficiency in pediatric medical education. Childhood poisonings are common, and toxicology should be incorporated into pediatric residency training, both from a public health and community advocacy standpoint. Given the limitations of the methodology of this study, we are developing a future study to survey pediatric residency program directors to further characterize toxicology education and identify potential barriers to incorporating toxicology into pediatric residency training programs.

KEYWORDS Toxicology curricula; pediatrics; residency education

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227. Toxicological treatment recommendation compliance rate with poison center recommendations

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Background: As a consultation service, poison centers recommend various treatments for poisoned patients. However, the decision to enact these recommendations belongs to the primary provider caring for the patient. A prior study determined that there was a 77% compliance rate for all recommendations made by Internal Medicine consultants, with decreasing compliance when more than 5 recommendations were made, and when recommendations involved physician or nursing actions as opposed to medications. Studies evaluating compliance with toxicological recommendations have focused on lay person compliance with follow up recommendations and not on treatment recommendations to providers, with three exceptions. Prior investigations have investigatedthe specific treatments such as hemodialysis for lithium toxicity, fomepizole use after toxic alcohol ingestion, and hyperinsulinemia and lipid emulsion use in beta blocker and calcium channel blocker overdoses.
Objectives: Our objective is to describe the overall treatment recommendation compliance rate of the National Poison Data System (NPDS) of the American Association of Poison Control Centers for the years 2016–2017. We describe specific treatment compliance rate, non-compliance rate, and the utilization rate of treatments administered without Poison Center recommendation.
Methods: De-identified treatment data was obtained utilizing standard nationwide enterprise reports from the NPDS for 2016 and 2017. Thirty selected treatments (selected by our investigators to have potentially the largest impact on disease course, morbidity, and mortality) were used to determine the overall treatment compliance rate. All treatments coded as "Not Given" or "Known Not Given" were assumed to not be administered. Basic statistical analysis was used to analyze the data.
Results: For the calendar years 2016–2017, there were 370,816 unique treatments administered. Overall treatment compliance was, similar to that of Internal Medicine, 72.3%. Benzodiazepines were the most commonly administered treatment (82,600 times), and the most commonly recommended treatment, recommended 49,648 times. Ventilators had the highest recommendation compliance, being employed 93.5% of the time recommended. This was followed closely by Fab antivenom and sedation. Of the treatments recommended but not performed, extracorporeal membrane oxygenation had the highest rate of noncompliance. Of the treatments provided without recommendation, those associated with intubation had the highest rate of utilization by the primary providers. Of note, both naloxone and flumazenil were commonly used without PC recommendation (91.8%).
Conclusion: The compliance rate of 72.3% is similar to the stated consult treatment recommendation compliance rate for Internal Medicine, potentially indicating effective communication when conveying the importance of treatments. However, some treatments are commonly inappropriately utilized despite their potential to cause adverse effects. This study also highlights the importance of clear and concise communication. Several potential areas are identified where Poison Specialists need to be aware their recommendations may not be followed, as well as areas where further education are needed to help prevent adverse effects of unwarranted treatments. Future study is warranted to determine what factors the variables influence this compliance.

KEYWORDS Poison center; treatment recommendation; recommendation compliance

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228. Development and validation of a risk predictive model for student alcohol intoxication associated with emergency department visits – a longitudinal data linkage study

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Objective: Available screening tool s for problem drinking were typically designed to identify students at high risk for binge drinking, which may not necessarily apply to students who are at risk of alcohol intoxication requiring emergency interventions. This study aimed to develop and validate a predictive model to quantify the risk of alcohol intoxication associated with emergency department (ED) visits among students.
Methods: We conducted a prospective cohort study of students enrolled to a U.S. public university from 2010/2011 to 2015/2016 academic years. Student admission and primary healthcare data were linked to subsequent ED visits with alcohol intoxication ascertained from ICD-9 and ICD-10 codes within 1 year following the first (index) enrollment. Multivariable logistic regression analysis was used to develop a risk predictive model based on the first 3 year (2010/2011–2012/2013) student cohort ($n = 93,289$), which was then validated in the following 3 year (2013/2014–2015/2016) student cohort ($n = 85,876$).
Results: Four hundred and twenty-eight students (46/10,000) in the derivation cohort and 496 students (58/10,000) in the validation cohort had an ED visit with alcohol intoxication within 1 year following enrollment. Student socio-demographic characteristics (gender, age, parental tax dependency), academic level, Greek life member, athletic participation, past year alcohol use, and having been diagnosed with depression or anxiety were statistically significant predictors. C-statistic of the model was 0.82 in the derivation cohort and 0.79 in validation cohort, with excellent calibration and no evidence of over- or under-prediction observed from calibration plots.
Conclusions: Based on routinely collected student data linked with clinical data, a robust risk predictive model was developed and validated to quantify absolute risk of alcohol intoxication associated with ED visits for every student at the time of enrollment. This model can provide a useful tool for clinicians or health educators to make real time decision to plan target interventions for students at elevated risk.

KEYWORDS Risk prediction; alcohol intoxication; emergency department

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229. Trends and determinants of student hazardous drinking – a comparative analysis using multiple datasets in a U.S. public university

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Objective: This study examined the trends in incidence and socio-demographic, organizational, academic, and clinical risk markers of student drinking associated with Emergency Department (ED) visits and incident reports from the University Incident Management Response System (IMRS).
Methods: A prospective cohort study of students enrolled in a U.S. public university from 2010/2011 to 2015/2016 was conducted. Student enrollment data were linked to primary healthcare data and subsequent ED visits with alcohol intoxication identified using ICD codes, and linked to alcohol-related incidents that occur on and off grounds recorded in the IMRS system within one year following the first (index) enrollment of each year. Incidence rate per 10,000 person-years for each of the 2 hazardous drinking outcomes was calculated, and annual trends in the incidence were analyzed using Poisson regression. Cox proportional hazard regression was used to provide adjusted hazard ratios (HR) (95% CIs) for the association between student characteristics and each of the hazardous drinking outcomes studied.
Results: The cohort consists of 204,423 students, 56% males, after excluding 5675 students (2.7%) with missing data on covariates. A total of 1041 students had at least one ED visit with alcohol intoxication and 5359 students had at least one alcohol-related incident within one year after the index enrollment; the overall incidence rate was 59/10,000 person-years and 311/10,000 person-years, respectively. There were a total of 455 students in both groups (7.6% of total students encountered). In the first 6 years from 2009–2010 to 2014–2015, incidence of student alcohol intoxication associated with ED visits increased linearly from 45/10,000 person-years to 71/10,000 person-years ($p < .001$). Similarly, incidence of alcohol-related incidents increased linearly from 249/10,000 person-years to 361/10,000 person-years ($p < .001$), but to a lesser extent (by 45% versus by 57%). In the last 2 years of the study period, incidence of both types of hazardous drinking showed a decline from 72 to 65/10,000 person-years (9%) and from 361 to 318/10,000 person-years (12%), respectively (Figure 1). These two hazardous drinking outcome measures share common risk markers, including: males (versus females), below 20 years of age (versus 25–30 years), Hispanic (versus Asian) students, parental tax dependency, Greek life member, undergraduate (versus graduate students), first time enrolled students, and having an existing diagnosis of depression and/or anxiety. In addition, African American, White, and multiracial students were at higher risk for alcohol-related incidents, while students who transferred from a prior institution were at lower risk. Past year alcohol use was significantly associated with higher risk for ED visits with alcohol intoxication. Being a member of a university athletic team appeared to be protective against alcohol intoxication associated with ED visits, but this protection was lost for alcohol-related incidents.
Conclusions: Data on student hazardous drinking captured in ED clinical data and the IMRS showed consistent trends in the period studied. Linking student admission data with ED clinical data and IMRS data can more fully capture and monitor student hazardous drinking behaviors and identify student groups at higher risk who subsequently can be targeted for intervention efforts.

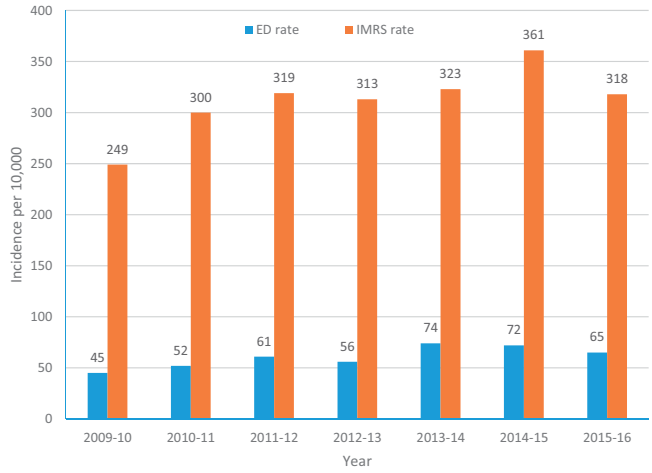

Figure 1. Trend in incidence of alcohol intoxication ED visits and alcohol-related incidents.

KEYWORDS Hazardous drinking; student; incidence
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230. Utilization of the PEHSU program as a poison center resource

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Background: The Poison Center system has provided consults on millions of toxic exposures since the first Poison Center was established in 1953. In 1998, the Pediatric Environmental Health Specialty Unit (PEHSU) program was established, which provides telephone consults on environmental toxic exposures, particularly in children and (recently) in pregnant women. Some PEHSU consults are actually referred from Poison Centers. Using this information, we further explored the nature and types of cases referred from poison centers to the PEHSU centers.
Methods: PEHSU specialists maintain consult records in a national Performance Tracking System database. Each first time caller to a PEHSU is asked how they were referred to PEHSU. We analyzed PEHSU consults initiated between January 2016 and March 2018 that were referred from Poison Centers.
Results: Between January 2016 and March 2018, the PEHSU program performed 1897 consults to first-time callers. One hundred and sixteen (6.1%) of these callers were referred to PEHSU from Poison Centers. Of these 116 Poison Center referral cases, 75 (64.6%) consults were provided to health professionals and 41 (35.4%) to the public. In 105 consults (90.5%), the primary reason for the call was to request information related to a specific potential exposure or health problem. In 112 cases (96.6%) the primary concern was an agent; in 4 cases (3.4%) a health problem. In 39 cases (33.6%), the primary agent/health problem prompting the consult was lead, followed by drugs, 25 (21.6%); fungus/mold, 7 (6.0%); mercury, 5 (4.3%); cleaning/disinfectant products, 4 (3.4%); natural gas, 3 (2.6%); carbon monoxide, 2 (1.7%); and perfluorinated chemicals (PFCs), 2 (1.8%). Other Poison Center referrals to PEHSUs involved: acetaminophen,

aluminum polish, anemia, artificial turf cooling pellets, bath salts, coal tar, cobalt, developmental delay, electromagnetic fields (EMF), epinephrine (EpiPen Jr. Autoinjector), foreign body in stomach, grain alcohol (ethanol), gases/fumes, metals (general), metoprolol succinate, nicotine gum, pesticides, polyurethane, Red Bull beverage, smoke/combustion products, toluene, vitamin D, volatile organic compounds (VOCs), and water toxins. In 5 cases (4.3%) the agent was unknown. Of the 40 cases (34.5%) where exposure timing was known, 27 cases (67.5%) were acute exposures, 7 (17.5%) were chronic exposures, and 6 cases (15.0%) were acute-on-chronic exposures. These consultations impacted 114 children and 31 adults (including 5 pregnant women).
Discussion: On occasion Poison Centers will refer cases to the PEHSUs for further evaluation. PEHSU expertise in pediatric and reproductive environmental health provides another resource for Poison Centers.
Conclusion: Poison Centers refer callers to PEHSUs on a variety of potential toxic environmental exposures and health concerns. The most frequently reported agent of concern was lead, which accounted for one-third of the calls. The majority of cases referred from PCs were acute exposures.

KEYWORDS Pregnant; pediatric; resource

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231. Development of a prototype software tool to assist with toxidrome recognition

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Background: Toxidrome recognition presents an ongoing challenge for medical trainees at all levels. Specialized computer software programs, often partnered with machine-learning algorithms, have been used to assist human operators with similar pattern-recognition problems in other fields. We created a simple web-based application to help with educational and clinical recognition of toxidromes by medical trainees and professionals.
Methods: Using a model-view-controller architecture, we created a web-based application that can be accessed via smartphone or internet-accessible computer. A Hypertext Markup Language (HTML) based front-end allows the user to input patient information including demographics, history, physical exam, vital signs, and symptoms in a standardized template similar to many Electronic Medical Record (EMR) systems. Python programming language scripts store the user input as a unique case in a Structured Query Language (SQL) database running on a cloud-based server. The core algorithm of the application iteratively checks the case against a database of known toxidromes and creates a ranked-list of potential toxidromes matching the case. Potential toxidrome matches are calculated based on the presence or absence of each possible data point (corresponding to history, vital signs, physical exam findings, and symptoms) entered by the user, weighted based on how relevant each data point is to each individual toxidrome. The algorithm outputs a dynamically-generated web-page containing the top five matching toxidromes, as well as a list of which missing data points would most alter the ranked toxidrome list if entered. From this page, the user is linked back to the input template and can enter additional data or correct mis-entered data. Suggestions for immediate tests and treatments, as well as links to additional information on each listed toxidrome, are provided for the matching toxidromes. Finally, all case information is retained in a central SQL database, allowing for administrative access and review of user-entered cases.
Results: As a proof-of-concept demonstration, a sample database of 15 toxidromes was created, with data weighting for individual symptoms and findings based on authors' clinical experience and gestalt. Using the prototype application, we were readily able to input cases, store them in the database, and generate a ranked differential. The application was able to match the correct toxidrome in a few simulated test cases successfully. Test cases included opioid, salicylate, and cholinergic toxidromes.
Conclusions: Our application appears valid as a proof-of-concept for checking a user-inputted case against a toxidrome database. The value-weighting of symptoms in the underlying toxidrome database requires improvement. The use of machine-learning algorithms to better weight symptoms based on a large database of clinical cases is planned. With improvements to the underlying database, this application will be a useful tool for clinical recognition of toxidromes and in toxicology education.

KEYWORDS Toxidrome; software; prototype

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232. Outreach on the web: collaborating coast to coast

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Background: Poison Centers across the nation are faced with the task of promoting center services in a cost effective manner. This is especially problematic for centers that cover large geographical areas with limited education staff and budget. In a service region such as ours, where the population exceeds 10 million, providing trainings and promoting services has been challenging. Over 20 years ago we developed an in-class instructor training program to address the issues of training volunteers to deliver poison prevention education on our behalf. Due to staffing, travel, and participant concerns (such as program content, program length, training location, and costs) significant changes were made to the program including the development and implementation of our online poison prevention training program.
Methods: Developed on a foundation of epidemiological data, education theory, and toxicological principles, the instructor training program became a way to encourage residents to adapt and share safe and healthy poison prevention habits. To further refine the delivery of our messages, we relied on program evaluations, annual surveys, and instructor report forms to keep our material relevant. Since its inception, the training manual has gone through 6 editions; a registration fee of $75 has now been waived, and class length has changed from an 8 h course to a self-paced online course that may take up to 3 h to complete. Today, registrants complete online training modules, quizzes, pre/post-tests, and an evaluation to familiarize themselves with our services and basic poison prevention. Upon completion, certificates are awarded with designated continuing education credits, a "Starter Kit" of materials they can use at their event(s) is supplied, and access to the online "Resource Center" that houses a collection of poison prevention tools and tips for conducting an event is made available.
Results: Our online poison prevention training program launched in 2015. We began expanding our outreach to other poison centers across the country in 2017 who were facing similar challenges as ourselves. As agreed upon between all participating centers, the goal of the partnership is to freely share

poison prevention education and materials, on a non-exclusive basis, by keeping the sites as consistent as possible. Quarterly meetings are held between the 7 educators to discuss adjustments to the content/program. Any additions/changes will be decided and agreed upon by the educators and then implemented on all the training sites.
Conclusions: Outreach education has been limited across our state as well as our partnering poison centers due to geographical barriers and cost. Between the 13 states/territories that have adopted the online training program, we cover a landmass of more than 1.6 million square miles reaching over 73 million people. The online training program has allowed us to use a consistent message to educate more people than previous methods that allotted for far more resources like time and travel. Our hope is that more poison centers will adopt this program and by doing so we will be able to make further improvements and educate more people.

KEYWORDS Education; online; prevention

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233. The "eyes" have it: healthcare provider survey on chemical eye exposures

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Background: Chemical eye exposures comprise a significant portion of calls to poison centers (PCs), and involve a variety of exposure scenarios and acuity levels. The purpose of this survey was to identify gaps between recommendations included in the PC management guideline for chemical eye exposures and trends in real world management of these patients in the emergency departments (EDs) of one state. A secondary objective was to identify educational needs that could be incorporated into the PC written guideline and consultation processes.
Methods: An electronic survey link was distributed by a local chapter of the American College of Emergency Physicians to members ($n = 138$) in one state served by a regional PC. The survey study was approved by the institutional review board of the PC's host institution. The survey questions were designed to mirror aspects of the PC's written guideline for management of chemical eye exposures.
Results: Twenty-one survey responses were received (response rate 15.2%). A majority (52.4%) indicated their ED does not have a written guideline for managing chemical eye exposures. Normal saline was identified as the preferred ocular irrigating solution by 57.9% of respondents, and 100% indicated they would always or sometimes use a Morgan Lens for irrigation. Respondents indicated that they always (79.0%) or sometimes (21.1%) utilize conjunctival pH testing in management of chemical eye exposures. The most important factors influencing their decision to check conjunctival pH were the specific substance involved, its pH (if known), ophthalmologist recommendations, and degree of patient discomfort. A majority indicated that they would test conjunctival pH before and after irrigation. There was considerable variability in the testing range specified by respondents for the pH paper available in their EDs. Although nearly half (46.2%) did not know the range, 53.9% did provide an estimate; of those just one was a narrow range (5–9). When only one eye is affected less than half (35.8%) indicated that they use the pH of the unaffected eye as a control. Phone consultation with an ophthalmologist was reported as an option by 94.4% of respondents, and 63.2% indicated that in-person ED consultation was available at all hours. None of the respondents reported availability of web-based consultation services. 52.6% reported calling the poison center sometimes, usually, or always for consultation on chemical eye exposures, while 47.4% reported rarely or never calling.
Discussion: Although the majority of respondents preferred normal saline for ocular irrigation, the pH of lactated ringers is closer to that of the normal conjunctiva, and considered by some to be more comfortable. However, the practical significance of this distinction is controversial. Variations in respondents' use and timing of conjunctival pH testing, and type of pH paper available to them indicates potential educational opportunities. The primary limitation to this study is the small sample size.
Conclusions: Results of this survey reveal opportunities for education through enhancements to PC's evidence-based management guidelines, consultation processes, and other professional educational activities. This may also increase awareness of the PC as a resource for managing patients with chemical eye exposures.

KEYWORDS Eye; chemical; poison center

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234. The development of medical toxicology specific quality healthcare measures

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Background: Medicare's well-established merit-based incentive payment system (MIPS) is designed to focus on quality health care delivery rather than quantity. As such, the Centers for Medicare and Medicaid Services (CMS) implemented a payment adjustment to promote reporting on quality measures. Yet, no CMS-approved quality measures have been designed for the practicing medical toxicologist. This absence makes quality reporting on medical toxicology measures impossible at a time when participating in such a value based system is increasingly important.
Methods: The American College of Medical Toxicology (ACMT) convened an expert committee of board-certified medical toxicologists. This committee researched, developed, optimized, and revised quality measures specifically designed for medical toxicology. Using the Toxic Investigators Consortium Registry (ToxIC) as a Qualified Clinical Data Registry (QCDR), medical toxicology quality measures were submitted to CMS for formal review.
Results: Nine medical toxicology-designed measures were submitted. Of these, CMS rejected 2, and accepted 7. In addition, CMS requested 2 measures merged into one. Both these measures involved acetaminophen toxicity (see measures 1 and 2). Therefore, 6 total measures were finalized for approval by CMS. See Table.
Conclusion: Six quality measures are now approved by CMS and are currently available for use on the ToxIC QCDR. Quality measure development provides financial stability to the field of medical toxicology, and engages medical toxicologists in quality health care delivery. Participation in the program can facilitate the development of benchmarks and encourage health care providers to improve the quality of toxicologic health care delivery.

Table. Medical toxicology quality measures proposed to the Centers of Medicare and Medicaid Services.

	Tile	Numerator	Denominator	Exclusions	Accepted
1*	Appropriate treatment for acute acetaminophen ingestion	Patients for whom n-acetylcysteine (NAC) was received within 2 h of presentation	Patients of any age with acute single acetaminophen ingestion with a Rumack-Matthew Nomogram result above the treatment line (150 mcg/ml)	Patients with an acute single acetaminophen ingestion occurring less than 4 h or more than 24 h prior to presentation, or patients who did not ingest pills in a single sitting	Y
2*	Appropriate discontinuation of intravenous n-acetylcysteine treatment in patients with acetaminophen poisoning	Patients for whom intravenous (IV) n-acetylcysteine (NAC) treatment was discontinued appropriately	Patients of any age with acetaminophen poisoning receiving IV NAC.	Hepatic failure as defined by hepatic encephalopathy and INR $\geq$ 2	Y
3	Repeat assessment of salicylate concentrations in overdose patients	Patients who received a second plasma salicylate concentration within 4 h following the initial test	Patients of any age with suspected drug overdose with an initial plasma salicylate concentration >15 mg/dl	Patients who died within 4 h of the initial test; Patients who did not experience a drug overdose; patients on hemodialysis within 4 h of initial test.	Y
4	Assessment of suspected ethylene glycol or methanol exposures	Patients for whom the appropriate laboratory testing was completed within 4 h of hospital presentation	Patients of any age with suspected exposure to ethylene glycol or methanol	Serum osmolality and quantitative ethylene glycol/methanol testing not available; unintentional accidental ingestions of ethylene glycol or methanol	Y
5	Screening for risk of opioid misuse/overuse	Patients who were screened for the potential risk of opioid misuse/overuse with a standardized tool (e.g., DAST, ASSIST) or assessed for the presence of any specific risk factors	Patients aged 12 years or older	None	Y
6	Pregnancy test in women who receive a toxicologic consult	Patients who receive a pregnancy test prior to emergency department discharge or within 24 h of hospital admission	Women of childbearing age (12–60 years) who receive a toxicologic consult	Women who have had a hysterectomy or oophorectomy; minor dermal caustic exposure; Woman who are post-menopausal	Y
7	EKG assessment in acute overdoses	Patients who have an EKG QRS and QTC duration assessment within 60 min of arrival to the emergency department	All intentional pharmaceutical overdoses of any age	Patients who present to the emergency department in cardiac arrest; exploratory pediatric ingestions with non-cardiotoxic ingestions	Y
8	Appropriate medical clearance	Patients who are medically cleared within 6 h of hospital presentation	Patients with a pharmaceutical overdose who remain asymptomatic with a normal physical exam, no evidence of vital sign changes, normal mental status, and no abnormal laboratory tests or elevated drug levels for the duration of the 6 h observation period	Patients who are receiving medications with delayed clinical effects	N
9	Occupational and environmental exposure history	Patients who had an occupational and environmental history obtained. The occupational and environmental history must include at least 2 items	Patients of any age seen in an outpatient clinic	Envenomation follow-ups	N

*Measures 1 and 2 were combined into one measure based on CMS recommendations.

KEYWORDS Quality measures; Centers for Medicare and Medicaid Services; Merit-Based Incentive Payment System
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235. Naloxone rescue kits used by participants of a syringe exchange program: is 0.4 mg intramuscular injectable dosing enough?

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Background: Poisoning/overdose is the leading cause of injury death in the United States (U.S.) as well as in this state which has been as high as is 4th in the nation for overdose deaths. Opiate overdoses account for greater than 60% of overdose deaths nationwide. One response strategy that has been implemented in many states and communities has been increased community member access to the opiate antagonist naloxone. Naloxone rescue kits used by non-medical laypersons have been documented to save thousands of lives across the United States. One of the most successful access points for placement of these layperson rescue kits has been in the setting of syringe exchange. With an increased presence of counterfeit fentanyls and fentanyl analogs in our communities, questions have been posed about the dosing of naloxone necessary in rescue kits such as these for community-based naloxone distribution.
Objective: To describe the reported use of intramuscular (IM) injectable naloxone rescue kits (containing 0.4 mg doses of naloxone) within a population of layperson participants in one syringe exchange services (SES) program.
Design/methods: Naloxone rescue kits were provided to participants in SES, each kit containing 2 doses of 0.4 mg naloxone vials and 2 syringes. Participants in SES are able to obtain multiple kits if desired. Participants were trained by SES staff on overdose recognition and naloxone administration. Reversal data, including the number of doses/vials of 0.4 mg naloxone used to achieve a reversal of an opiate overdose, were collected anonymously via self-report to a staff member of the SES. Participants were assigned unique ID codes and data were stripped of identifying information before being given to the research team.
Results: One hundred and fifty-seven individuals reported the use of a naloxone rescue kit over 14-months (February, 17–March, 2018). Kits had been provided to them during SES outreach services by one entity. The reported use was on a friend/acquaintance (68%), family member (10%), self (10%), spouse (2.5%), other (0.5%), and unreported (10%). One dose of naloxone (0.4 mg IM) was used to reverse the overdose 18.5% (29) of the time, two doses 66% (103), 3 doses 10% (15), and 4 doses 0.5% (1). The number of doses used was unknown in 5% (8) of the reports. There were 3 unsuccessful reversals reported during this time period using 2, 3, and 2 vials of naloxone.
Conclusions: Individuals participating in a syringe exchange services program self-reported use of naloxone rescue kits that had been provided to them. The majority of the kits were used on a friend, family member, or were reported used on the participant themselves. Over 86% of the reversals were reported successful with 1 or 2 doses of 0.4 mg IM injectable naloxone. There is no indication from these results that increased doses of naloxone are required or needed in layperson naloxone kits in this community.

KEYWORDS Naloxone; opiate overdose; harm reduction
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236. Characteristics and predictors of severe buprenorphine outcomes reported to the poison centers

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Background: Buprenorphine use has increased dramatically 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 severe outcomes associated with buprenorphine has not been clearly delineated. In the present study, we investigated the characteristics and risk factors of severe buprenorphine exposures reported to the U.S Poison Centers (PCs).
Methods: We retrospectively queried the National Poison Data System (NPDS) for exposures to buprenorphine from 2011 to 2016. Severe buprenorphine exposures (SBE) were defined as exposures that resulted in either a death or major clinical outcomes. Trends in the SBE were tested using Poisson regression with percent changes during the study being reported. Characteristics of exposures were descriptively assessed using the chi-sq test, stratifying them according to the baseline severity of outcomes (SBE versus non-SBE). Logistic regression was used to evaluate the predictors of SBE, with adjusted odds ratios (AOR) and 95% confidence intervals (95% CI) being reported.
Results: The number of buprenorphine exposures reported to the PCs (21,364) increased from 3625 calls in 2011 to 3733 calls in 2016. There were 967 cases of SBE, with these exposures increasing by 66.6% during this period (114–190, $p < 001$). Cases between ages 20 and 49 years (76% versus 53.8%) were more common among the SBE group, whereas the gender distribution was similar among both groups. Intentional abuse (24.9% versus 20%) and suspected suicides (37.5% versus 13.7%) were significantly higher among the SBE group. The majority of the SBE cases were en-route to a healthcare facility when the PC was called (what percentage were?). The proportion of severe outcomes was lower within the southern states (36.4% versus 38.4%), with Michigan (69) demonstrating the highest reported SBE cases during the study period. Multi-substance exposures were significantly higher among the SBE cases (71.4% versus 36.4%). Additional co-occurring opioids were more commonly reported for the SBE cases (20.8% versus 10.7%), with 83% of such co-occurring opioid SBE cases reporting only one additional opioid. The most commonly reported opioids were methadone and hydrocodone while benzodiazepines were the most frequent non-opioid substances in multi-substance exposures. This risk of severe exposures increased with age, with cases between 20 and 39 years (AOR: 1.4, 95% CI: 1.1–1.7), and adults above 60 years (AOR: 1.9, 95% CI: 1.3–2.7) demonstrating significantly increased the odds of such outcomes. Cases of suspected suicide (AOR: 6.3, 95% CI: 4.3–9.1) and abuse (AOR: 1.4, 95% CI: 1.4–2.6) were significantly more likely to result in a SBE. Co-occurring opioid exposures increased the risk of a SBE by 66% (AOR: 1.4, 95% CI: 1.4–1.9). The Midwest region (AOR: 1.2, 95% CI: 1.1–1.4) demonstrated a higher risk of SBE compared to the northeast.
Conclusions: This study reflected an increase in the reported calls to poison centers for SBE. This increase parallels the increase

in the buprenorphine prescriptions. Several key characteristics, including reasons for exposure and presence of co-occurring opioids significantly increased the risk of SBE.

KEYWORDS Buprenorphine; severe outcomes; NPDS

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237. Epidemiology of naloxone administration prior to poison center recommendation

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Background: Opioid misuse is a growing public health challenge, with more than 4% of the adult United States (U.S.) population misusing prescription opioids. As deaths due to opioid overdose have risen, there has been growing momentum to increase public access to naloxone. Poison Centers (PCs) are in a unique position to track the trends of naloxone and the related outcomes. The objective of this study is to evaluate the use of naloxone in patients prior to communication with U.S. poison centers (PCs).
Methods: A retrospective study was conducted utilizing the National Poison Data System (NPDS). All cases where naloxone as therapy was performed prior to recommendation from PCs, also known as not recommended but performed (NRP), from 2000 to 2016 were evaluated. Descriptive statistics were used to analyze the characteristics of naloxone reports made to the PCs. Poisson regression models were used to evaluate the trends in the number and rates of reports, with percent changes during the study period being reported with the 95% confidence intervals (95%CI). Incidence of naloxone reports at the state- and national-level were calculated.
Results: There were 218,861 calls to the PC where naloxone was used as therapy prior to PC recommendation and these calls demonstrated a four-fold increase from 5693 in 2000 to 21,864 in 2016, despite an overall drop in PC calls during the same time period. Exposures mainly occurred at the cases' residence (87.7%). Cases that received naloxone were predominantly between ages 20 and 39 years (40.9%) or 40 and 59 years (36.3%), with teenagers constituting 8.9% of the sample. The proportion of females (52.5%) was higher among cases. Multiple substance exposures accounted for 59.3% of the cases, with the number of substances ranging from 2 to 30. Multiple substance exposures were more commonly seen in older age groups receiving NRP naloxone. In regards to severity, major medical outcomes were seen in 22.7% cases, while the cases fatality rate was 1.5% with 3300 deaths reported during the study period. One-fourth of the intentional abuse cases exhibited major clinical effects. Hydrocodone (14.6%) and oxycodone (13.6%) were the most frequently reported opioid exposures that resulted in NRP naloxone therapy, while benzodiazepines was the most common co-occurring substance. The national incidence of NRP naloxone was 264.3 per 100,000 persons, with West Virginia being the state with the highest reported incidence. During the study period, the frequency of NRP naloxone increased significantly by 284% (95% CI: 272.9%, 295.4%; $p < 001$), while the rate per 100,000 NPDS exposures increased by 271.8% (95% CI: 225.1%, 324.1%; $p < 001$).
Conclusions: There was an increasing trend of naloxone being administered prior to any communication with the PC. Cases demonstrated significant clinical effects with opioids as the most frequently reported exposures and attempted suicide being the most common reason for exposure. Though a potentially important measure to address the current opioid crisis, several challenges exist in expanding access to naloxone, including the appropriateness of use. PCs could play a key role in this process.

KEYWORDS Naloxone; poison control; opioids

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238. Poison centers respond to a state's opioid crisis

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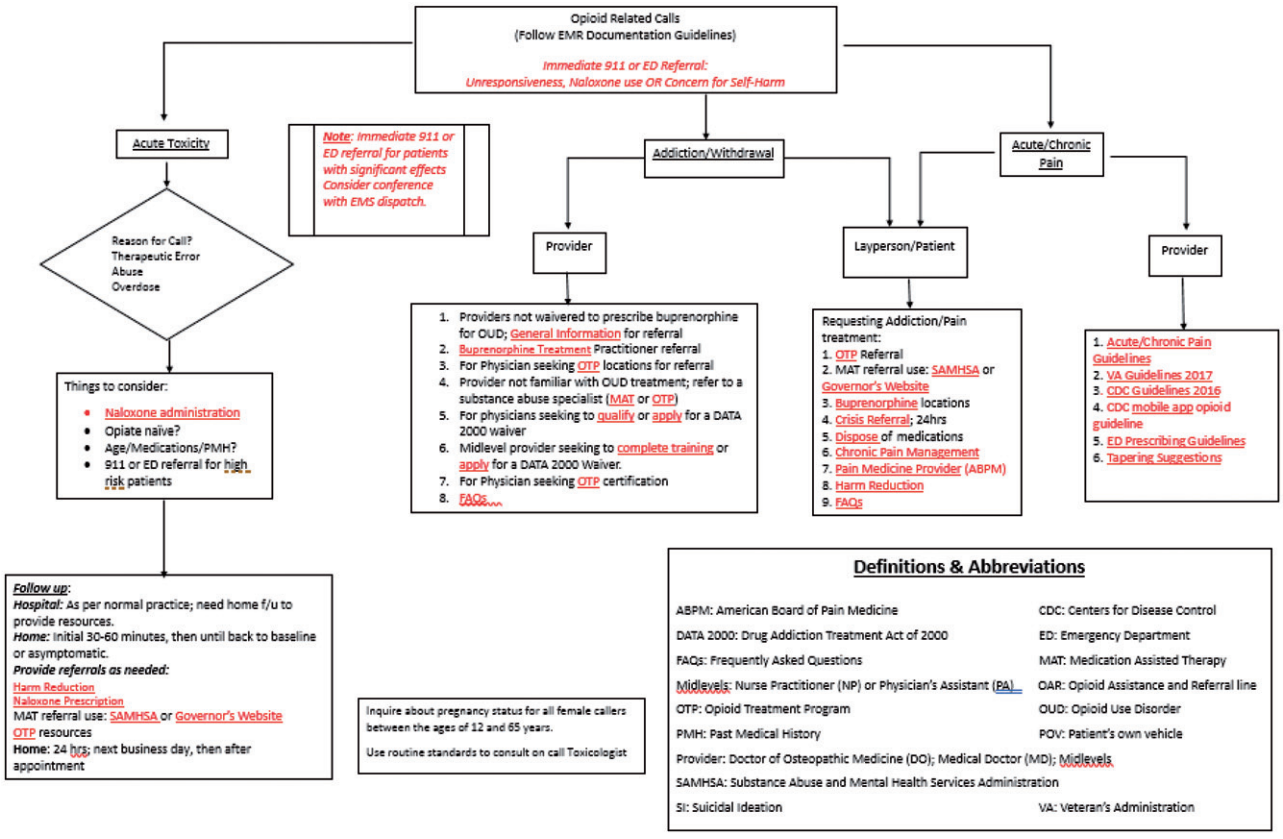
Background: The United States opioid epidemic has caused increased morbidity and mortality, and added to the burdens of health care systems across the nation. Our Poison Control System (PCS) partnered with the Department of Health Services (DHS) and other community health care organizations, to develop the Opioid Assistance and Referral (OAR) Line, as part of a state-wide systematic response to this crisis.
Method: On June 5, 2017, the Governor declared a state of emergency due to the opioid overdose epidemic. Our PCS participated in stakeholder meetings, convened by the Governor's Office and DHS, to help form the state's response to this crisis. The resulting Opioid Action Plan was submitted by the DHS to the Governor's Office on September 5, 2017, with 12 key recommendations. One of these recommendations included the implementation of a 24/7 Opioid Assistance and Referral (OAR) Line. The purpose of this line was to provide clinical guidance to prescribers, as well as management and referrals to the general public, and paralleled existing services and expertise provided by the PCS. Specific PCS directors and staff were identified to review research, develop standard operative procedures (Figure 1), identify community resources, and generate frequently asked questions. A two-part roll out was planned, initially to prescribers and subsequently to the general public.
Results: On February 26, 2018 the OAR Line was initiated, with an advertised Go Live date on March 26, 2018 at 0700. Anticipated calls included: prescribing guidance, managing complex pain and/or opioid use disorder, crisis interventions, naloxone administration and education, substance abuse and behavioral health treatment resources, harm reduction programs, medication assisted treatment, and buprenorphine waivered training.
Conclusions: Poison and Drug Information Centers have a unique opportunity to enhance their roles in the opioid crisis, and other public health projects, by working closely with lawmakers and Health Departments. Further research and data



analysis will be required to evaluate and improve such interventions.

KEYWORDS Opioid; epidemic; assistance

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239. Using the quality assurance process to learn about poison center callers

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Objectives: The objectives of this initiative were to learn more about existing poison center callers and to encourage repeat use by adding data collection and a brief intervention to the standard quality assurance process.

Methods: Between 2016 and 2017, student rotators re-contacted 1762 poison center callers within 24 h to assess their satisfaction and their likelihood of calling again under similar circumstances, i.e. an exposure at home. In addition to these routine questions, each year we added two new questions designed to help us better understand callers' information-seeking behavior. In 2016, callers were asked if this was their first call to poison control, and how they first learned about poison control. In 2017, we asked if callers had sought help anywhere else prior to calling the poison center, and if they preferred speaking to a specialist or interacting via chat/text. Callers were also encouraged at the close of each call to save 1-800-222-1222 into the phone to make calling the poison center again quick and easy.

Results: Overall, 98.7% of callers who completed surveys indicated they were satisfied with their call and 99% indicated they would call again "if necessary." Survey refusal rates were estimated by rotators to be under 10%. 73.2% of callers indicated the subject call was their first call to poison control. The other 26.8% indicated they were a repeat caller. Callers most commonly indicated they "first learned about poison control" online (32.8%), from their doctor or pediatrician (19%), via a product label (9.8%) or from family/friend (9.5%). Other common responses under "other" sources included workplace, nurse/insurance hotline, poison center media (billboard, website, TV), hospital, school or Siri. Nearly 23% of respondents reported they sought help somewhere else before calling the poison center, while 77% of respondents indicated they called the poison center first. Callers expressed an overwhelming preference for speaking directly with a poison specialist (97.6%). Only a tiny percentage preferred text or chat (1.2%), or had no preference (1.2%). All 1762 callers were individually encouraged to save the hotline into their phones and to call again if needed, thus normalizing the use of the poison center. Very few callers (<5%) rejected this suggestion.

Conclusions: The quality assurance follow-up call is an ideal opportunity to collect data and positively reinforce callers' use of the poison center. The results of this study indicate that most callers are first-time callers, that callers obtain information about poison control from multiple sources, primarily the internet, and that poison centers are competing with other sources of health information. These findings have important implications for outreach. First, poison centers must continue to promote themselves through search engine optimization, physicians, and mass media as these channels appear to be effectively generating calls. Second, educators should promote the poison center as a resource for a variety of exposures over a lifetime, as opposed to singular life-or-death emergencies. Finally, this study suggests that any attempt to switch poison center services to being

primarily chat- or text-based would be highly unpopular with existing users.

KEYWORDS Education; caller preferences; quality assurance

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240. Can the intranet be an effective tool for primary and secondary poison prevention?

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Background: As a means of public education, the staff at one regional Poison Control Center (PCC) offers free poison prevention packs to the community. On average, about 50 free packs are distributed monthly to community members who request them. Packs include various education material and are designed to increase primary and secondary poison prevention behaviors. Primary prevention aims to avert a poison exposure; secondary prevention seeks to limit the effect of an exposure by improving access to poison control services. An educational intervention was designed to discover whether offering packs via the intranet would increase the practice of primary and secondary poison prevention.
Methods: Partnering with its host institution during National Poison Prevention Week, the PCC utilized the host institution's intranet to promote poison prevention packs to about 40,000 employees. Packs could be ordered via a click-through banner on the homepage, and the promotion was held over a 4-d period. Employees clicking the banner arrived at a landing page with poison prevention information and a link to order the poison prevention packs of their choice. Individuals could order up to four free packs.
Results: Through the intranet promotion, 1368 poison prevention packs were ordered. The intranet landing page was visited 2841 times, 2753 of which were unique visits. The average time spent on the landing page was four min 21 s, nearly triple the amount of time typically spent on an intranet landing page. Shortly after pack distribution, consumers were emailed a survey measuring their intent to make behavioral changes upon review of the information. One hundred nine respondents participated in the survey: 55% said they were planning on taking steps to prevent or mitigate a poisoning, 36% were unsure if they would take additional steps, and 9% reported they would not take any additional steps. For those planning to make changes, the most often sited behavior modifications included storing chemicals/medicines out of reach (24%), taking medicines more safely (20%), knowing more about plant and snake hazards (17%), and talking to someone else about poison prevention (17%).
Conclusions: The intranet campaign provided an opportunity to reach a large population in a short amount of time. Additionally, over half of survey respondents reported that they were likely to make behavioral changes that could either prevent a poison exposure from occurring or minimize the effect of an exposure. Challenges to implementing the intervention may include locating the appropriate people within the host institution to approve intranet placement and ensuring that enough education material is available to accommodate the spike in volume. Overall, the intranet can be a valuable means of educational delivery and can increase primary and secondary poison prevention awareness.

Pack type	Number of packs ordered	Hits to store page
Parent pack	460	1432
Snake pack	322	995
Senior pack	238	661
Babysitter pack	173	646
Teen pack	158	589
Spanish pack	17	59

KEYWORDS Poison prevention; public education; intranet outreach

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241. Severe delirium and bradycardia associated with a synthetic cannabinoid outbreak

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Background: Synthetic cannabinoids (SC) have risen in number & availability with recreational use expanding in the US over the past decade. SC are often sold as "potpourri" or "herbal incense" "not for human consumption". Numerous "brands" of SC have been detected in illicit use. Outbreaks of delirium, illness & death associated with SC use have been reported. Morbidity may be expected to increase as labs produce new SC in attempts to circumvent regulation. Accordingly, SC pose a significant & growing public health threat. We report severe SC effects that heralded an apparent outbreak in our community.
Case reports: Two patients with similar symptoms arrived in our ED via EMS. The first was obtunded, became combative after receiving naloxone from EMS, & was sedated with midazolam. Upon clearing, the second stated they both had used methadone & smoked SC. He provided a sample of the SC material. A third patient used the SC, was transported to a neighboring hospital & had delayed onset of a bradycardic event. On arrival patient 1, a 43-years-old male, had markedly altered mental status & slightly asymmetrical pupils with a stable airway. He became bradycardic (HR 40), was given 2 mg of naloxone with minimal response, had a 12 s cardiac pause & responded to atropine 1 mg IV. He then required intubation. Upon transfer to the ICU he became hypotensive (MAP 60s) & responded to a 1 L LR bolus. He stabilized, improved & was d/c on day 4 on methadone maintenance. Patient 2, a 49-years-old male was found unresponsive by EMS & arrived with agitated delirium unable to follow commands. HR 50 resolved after atropine 0.5 mg atropine IV and 1L NS. Mental status cleared after naloxone 1 mg IV. The patient stated that he & his friend had smoked a new brand of "K2." He left the hospital against medical advice.
Discussion: Reported effects of SC include excited delirium, psychosis, seizures, coma, acute kidney injury, cardiotoxic effects, & death. Inability of common immunoassay drug screens to detect SC may obfuscate diagnosis of affected patients. The sample submitted was confirmed by the U.S. DEA Lab as "Synthetic Cannabinoid ADB Fubinaca," a Schedule 1 Controlled Substance. Cooperation between patients, emergency physicians & law enforcement has resulted in rapid intervention & harm reduction in similar outbreaks. A flurry of patients with delirium & similar clinical effects was noted in our area over several days, then subsided, perhaps facilitated by targeted law enforcement efforts & increased awareness of dangerous SC in the community.
Conclusion: Unlike naturally occurring cannabinoids often regarded by clinicians as relatively benign, use of SC use has been associated with morbidity & mortality. Users of SC and clinicians are often unaware of the severe and potentially lethal

effects of SC and appropriate treatment. Detection of novel SC in the community may facilitate DEA scheduling, limit sources and use of SC. Education targeted toward clinicians may increase awareness of these potentially potent agents, encourage reporting & facilitate successful treatment of affected patients.

KEYWORDS Synthetic cannabinoid; public health; ADB Fubinaca

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242. "Thinking (2700 miles) outside of the box"

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Background: Our poison center (PC) is one of the busiest in the country, handling over 72,000 human exposure calls on an annual basis. We are fortunate to have a highly engaged workforce that is willing to go above the normal call of duty. We also have leadership that strongly encourages staff, both clinical and non-clinical, to participate in other activities outside of the normal day-to-day call center routines. In particular, our PC strongly encourages staff to participate in a wide variety of NAACT related activities, which allows them to share interesting cases and research on a wide variety of clinical toxicology topics and issues. In 2017, this PC had over a third of its SPI staff have abstracts accepted for the upcoming annual NACCT meeting. This created a unique dilemma for the executive team. How do we reward our SPI staff for their accepted abstracts and not disrupt the delivery of services we provide to the community we serve? The solution was simple. Setup a PC 2700 miles away in Vancouver, B.C. with SPIs agreeing to work shifts and present accepted work without sacrificing our call center business.
Methods: With the approval of the leaders of the AAPCC and AACT, meeting organizers, the cooperative efforts of our telecom partner CNP Technologies, and guidance from our Health System's Legal department, we embarked on a plan to set up and bring up a remote PC on foreign soil. To do this effectively, we first had to upgrade our automatic call-distribution software to an entirely new web-based platform. We then faced the daunting challenge of training staff on the new telecom features in the four weeks leading up to the NACCT meeting. We then purchased and configured laptop computers and monitors. We developed plans to create a virtual private network utilizing a 100 mbps internet line that basically connected our remote center back to our home base. We negotiated on a location where we would configure and set-up our remote site. Finally, we secured furniture and acoustic paneling to provide ourselves with as much privacy as was possibly. We solved our biggest problem of how this was all going to be paid for by getting CNP Technologies to underwrite over 95% of the costs.
Results/conclusions: With assistance from one of our own IT specialists who was flown in specifically to turn this vision into reality, we were able to fully configure 3 functional work stations within a 2-h period. SPIs attending the meeting were able to present their abstracts, work pre-determined shifts, and partake in many conference activities with no disruption in call center activities. This PC was able to reward staff who got abstracts accepted with an all-expense paid trip to the NACCT meeting and keep the PC running at full capacity. By creating a remote center 2700 miles away, it also allowed the PC to test a major component of its disaster recovery plan. We were able turn pages of this plan into a real world working application.

KEYWORDS Teleworking; disaster recovery; partnerships

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243. Drain cleaners: are non-professional users aware of the health risks?

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Background: In 2017, the Dutch Poisons Information Center (DPIC) was consulted 170 times about human exposure to drain cleaners. As these exposures can result in serious health effects, information about the circumstances of exposure is valuable for developing preventive measures. The DPIC participated in a follow-up study of the International Association for Soaps, Detergents and Maintenance Products (A.I.S.E), studying these circumstances.
Methods: From November 2017 onwards, human exposures to drain cleaners were investigated. Follow-up (telephone interview using a standardized questionnaire) was performed in accidental exposures in which the patient, or parent in case of children <16 years, granted permission. If no follow-up was possible, data from the initial contact with the physician was used. The study protocol was approved by the medical ethical committee.
Results: In the first four months of the study period the DPIC received 72 information requests concerning accidental exposure to drain cleaners. Eight cases were excluded (minimal information, no consent, doubtful exposure). Most exposures involved adults (54/64), and 10 incidents involved children up to 4 years. Skin contact was the predominant route of exposure, either as the only route of exposure (39%) or as part of a combination of several routes of exposure (56%). Oral exposure was reported in a total of 19 cases (15 oral exposures and 4 multiple routes of exposure), including 7 children. Symptoms occurred in 57 out of 64 (89%) patients. Minor symptoms (such as skin, eye or mucous membrane irritation) were reported in 47 patients and moderate symptoms (such as chemical burns, erosion or ulceration of the mucous membranes) in 10 cases. Most incidents were directly related to product use (78%) and involved the person handling the product (35 cases) or the person working on the drain after application of the drain cleaner (7 cases). Three times a bystander was exposed. The main causes of work-related exposure were physical unblocking of the drain after application of the product (12 cases) and spilling or splashing while preparing or using the product (10 cases). When using the product or unblocking the drain afterwards, only 7 patients wore gloves (light duty) and none used protective glasses. Eight exposures (one adult and 7 children) occurred at the moment the product was ready to use or not yet stored away. The adult was exposed because of a falling bottle. The children grabbed the drain cleaner in an unguarded moment. Four adults mistook drain cleaner for a drink.
Conclusions: Accidental exposures to drain cleaners often occur during (due to spilling or splashing) or directly after product use while working on the drain (during physical unblocking). Despite the product labelling as a corrosive substance, most users do not use protective equipment, such as gloves or glasses. As a commonly used product, general consumer awareness of the possible health risks of drain cleaners is low. Better information on the packaging might raise awareness about the potential health risks and contribute to a reduction in the number of exposures.

KEYWORDS Drain cleaner; accidental exposure; prevention

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244. Analytical testing of blood specimens in patients presenting after near-fatal overdose

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Background/Objectives: The prevalence of clandestine opioids within the illicit drug market is thought to be driving significant increases in non-fatal and fatal opioid overdoses. Little is known about the incidence, identity, and clinical impact of these substances in near-fatal overdose, and individuals are often unaware of their presence. Additionally, traditional analytical instrumentation used in clinical settings is often unable to detect novel clandestine opioids. To better elucidate causes of near-fatal overdose in our patient population, we obtained rigorous analytical testing on blood specimens obtained from patients presenting for acute care of suspected opioid overdose.
Methods: Adults presenting to an urban, tertiary care emergency department (ED) after a reported opioid overdose were eligible for enrollment if they had received naloxone. Verbal consent was obtained either pre-or post-specimen collection, based on mental status, with collections performed at the time of clinically-related blood draws only. Samples were stored at −80 °C until shipped on dry ice to a research laboratory, where they were analyzed using Liquid Chromatography Quadrupole Time-of-Flight Mass Spectrometry (LC-QTOF-MS).
Results: We obtained 16 blood specimens at the time of ED presentation (median time from triage to specimen acquisition 42 min). Demographics are listed in Table 1. Of the 16 study participants, only four patients had any heroin metabolite identified. Sixteen of the 16 patients tested positive for fentanyl, with only six patients positive for norfentanyl. Acetylfentanyl was found in two specimens; carfentanil was identified in one (see Table 2). Cocaine itself was present in six specimens. The doses of required naloxone are detailed in Table 3. The highest dose of naloxone (10 mg total – 4 mg intranasal, 2 mg intramuscular, and 4 mg intravenous) was administered to a patient who tested positive for carfentanil and heroin metabolites. Of note, three of the patients in this cohort reported intended use of pharmaceuticals (e.g., Percocet®, Suboxone®, and a "sleeping pill'). These individuals reported oral use ($N = 2$), and intranasal use ($N = 1$).
Conclusions: In our previous work studying urine specimens after opioid overdose, we found nearly universal exposure to fentanyl. However, we could not confirm that fentanyl was a culprit agent. While we are awaiting quantitation in the blood specimens, the role of fentanyl in causing near-fatal overdose in our population is undeniable. Moreover, we are increasingly finding evidence of fentanyl exposure through counterfeit pharmaceuticals, with oral ingestion as the ultimate route in two patients described here.

Pack Type	Number of Packs Ordered	Hits to Store Page
Parent Pack	460	1432
Snake Pack	322	995
Senior Pack	238	661
Babysitter Pack	173	646
Teen Pack	158	589
Spanish Pack	17	59

KEYWORDS Opioid; overdose; LC-QTOF-MS

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245. Crushing counterfeits: deaths due to illicit and inadvertent use of potent opiate analogues

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Background: Amidst the roaring crescendo of the American opiate epidemic, abuse of progressively potent opiates is trending through the nation. Fentanyl and its analogues increasingly account for opioid-related deaths due to their high potency. As the tides of law enforcement begin to sweep control over commonplace opiates, novel agents and counterfeit compounds have cropped up to meet street demand; these novel formulations are sold to illicit users, who are generally unaware of these formulary variations. Furanylfentanyl is one such drug, which mimics the extremely potent fentanyl, belonging to the class of novel psychoactive substances. U-47700 is a second synthetic agent, belonging to the class of benzamides. These agents are extremely potent, generally requiring four times the usual dose of Narcan for reversal. We report three deaths, two with confirmed exposure to furanylfentanyl and U-47700, and one with confirmed exposure to furanylfentanyl, U-47700 and acetylfentanyl. These cases present a timely illustration and definitive evidence of the dramatic and hidden toxicity of these novel formulations. These cases have exciting implications to toxicological exposure management, law enforcement, and national health.
Case reports: The first case is a 24-year-old male found unresponsive and non-resuscitatable after snorting what appeared to be Percocet®. Chemical analysis of tablets and drug paraphernalia obtained from the scene tested positive for furanylfentanyl, U-47700, cocaine, and alprazolam. No autopsy was performed, but postmortem blood testing revealed furanylfentanyl (2.8 ng/ml), U-47700 (76 ng/ml), benzoylecgonine, alprazolam, THC, and Gabapentin. The second case is a 20-year-old male with a history of substance, found unresponsive in full rigor. Evidence from the scene suggests the subject snorted pills appearing to be oxycodone. These counterfeit pills tested positive for furanylfentanyl, U-47700, and acetylfentanyl. Postmortem blood testing resulted positive for furanylfentanyl, U-47700, and acetylfentanyl. The third case is a 21-year-old female with substance use disorder (SUD) found on the bathroom floor by her boyfriend after snorting what appeared to be oxycodone. She was intubated and attempts to resuscitate her were unsuccessful. Drug paraphernalia seized by police was subjected to DEA chemical analysis, which resulted positive for furanylfentanyl and U-47700. Postmortem peripheral blood testing resulted positive for furanylfentanyl and U-47700. The cause of death was determined to be opioid toxicity in all three cases.
Discussion: As opioid-involved deaths continue to increase in the United States, fentanyl, its analogues, and other synthetic opioids have both overtly and surreptitiously seeped into the illicit drug market. Due to the greater potency of these synthetic opioids, the risk of respiratory depression and death is higher than with more common opioids, and treatment of overdose requires much higher doses of reversal agents.
Conclusion: We report three opiod-induced deaths from counterfeit pills with scene and postmortem confirmation of synthetic

opioids. Clearly, furanylfentanyl, acetylfentanyl, and U-47700 are novel but increasingly pervasive synthetic opioids that are of great public concern, with a higher risk of respiratory depression and death. These considerations have important implications to EMS and emergency personnel, law enforcement, and public health and safety.

KEYWORDS Counterfeit; opiod; overdose

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246. The Arsenic Herbicide Debacle

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Background: A herbicide from the golf course where Dad works was brought home to use on the yard. His 3-year-old son drank from the herbicide bottle which contained Monosodium Methyl Arsonate (MSMA) elemental Arsenic (22.30%).
Case report: Dad called the poison center and the child was referred to a Health Care Facility. Forty minutes after ingestion, the child vomited eight to ten times. CBC and CMP were normal. An Abdominal radiograph revealed radiopaque fluid in the stomach. The blood Arsenic concentration was 369 μg/l. BAL (37.25 mg) IM was administered and the child was transferred to a pediatric hospital. Vital signs were 96/70 mmHg, HR 115 bpm, RR 20, temp 97.1 . BAL administration was repeated. EKG was normal. The treating physician called and spoke with our Medical toxicologist who advised obtaining a spot urine and switch treatment to Succimer. A 24-h urine was also collected in an Acid washed container and fractionated into organic and inorganic arsenic. The next day the child was doing well taking oral Succimer. The spot urine revealed >1000 μg/l. Inorganic arsenic concentration was 560 μg/l. Chelation was continued and labs were periodically checked. A repeat spot urine 3 d later revealed Arsenic 276 μg/l. The 19 d course of Succimer was completed and two weeks post chelation labs (CBC and CMP) remained WNL and repeat Arsenic blood concentration 8 μg/l (normal range 2–23 μg/l). A repeat 24-h urine was not available due to sample error.
Case discussion: Arsenic is well absorbed after ingestion. Diagnosis is based on the history of ingestion and symptoms. Acute arsenic poisoning causes significant nausea, vomiting and watery diarrhea. Hypotension and metabolic acidosis can ensue. QT may be prolonged. Some arsenic compounds are radiopaque and can be seen on X-ray. In the first few hours and days the urine arsenic concentration can exceed 1000 mcg/l. (Normal organic arsenic concentration is <50 mcg/l.) Blood levels may be elevated initially but quickly return to normal range as arsenic distributes into the tissues. CBC and CMP should be followed since Succimer can cause bone marrow depression and transaminitis. Chelation should not be delayed while awaiting arsenic concentration. Dimercaprol (BAL) is a peanut oil-based product so peanut allergies should be questioned prior to administration. BAL is given at 3–5 mg/kg every 4–6 h and the injection is extremely painful. If the patient is able to take oral supplements Succimer (DMSA) can be considered because it is extensively bound to protein and protects against the toxic effects of arsenic.
Conclusion: Arsenic is well absorbed after ingestion and can quickly lead to life threatening toxicity. BAL distributes to the tissues forming complexes that increase excretion of arsenic in the urine however, BAL increases distribution of arsenic to the brain. Succimer has a higher therapeutic index and does not redistribute arsenic to the brain. Chelation was administered without delay resulting in a favorable outcome for this patient.

KEYWORDS Arsenic; BAL (Dimercaprol); succimer (DMSA)

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247. Intentional single ingestion cyclobenzaprine trends in pediatric patients

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Background: Cyclobenzaprine is a popular muscle relaxer prescribed primarily for the relief of musculoskeletal pain. Reported poisoning may result in both central nervous system effects (obtundation, hallucinations, lethargy, confusion) and cardiovascular toxicity (tachycardia, dysrhythmias, QRS widening). The aim of this study is to report trends in pediatric patients associated with intentional single ingestion cyclobenzaprine over a 16 year period from one regional poison center (RPC).
Methods: Electronic RPC records coded for cyclobenzaprine (January 1, 2002–December 31, 2017; single ingestion; intentional; age 6 to 19 years) were queried. Numbers and trends were compared for 1) total cases; 2) intubations; 3) tachycardia (>120 BPM); 4) QRS >120 ms; and 5) mortality.
Results: A total of 504 cyclobenzaprine cases in patients aged 6–19 years were reported to the RPC during the study period. There were 188 intentional single ingestion (mean; 16-years-old) cases meeting inclusion criteria. A consistent upward trend in cases reported per year occurred over time revealing a 360% increase between 2002 (5 cases) and 2017 (23 cases). Only 4 patients required intubation during the study period. Tachycardia (range; 50–173) was present in only 18% of cases and QRS widening was nonexistent. All patients were discharged in good health and no deaths were reported.
Conclusions: Intentional single ingestion cyclobenzaprine pediatric cases reported to this RPC have increased noticeably. Potential reasons for this are speculative and require further study. In this series, single ingestion cyclobenzaprine cases remained benign for the most part and resulted in only a few serious effects and no mortalities.

KEYWORDS Cyclobenzaprine; pediatrics; trends

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248. Hepatotoxicity in a child following an accidental overdose of liquid acetaminophen

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Background: Accidental paediatric liquid acetaminophen exposures are common due to its availability. Most children ingest

less than a toxic dose of 200 mg/kg and treatment with acetylcysteine and hepatotoxicity are rarely required. Children aged between 1 and 5 years are thought to be less susceptible to acetaminophen-induced hepatotoxicity than adults and older children. We present a case of an accidental liquid acetaminophen overdose in a child who developed hepatotoxicity despite having an initial acetaminophen concentration below the treatment nomogram line (150 mg/l at 4 h).

Case Summary: A 3-year-old (15.4 kg) girl presented 1 h post-accidental ingestion of up to 150 ml of 24 mg/ml liquid acetaminophen, equating to 3.6 g (240 mg/kg). She had been unwell with vomiting, mild rhinorrhoea and low-grade fever for 4 d prior to presentation. She had no diarrhoea or abdominal pain prior to her presentation and had been administered only one dose of acetaminophen (9.6 mg/kg) 2 d earlier. She was otherwise well and examined normally. As per national consensus guidelines an acetaminophen plasma concentration was measured 2 h post ingestion and was 105 mg/l. Because the 2 h acetaminophen plasma concentration was less than 150 mg/l, no further treatment was required as per guidelines. However, a repeat acetaminophen plasma concentration at 4 h post-ingestion was 97 mg/l there was mild liver injury with ALT 52 U/l (RR: < 30 U/l) and AST 60 U/l (RR: < 30 U/l). She was admitted for observation and repeat ALT and AST at 17 h post ingestion had risen to 219 U/l and 217 U/l respectively. After consultation with the local Poisons Information Centre she was commenced on standard intravenous acetylcysteine at 25 h post-ingestion. Her ALT continued to rise and peaked at 1393 U/l 5 d post-ingestion, with a peak INR of 1.5 at 44 h post-ingestion. Acetylcysteine was continued for 64 h in total. She made an uneventful recovery and her ALT had returned to normal on review a month later.

Discussion: We present a case of hepatotoxicity in a child following liquid acetaminophen ingestion which is uncommon, and this occurred despite the acetaminophen plasma concentration being below the 150 mg/l threshold at 4 h on the nomogram line. Pharmacokinetic modelling estimates that <5% of children under 6-years-old with acetaminophen concentrations above the nomogram treatment line are at risk of only transient hepatic abnormalities, hence this case is notable. It could be hypothesised that that her intercurrent illness may have made her more susceptible to a hepatic injury, because of poor oral intake resulting in glutathione depletion.

KEYWORDS Paediatric; acetaminophen; hepatotoxicity

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249. Tragic "Tryp": confirmed fatal N,N-dipropyltryptamine (DPT) exposure in a teenager

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Background: Tryptamines are a class of compounds including serotonin, psilocybin, and N,N-dimethyltryptamine with substituted monoamine groups. Fatalities related to tryptamines are associated with intense sympathomimetic effects and/or severe serotonin toxicity. Less is known about the pharmacokinetic properties and clinical manifestations of synthetic tryptamines such as N,N-dipropyltryptamine (DPT). We report a case of confirmed DPT use leading to brain death in a teenager.

Case report: A 17-year-old boy was found down outside 12 h after he was reported missing. A friend reported both had insufflated "DPT." The patient was found shaking in apparent convulsions near a watery marsh. He was moved to solid ground, but when EMS providers arrived he was pulseless and apneic. Pupils were 5 mm and reactive, extremities were cool, skin was cyanotic. GCS was 3; blood glucose was 300 mg/dl. Naloxone (2 mg IV) resulted in no response. He was intubated prehospital. Cardiopulmonary resuscitation (30 min) and 4 mg of epinephrine resulted in return of spontaneous circulation (ROSC). Post-ROSC vital signs included blood pressure 119/52 mmHg, pulse 112 beats/min, and temperature of 35 °C. EKG revealed a QRS duration of 116 msec; 7 ampules (50 mEq/ampule) of bicarbonate were given with minimal response. On hospital arrival he made no purposeful movements without sedation. Initial labs were as follows: venous pH 7.26, serum bicarbonate 14 mEq/l, creatinine 1.86 mg/dl, troponin I 0.213 mcg/l, lactate 6.5 mmol/l, and creatinine kinase 3310 IU/l (peak 16,020 IU/l). Brain imaging was concerning for global hypoxic injury; therapeutic hypothermia was performed. The following morning he developed hypertension, anisocoria, and non-reactive pupils. Cerebral edema was confirmed by brain imaging. Neurosurgery placed a ventriculostomy but intracranial pressures rose despite aggressive management with mannitol and hypertonic saline. He was subsequently declared brain dead on hospital day 3. His urine drug screen by mass spectrometry done by the medical examiner laboratory was negative for all basic and neutral drugs in the reference catalog. Drug paraphernalia from the scene was confiscated by law enforcement and tested positive only for DPT. Local media reported this product was purchased for $400 online and shipped from China.

Case discussion: In the years preceding this case, 1–2 deaths per year due to tryptamines were reported to the National Poison Data System. Synthetic tryptamines are part of the epidemic of novel psychoactive substances sold online as "legal highs." This patient developed seizures, cardiopulmonary arrest, and evidence of early hypoxic-ischemic injury with multi-organ injury. It is unknown if seizures were due to anoxia or direct effects of DPT. Complete autopsy results were not available, however direct contact with law enforcement indicated this death was not attributable to drowning and was in fact due to direct drug intoxication.

Conclusion: N,N-dipropyltryptamine (DPT) is a potentially lethal drug easily purchased online. Parents, law enforcement, and poison educators should continue to warn the adolescent community about the risk of so called "legal highs."

KEYWORDS Tryptamines; pediatric; fatality

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250. Six-year analysis of accidental liquid laundry detergent pack ingestions treated in a healthcare facility

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Background: US Poison Centers (PCs) frequently respond to accidental childhood ingestions involving Single Use Liquid Laundry Detergent Packs (LLDP). Previous case series have demonstrated that the majority of ingestions reported to PCs do not result in

serious injury, however a significant proportion (>40%) are managed in a healthcare facility (HCF). We sought to further analyze exposure management trends among patients evaluated in a HCF using data from an ongoing, multi-center, prospective study.
Methods: This is a trend analysis of accidental LLDP ingestions involving children (age <6 years) evaluated in a HCF setting from 2012 to 2017, as reported to 12 US poison centers (PCs) participating in the prospective study (serving 24% of US population). The PC exposure narrative was obtained to verify the accuracy of coded data (patient demographics, clinical effects, therapies, level of care provided, medical outcome) and to extract information pertaining to diagnostic procedures performed within the HCF setting (e.g. endoscopy, chest x-ray, etc.).
Results: During the 6-year period (2012–2017), PC study sites reported 13,453 childhood ingestions (age <6 years), of which 37.5% ($N = 5046$) were managed in a HCF and 92.2% involved children <=3-years-old. The proportion of patients evaluated in an HCF declined from 41.9% (2012) to 28.7% (2017), corresponding with a reduction in the number of PC patient referrals. Among patients who could be followed to a known medical outcome and confirmed HCF disposition ($N = 4473$, 88.6%), the proportion of patients 'treated and released' after a brief observation period increased from 2012 (83.7%) to 2017 (92.4%). This increase corresponded with a 76.8% decline in the percent of patients admitted to an intensive care unit (ICU) from 2012 (8.6%) to 2017 (2.0%), and a 27.7% decline in non-ICU admissions (7.7% to 5.6%, respectively). Additionally, the percent of patients with a moderate/major effect outcome decreased by 71% from 2012 (18.5%) to 2017 (5.4%), and was most notable among patients who were treated and released (9.8% to 1.9%, respectively). The proportion of patients with a 'No effect' outcome was significantly higher for patients who were brought to a HCF without consulting a PC (16.3%, $N = 468$) versus patients who were referred by the PC (3.29%, $N = 55$); however, the proportion of patients with a minor effect outcome was similar (91.8% versus 85.5%, respectively).
Conclusion: During the period of analysis (2012–1017), the proportion of childhood LLDP ingestions managed in a HCF declined, and the vast majority of patients did not develop symptoms requiring emergency medical care support. Additional efforts are needed to establish a PC consensus triage guideline to reduce unnecessary referrals and to improve PC consultation prior to seeking care in a HCF.

KEYWORDS Laundry detergent pack; unintentional exposure; healthcare facility

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251. Analysis of childhood exposure reporting rates involving liquid laundry detergent packs in the U.S. (2012–2017)

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Background: Following the widespread introduction of Single Use Liquid Laundry Detergent Packs (LLDPs) in the US (early 2012), a prospective observational study was initiated among 12 US poison centers (PCs) serving 24% of the total US population. Soon after introduction, LLDP manufacturers began to implement exposure reduction strategies, which were used to finalize a new ASTM safety standard addressing LLDP product, packaging, and labeling requirements (ASTM F3159). This new standard was broadly adopted by the major LLDP manufacturers and transitioned throughout 2016. This is a 6-year trend analysis (2012–2017) of childhood exposure reporting rates using data from the ongoing, prospective study to evaluate the impact of accidental exposure reduction strategies.
Method: LLDP exposures involving children (age <= 5 years) reported to the 12 PC study sites between 2012 and 2017 were extracted from the study database. The case narrative was reviewed to verify medical outcome, clinical course, and key situational and product characteristics. Multi-route exposures were assigned a 'primary route' based on the patient's clinical presentation and exposure history. Coding discrepancies were reconciled with the contributing PC. Trend and comparative analyses were performed on absolute case counts, relative proportions, and exposure reporting rates, which were normalized using Nielsen consumption data as a surrogate for household availability and expressed as 'exposures per million units purchased' (EMU). To more accurately reflect reporting rates for the entire US population, reporting rates were adjusted by a factor of 4.
Results: During the period of analysis (2012–2017), 16,837 LLD Pack childhood exposures were reported and the primary route of exposure was ingestion (79.9%), followed by ocular (16.6%), and dermal (3.5%). The total case count increased from 2012 ($N = 1824$) to 2014 ($N = 2982$), stabilized between 2015 ($N = 3155$) and 2016 ($N = 3190$), and declined in 2017 ($N = 2678$); however, normalized exposure reporting rates declined annually (56% overall) from 2012 (4.25 EMU) to 2017 (1.86 EMU). The exposure reporting rate for ingestion cases with a moderate/major effect outcome (serious cases) declined 92% from 2012 (0.239 EMU) to 2017 (0.018 EMU). During the first four years (2012–2015), the proportion of serious cases was 3-fold higher for ingestions involving a single-compartment LLDPs (10.6%) versus multi-compartment LLDPs (3.7%); however, this finding was not present for ingestions reported after 2016 (1.2% for all products). The exposure reporting rate for ocular cases with a moderate/major outcome declined 61% from 2012 (0.160 EMU) to 2017 (0.061 EMU), with no observed difference in the proportion of cases involving single versus multi-compartment LLDPs.
Conclusion: Accidental childhood LLDP exposures declined in frequency and severity over the 6-year period evaluated, suggesting that exposure reduction strategies are having an impact. Ongoing, collaborative efforts to further reduce and sustain lower rates of accidental exposure are needed.

KEYWORDS Laundry detergent packs; unintentional exposures; exposure reduction strategies

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252. Characterizing essential oil ingestions in children less than 7-years-old

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Introduction: According to the American Association of Poison Control Centers Annual Report, essential oils were listed as one of the Top 25 Pediatric exposures in children under 5 years of age. In 2015, there were 11,657 exposures, 11,044 of which were single substance exposures.1 Essential oils are widely available and able to produce numerous toxic effects. In severe cases, children may suffer severe toxicity such as central nervous system depression, seizures, respiratory compromise and even death.2

Home management of essential oil exposures in young children has not been previously reviewed. The primary objective of this study was to characterize the frequency and timing of phone call follow-up for pediatric patients with essential oils ingestions by Specialists in Poison Information (SPIs) at our poison center (PC).
Methods: A retrospective chart review of the Toxicall database at our PC was performed. Inclusion criteria were essential oil exposure calls involving children less than 7 years from private residence 2015 to 2016. Variables of were collected and descriptive statistics were performed. The study protocol was submitted to the IRB and deemed to be exempt from full review.
Results: In 2015–2016, 162 calls were received involving ingestion of essential oil products in children under the age of 7. Of 162 calls, 4 calls involved more than one oil. Specifically, 83 cases were defined under the general term of "essential oils," 42 cases of melaleuca oil, 21 camphor, 8 eucalyptus oil, 2 lavender, 2 lemon, and one case each of clove, frankincense, peppermint, and wintergreen. All cases involved oral ingestion as the primary or sole route of exposure. Sixty cases (37%) involved a single lick or taste. Four cases (0.025%) required immediate referral to a health care facility. More cases involved females ($n = 93$, 57%) compared to males ($n = 69$, 43%). The most common age of children that ingested essential oils was age 2 years ($n = 69$, 60.5%), followed by 3 years ($n = 35$, 21.6%), 4 and 5 years (both $n = 9$, 5.6%), less than 12 months ($n = 7$, 4.3%) and 6 years ($n = 4$, 2.5%). No ingestions were reported in children aged 13–23 months. Of home-managed cases not immediately referred to a health care facility, 61.4% ($n = 97$) of calls received a follow up call. 54.4% ($n = 86$) of all home-managed cases received a follow up call in the first 6.5 h. Of these, 57% ($n = 49$) were called in the first 3 h, 15.1% ($n = 13$) between 3 and 5 h, and 28% ($n = 24$) were contacted after 5–6.5 h. An additional 11 cases were contacted more than 6.5 h later. Of 158 home managed cases, one case was identified as being referred to a health care facility on call back, representing less than 1% of home managed cases.
Conclusion: In this retrospective review of essential oil ingestion cases in young children called into our poison center, phone call follow up calls were made at variable time frames. The vast majority of cases were managed at home. Management was very rarely changed due to follow-up calls.

KEYWORDS Essential oil ingestions; pediatrics; follow up

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253. Exposure to topical drugs used in pediatric dermatology in children age 0–12 years: descriptive analysis of calls to United States Poison Controls Centers from 2000 to 2014

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	Topical Beta Blockers		Topical Steroids		Vitamin D Analogs		Tacrolimus, Pimecroli		Topical Lidocaine		Topical Minoxidil	
	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous
No Effect	19	0	12219	248	52	8	1012	22	138	11	428	8
Minor Effe	2	0	1079	77	3	2	70	31	12	4	42	2
Moderate	1	0	28	11	0	1	4	3	0	12	17	0
Major Effe	1	0	0	0	0	0	0	0	0	5	0	0

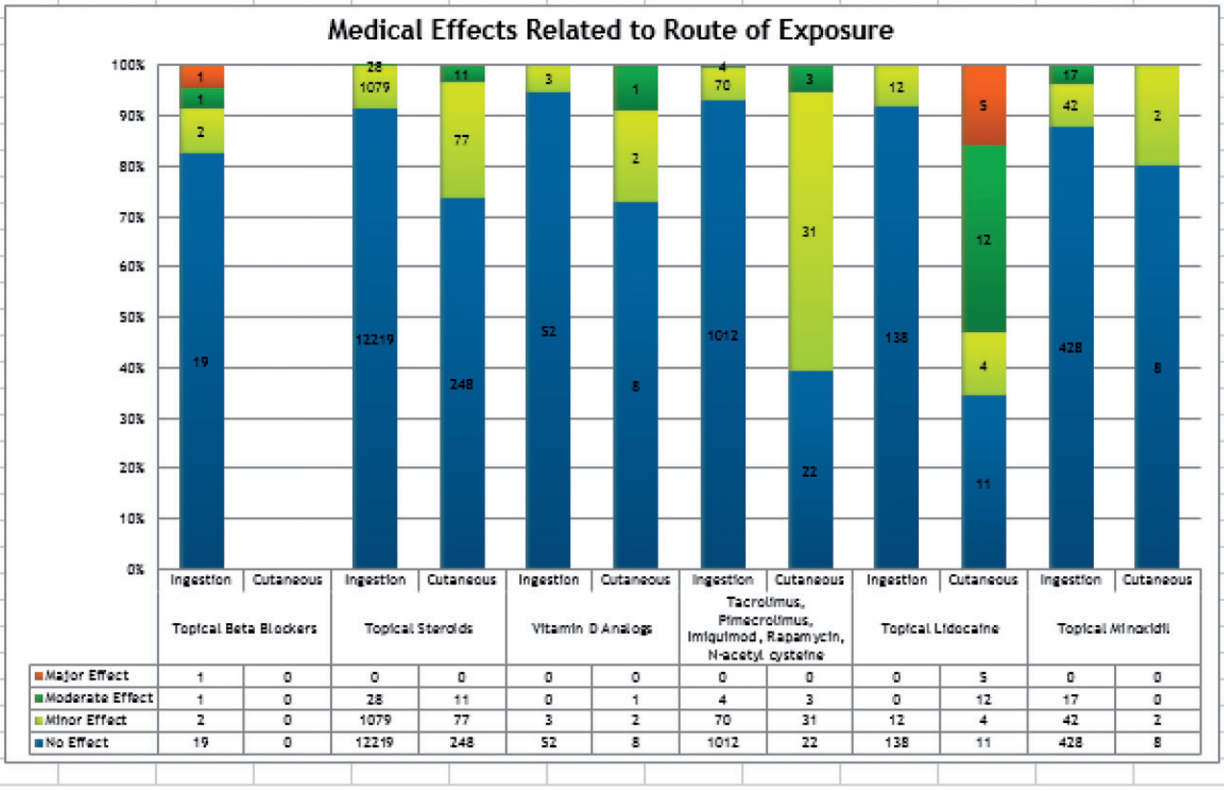

Figure 1. Medical outcomes in patients exposed to topical beta-blockers, topical steroids, vitamin D analogs, tacrolimus, pimecrolimus, imiquimod, rapamycin, N-acatyl cysteine, and topical lidocaine divided by ingestion and cutaneous exposure.

	Topical Beta Blockers		Topical Steroids		Vitamin D Analogs		Tacrolimus,		Topical Lidocaine		Topical Minoxidil	
	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous	Ingestion	Cutaneous
Managed in Non Health Care Facility	9	0	12857	307	54	9	987	49	91	7	284	9
Treated, Evaluated, and Released	12	0	405	16	1	1	82	4	45	12	160	0
Admitted to Critical Care	0	0	4	0	0	0	0	1	3	9	14	0
Admitted to Non Critical Care	1	0	5	0	0	0	9	0	10	4	15	0
Admitted to Psych	0	0	1	0	0	0	0	0	0	0	0	0
Patient Refused	0	0	2	3	0	0	4	2	1	0	7	0
Patient Lost to Follow Up	1	0	23	6	0	0	1	0	0	0	3	0
Other/Unknown	0	0	29	4	0	1	3	0	0	0	4	1

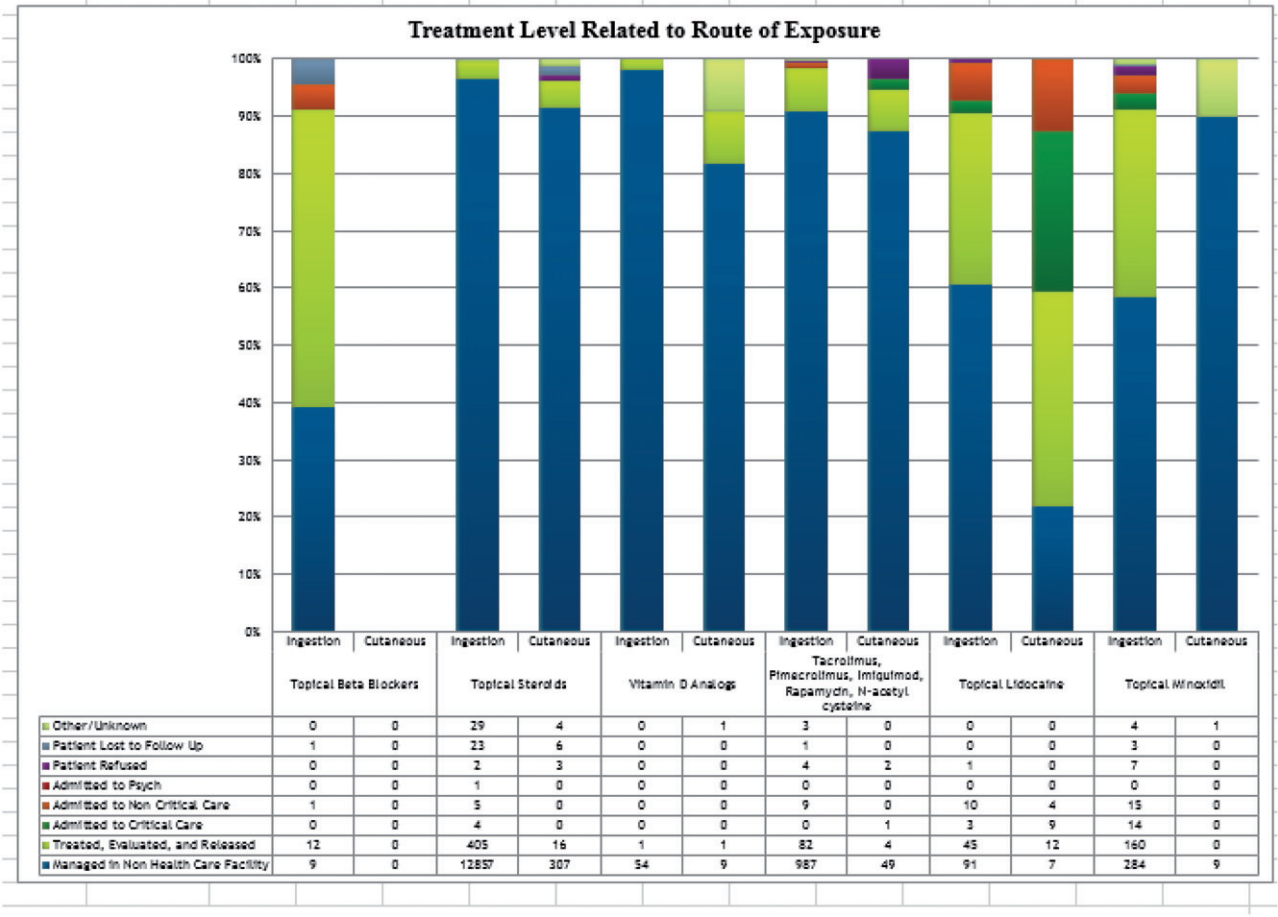

Figure 2. Level of treatment for patients exposed topical beta-blockers, topical steroids, vitamin D analogs, tacrolimus, pimecrolimus, imiquimod, rapamycin, N-acatyl cysteine, and topical lidocaine divided by ingestion and cutaneous exposure.

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Background: Although the American Association of Poison Control Centers (AAPCC) releases reports yearly, there has not been a report regarding exposure to dermatologic sources. Many topical medications used in dermatology, specifically pediatric dermatology, are used off-label though they have been approved by the Food and Drug Administration (FDA) for other indications. The safety profiles of these products are not well delineated in young children; however, they are generally assumed to be safe. We sought to summarize pediatric exposures to several products used in pediatric dermatology that were reported to the National Poison Data System over a 15-year period.
Methods: Exposures in children age 0–12-years-old involving topical formulations of beta blockers, steroids, vitamin D analogs, tacrolimus, pimecrolimus, imiquimod, rapamycin, N-acetyl cysteine, lidocaine, and minoxidil were requested from the NPDS from January 1, 2000 to December 31, 2014. Products were grouped by generic case code and products whose generic code included oral or IV medications, such as beta blockers, were narrowed down to topical preparations using specific product codes. Descriptive statistics were used to analyze route of exposure, medical outcomes, level of treatment, and clinical effects. (See supplemental Table 1 for descriptions). Only cases that were followed for medical outcome were included in analysis.
Results: In total, there were 15,127 cases reported to the NPDS regarding ingestion and 445 cases regarding cutaneous exposure to the listed topical medications that were followed for medical outcome. Medical outcomes related to each product group is shown in Figure 1. No clinical effects were reported in 92% of ingestions and 67% of cutaneous exposures. Major effects were reported in relation to topical beta blockers and topical lidocaine. One case reported bradycardia and hypoglycemia after ingestion of a topical beta blocker. Five cases with major effects related to cutaneous exposure to topical lidocaine were reported, the most common being cyanosis and seizures. Level of treatment related to each product group is shown in Figure 2. Of all the cases reported, approximately 5% were referred to a healthcare facility and less than 1% were admitted for further treatment. Ingestion of topical beta-blockers resulted in the greatest number of referrals (57%) and cutaneous exposure to topical lidocaine resulted in greatest number of admission for further treatment (14%).
Conclusion: Exposures to topical products effective in the treatment of several pediatric dermatologic conditions resulted in no effects in 91% of followed exposures. Hypoglycemia and bradycardia are possible following ingestion of a topical beta-blocker. Cutaneous exposures to topical lidocaine resulted in the most severe outcomes necessitating more advanced care. These data suggest lidocaine and beta-blockers are high-risk dermatologic preparation exposures in children and as such should be monitored more closely.

KEYWORDS Pediatrics; topical formulations; cutaneous exposure

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254. Treatment of ventricular fibrillation due to ammonium bifluoride poisoning with hemodialysis

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Background: Ammonium bifluoride is an inorganic, fluoride--containing compound found in glass and metal etching products, as well as wheel cleaners. Fluoride toxicity is a common cause of preventable poisoning, and has been reported to cause life-threatening ventricular dysrhythmias. We report a case of recurrent ventricular fibrillation secondary to ingestion of ammonium bifluoride treated with hemodialysis.
Case report: A 21 kg 4-year-old girl presented to an emergency department with vomiting and coma shortly after ingestion of reportedly "just a sip" of "Meguiar's Professional's Choice Detailer, Wheel Brightener," with the safety data sheet indicating the presence of 5–10% ammonium bifluoride as well as water (70–90%), sodium xylene sulfonate (1–5%), ethoxylated alcohols (0.5–1.5%) and ammonium fluoride (<0.5%). The patient was hypotensive (blood pressure 75/39 mmHg) and required intubation for unresponsiveness. Arterial blood gas revealed pH 7.156, pCO_2 44.3 mmHg, pO_2 115.7 mmHg, HCO_3 15.7 mmol/l. A point of care ionized calcium was 0.88 mmol/l. Serum chemistries were notable for a potassium of 3.4 mmol/l, magnesium 2.2 mg/dl, calcium 6.0 mmol/l, lactate 1.1 umol/l, and bicarbonate level of 18 mmol/l with an anion gap of 16 mEq/l. The patient was given 1.6 g of calcium gluconate and sodium bicarbonate. Ninety minutes after arrival, she had a brief ventricular fibrillation cardiac arrest, which was successfully treated with defibrillation. Thereafter, another 1.6 g calcium gluconate was given; 110 min after arrival, two additional episodes of ventricular fibrillation were defibrillated. An infusion of calcium gluconate at 400 mg/h was then started and 4 g of magnesium sulfate were given. A repeated ionized calcium level was 1.33 mmol/l; blood testing showed hypophosphatemia (0.9 mg/dl), which was repleted. An EKG revealed sinus tachycardia (rate 123/min) with normal intervals. En route to a tertiary center, the patient required two additional defibrillations for ventricular fibrillation despite the ongoing infusion of calcium gluconate and a normal point of care ionized calcium on arrival (1.23 mmol/l). Five hours after ingestion and within 1 h of the last episode of ventricular fibrillation, the patient was started on hemodialysis; no further episodes of dysrhythmia occurred and the patient recovered with a favorable neurologic outcome and no caustic injury. A fluoride level obtained 90 min into HD was 0.37 mg/l (reference range < 0.2 mg/l).
Case discussion: We report a rare case of confirmed fluoride toxicity from ammonium bifluoride ingestion with five episodes of ventricular fibrillation cardiac arrest. Dysrhythmia from fluoride poisoning is thought to be due to electrolyte abnormalities, most notably hypocalcemia; however, correction of hypocalcemia did not prevent dysrhythmia in this case, likely due to direct effect of fluoride on the myocardium, which has been shown in animal models. Fluoride is amenable to removal via hemodialysis, and its use in this case is supported by the fact that no further dysrhythmia occurred after hemodialysis was initiated. Marked hypophosphatemia was also observed and may have contributed to dysrhythmia.
Conclusion: Ammonium bifluoride is a rarely reported source of fluoride ingestion, hemodialysis should be considered, in addition to electrolyte repletion including calcium and phosphate, in the management of life-threatening toxicity.

KEYWORDS Ammonium bifluoride; cardiotoxicity; hemodialysis

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255. Prevalence of "one pill can kill" medications in blister packs: a single center study

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Background: In the United States, polypharmacy has increased over the last 20 years and has been associated with medication regimen noncompliance. Medication organizers, such as monthly blister packs, have been demonstrated to improve rates of adherence, and healthcare providers often recommend them to their patients. Although beneficial for patient compliance, many medication organizers are not child resistant, which increases the likelihood of exposure. One study suggested that medication organizers were involved in over half of unintentional medication exposures in children less than 6-years-old that presented to a single Emergency Department. This study did not detail if any "one pill can kill" (1PCK) medications were involved. 1PCK medications can be lethal in pediatric patients, particularly under age 2-years-old, with only the ingestion of a single tablet or capsule. Individual medications and therapeutic classes identified as 1PCK include tricyclic antidepressants (TCA), beta blocker (BB), calcium channel blockers (CCB), opioids, sulfonylurea, benzonatate, hydrochloroquine, chloroquine, chlorpromazine, clonidine, clozapine, olanzapine, bupropion, diphenoxylate-atropine, theophylline, venlafaxine, and thiazolidinediones. The primary purpose of our study is to characterize the type and quantity of 1PCK medications found in monthly medication blister packs.
Methods: This is a retrospective study that describes the presence of 1PCK medications found within blister packed medications filled at a single institution's outpatient pharmacy from September 1, 2017 to September 30, 2017. All patients receiving blister packed medications were identified using a report from the outpatient pharmacy and patients less than 18-years-old were excluded. The primary outcomes of this study are the quantity and type of 1PCK medications included in each patient medication blister pack. All parametric data will be analyzed by a Student's t-test for 2-group comparisons. All nonparametric comparisons will be made by Mann Whitney U for 2-group analysis and Kruskal Wallis with post hoc Dwass-Steel-Critchlow-Fligner test.
Results: After excluding 3 pediatric medication blister packs, 450 patients received 486 monthly medication blister packs in September 2018. 75.5% of all medication blister packs contained at least one 1PCK medication. Blister packs contained 1 (60.8%), 2 (29.7%), 3 (7.9%), or 4 (1.6%) 1PCK medications. The 1PCK medications included CCB ($n = 240$, 49.4%), BB ($n = 206$, 42.4%), sulfonylurea ($n = 60$, 12.3%), TCAs ($n = 21$, 4.3%), clonidine ($n = 13$, 2.7%), bupropion ($n = 12$, 2.5%), venlafaxine ($n = 4$, 0.8%), hydroxychloroquine ($n = 3$, 0.6%), olanzapine ($n = 2$, 0.4%), and thiazolidinediones ($n = 1$, 0.2%). Delayed or extended release preparations represented 40.9% of all 1PCK medications in the blister packs. Opioids, benzonatate, chloroquine, chlorpromazine, clozapine, theophylline, and diphenoxylate-atropine were not in any blister packs. Blister packs containing 1PCK medications were more likely to contain more medications (8.5 ± 2.9 versus 5.7 ± 2.9 medications, $p < 0001$) and belong to older individuals (69.1 ± 12.6 versus 62.6 ± 16.7-years-old, $p < 0001$) than blister packs without 1PCK medications. There was no significance difference in gender between groups.
Conclusions: Medication blister packs commonly contain 1PCK medications. Patients should routinely be asked about the presence of children in the household and counseled on storing blister packs "up and away." Further research is needed to determine the extent of medication organizers in unintentional pediatric exposures.

KEYWORDS One pill can kill; pediatric; medication organizer

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256. Probiotics in acute gastroenteritis-benefit or harm?: a multicenter, randomized, double-blind, placebo-controlled clinical trial

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Background: Globally, Acute gastroenteritis (AGE) is responsible for over 800,000 deaths each year in children <5 years. In the U.S., 179 million episodes of AGE occur annually resulting in 1.7 million emergency department (ED) visits by children, 600,000 overall hospitalizations and 5000 deaths. Providers have little to offer to modify the disease course. Probiotics represent an expanding, multi-billion dollars industry, with potential clinical benefits. We conducted a clinical trial to determine whether probiotic treatment improves outcomes in children who seek ED care for AGE.
Methods: We conducted a multicenter, randomized, double-blind, placebo-controlled clinical trial. Eight hundred and eighty-six children aged 3 months–4 years with AGE (had ≥3 episodes of watery stools in a 24-h period)were enrolled in six Canadian university-affiliated pediatric EDs, between November, 2013 and April, 2017 (Figure 1). Participants were randomly assigned to receive a commercially-available probiotic (Lacidofil® STRONG), containing Lactobacillus rhamnosus R0011 and Lactobacillus helveticus R0052, 4.0×109 CFU, in a 95:5 ratio or placebo, twice daily, for 5 d. Sachets containing probiotics and placebo were identical in appearance, smell and weight. Rectal swabs/stool specimens were collected during the enrollment visit for enteric bacterial culture plus a multiplexed nucleic acid syndromic panel for 15 enteric viruses, bacteria and parasites (Luminex xTAG). Primary outcome was the development of moderate-severe disease within 14 d of randomization, defined by a Modified Vesikari Scale score ≥9. Secondary outcomes included duration of diarrhea and vomiting, subsequent unscheduled physician visits and adverse events.
Results: The proportion of participants experiencing moderate-severe disease (MVS ≥ 9) within 14 d after enrollment was similar between the study groups [probiotics–108/414 (26.1%) versus placebo–102/413 (24.7%); difference, 1.39%; 95%CI,

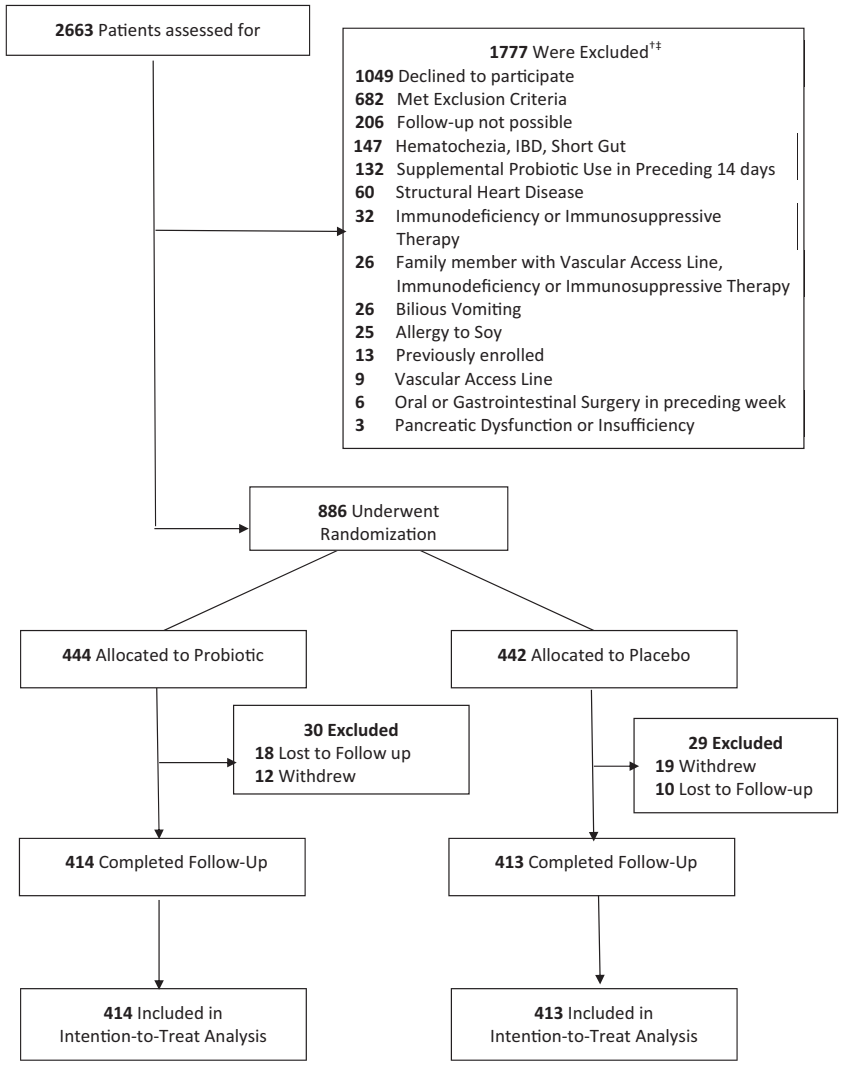

Figure 1. Enrollment and outcomes. IBD: inflammatory bowel disease; †Patients may have met more than one criterion.

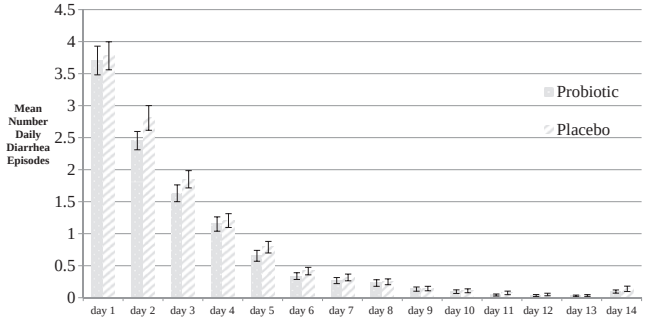

Figure 2. Mean number of episodes of diarrhea per 24-h period following randomization by Treatment Group. Diarrhea: incidence rate ratio: 0.98; 95% CI: 0.85, 1.13; $p = .78$ (probiotic versus placebo).

−4.54 to 7.30%; $p = .65$]. Regression analysis adjusted for site found no benefit with probiotic use (OR: 1.06; 95%CI: 0.77, 1.46; $p = .72$). After adjustment for site, age and frequency of vomiting and diarrhea, treatment assignment did not predict moderate-severe disease (OR, 1.06, 95%CI: 0.76, 1.49; $p = .74$). In probiotic versus placebo groups, there were no differences in median (IQR) duration of diarrhea [52.5 (18.3, 95.8) versus 55.5 (20.2, 102.3) h; $p = .31$; Figure 2] and reported risk of adverse events (32.9% versus 36.8%; OR 0.83; 95%CI: 0.62, 1.11; $p = .21$). Two serious adverse events were reported, both in the placebo group. Vomiting was more common in the probiotic compared with placebo group [IRR: 1.36; 95%CI: 1.13, 1.63; $p < 001$]. The proportion of children experiencing unscheduled health-care provider visits did not differ between groups-[probiotic −30.2% (125/414) versus placebo −26.6% (110/413); OR: 1.19; 95%CI 0.87, 1.62; $p = .27$]. Rotavirus was identified in probiotic group participants more often. End point outcomes are depicted in Figure 3.

Conclusions: In children presenting to an ED with acute gastroenteritis, twice daily administration of 4.0×109 CFU of a Lactobacillus rhamnosus/helveticus probiotic does not prevent development of moderate-severe disease within 14 d. Among children with predominantly viral AGE, probiotics did not result in benefits related to primary or secondary outcomes.

End-Point	Number Included in Analysis	Probiotic N (%)	Placebo N (%)	Odds Ratio (95%CI)	P Value
Primary Efficacy End-Point: MVS Score ≥ 9¶					
All Participants – no. (%)	827	108/414 (26.1)	102/413 (24.7)	1.06 (0.77, 1.46)	0.72
Age < 1 yr – no. (%)	284	45/134 (33.6)	48/150 (32.0)	1.01 (0.60, 1.71)	0.97
Exclusively Breast Fed – no. (%)	53	7/22 (31.8)	10/31 (32.3)	0.82 (0.18, 3.61)	0.79‡‡
Antibiotics, 14 Days pre-index Visit – no. (%)	110	12/51 (23.5)	17/59 (28.8)	0.86 (0.35, 2.11)	0.74§§
Greater Than 70% Compliance – no. (%)	598	72/295 (24.4)	66/303 (21.8)	1.16 (0.79, 1.71)	0.45
Secondary Efficacy End-Points					
Median Duration of Diarrhea, hr, (IQR)	827	52.5 (18.3, 95.8)	55.5 (20.2, 102.3)		0.31
Median Duration of Vomiting, hr, (IQR)†	409	17.7 (0, 58.6)	18.7 (0, 51.6)		0.18
Health-Care Provider Visit – no. (%)¶	827	125/414 (30.2)	110/413 (26.6)	1.19 (0.87, 1.62)	0.27
Safety					
Any Adverse Event – no. (%)‖	827	136/414 (32.9)	152/413 (36.8)	0.83 (0.62, 1.11)	0.21
Tertiary Efficacy End-Points					
Days of Daycare Missed, Days, Median (IQR)‡	331	1.0 (0, 2.0)	1.0 (0, 2.0)		0.55
Hours of Work Missed, Median (IQR)§	653	0 (0, 8.0)	0 (0, 8.8)		0.18
Emergency Department Revisits – no. (%)¶	827	83/414 (20.0)	76/413 (18.4)	1.11 (0.77, 1.60)	0.56
Revisit with IV Fluid Administration – no. (%)¶	827	36/414 (8.7)	26/413 (6.3)	1.57 (0.75, 3.28)**	0.23
Revisit with Hospitalization – no. (%)¶	827	33/414 (8.0)	22/413 (5.3)	1.65 (0.66, 4.12)††	0.28

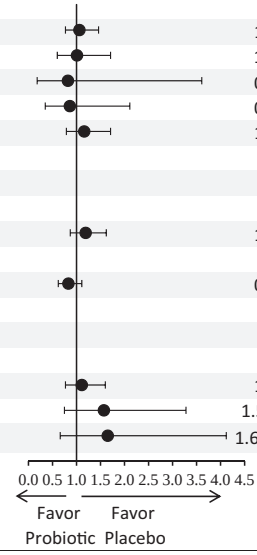

Figure 3. Study end-points.* MVS: Modified Vesikari Scale; hr: hours; IV: intravenous. *Plus-minus values are means ± SD. †Includes only participants with ≥ three episodes of vomiting in the 24 h prior to enrollment. ‡Includes only children who attend daycare; analyzed employing Van Elteren test stratified by participant enrollment site; no imputation was performed for participants with missing daycare absenteeism data. §Includes only caregivers who work; analyzed employing Van Elteren test stratified by participant enrollment site; no imputation was performed for participants with missing work absenteeism data. ¶Analyzed employing logistic regression with model adjusted for participant enrollment site. |Analyzed employing logistic regression with model adjusted for participant enrollment site however no imputation was performed for participants with missing adverse event reporting data. **Regression analysis excluded participants from a single site since none of the 11 emergency department revisit cases at this site received IV fluids, thus this site could not be included in the regression model. ††Regression analysis excluded participants from three sites since none of the 23 emergency department revisit cases at these sites were admitted, thus these sites could not be included in the regression model. ‡‡Regression analysis excluded participants from three sites as all exclusively breastfed children at these sites all were either in one group (probiotic or placebo) or had the outcome of interest thus these sites could not be included in the regression model. §§Regression analysis excluded five participants from one site as they all experienced the outcome of interest thus this site could not be included in the regression model.

KEYWORDS Probiotics; gastroenteritis; randomized clinical trial

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257. Latrogenic pediatric hydroxocobalamin overdose

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Background: Hydroxocobalamin, a precursor molecule to vitamin B12, has emerged as the preferred treatment for patients with known or suspected severe cyanide toxicity. Hydrogen cyanide is an inhalational toxicant often found in structure fires due to the use of synthetic building and furnishing materials. Hydroxocobalamin is most often administered in the United States for empiric treatment of patients rescued from enclosed-space fires with concern for inhalational injury and potential concomitant cyanide toxicity. However, limited data exist on the effects of hydroxocobalamin toxicity, particularly in pediatric patients.

Case report: A healthy three year-old girl was rescued by firefighters from an apartment fire. She was breathing and moving all extremities without signs of cutaneous burns, but emergency medical services (EMS) personnel electively intubated the child after finding soot around the nose and mouth. The patient received etomidate and three weight-adjusted doses of succinylcholine during the intubation followed by midazolam and fentanyl. She also received 5 g (373 mg/kg) of intravenous hydroxocobalamin given concern for potential cyanide toxicity, an amount equivalent to one standard adult dose but over five times the appropriate weight-adjusted dose for this 13.4-kilogram child. On emergency department (ED) arrival, her vital signs were: temperature 35.9 °C, heart rate 54 bpm, blood pressure 111/83 mmHg, respirations 26 per min, and pulse oximetry 99% on 100% oxygen by bag-valve mask. Her exam was notable only for chromaturia and diffuse erythroderma, thought to be secondary to hydroxocobalamin administration. Bradycardia resolved without intervention after two h, and bronchoscopy revealed a small number of carbonaceous deposits in the proximal bronchi, consistent with grade 1 inhalational injury. The patient was extubated approximately 4 h after prehospital intubation, and observed overnight without incident. She was discharged the following morning in good condition with persistent erythroderma. Skin color had returned to normal at time of telephone follow-up 2 d later.

Case discussion: We believe this to be the first reported case of iatrogenic pediatric hydroxocobalamin overdose for the treatment of suspected cyanide toxicity. The patient developed erythema and chromaturia, both of which are expected even with therapeutic levels of hydroxocobalamin. Along with minor airway burns, the only other finding was a transient and hemodynamically neutral bradycardia, which occurred shortly after prehospital intubation. Laryngoscopy in children can stimulate a vagal response, and succinylcholine is known to cause sinus bradycardia via agonism of sinoatrial muscarinic receptors, the risk of which is significantly increased with repeat succinylcholine

administration. Given these plausible alternative explanations, it seems unlikely that hydroxocobalamin toxicity incited a negative chronotropic response in this patient. Previous studies have found an association between hydroxocobalamin and transient hypertension, but that was not observed in this case. In all, we were unable to appreciate any complications due to excess hydroxocobalamin administration.

Conclusions: We believe this to be the first reported case of iatrogenic pediatric hydroxocobalamin overdose in the treatment of suspected cyanide toxicity, which the patient tolerated well without life-threatening complication or adverse effect.

KEYWORDS Hydroxocobalamin; cyanide; Iatrogenic

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258. Pediatric benzodiazepine exposure and overdose in the United States: 16-years of poison center data

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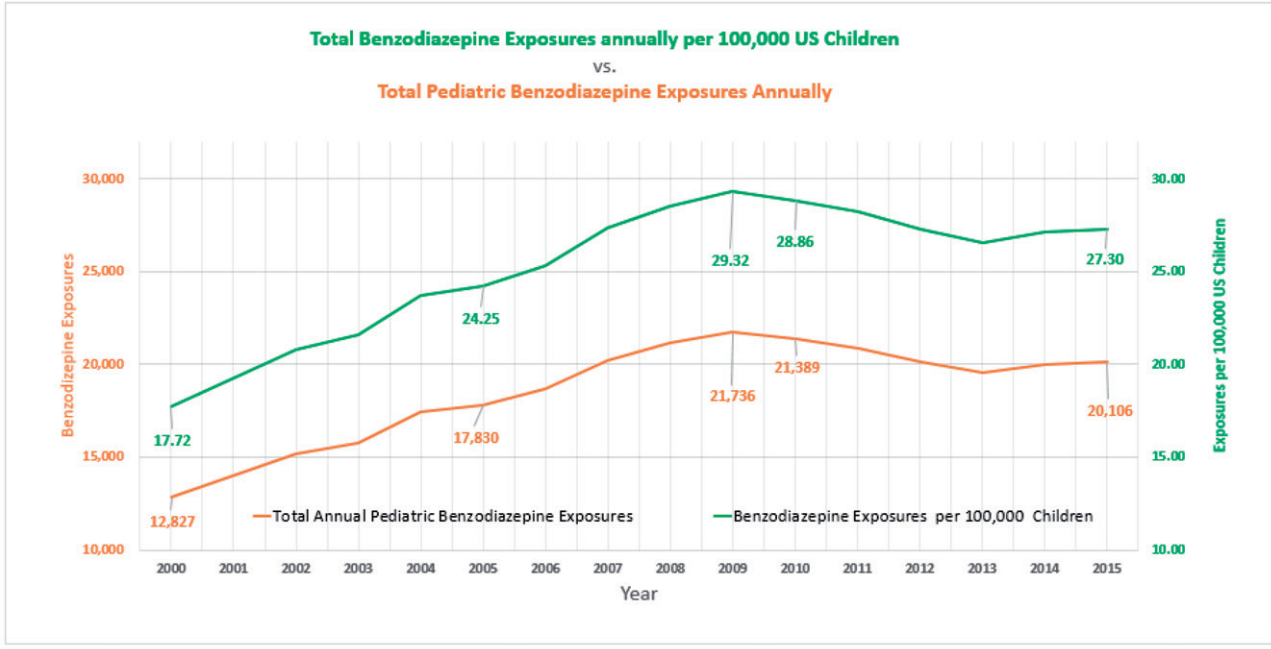
Background: In recent years, there has been a significant increase in prescription drug abuse and related fatalities. Although opioid analgesics have been most commonly implicated, there have additionally been significant increases in the prevalence of benzodiazepine exposure, abuse, and overdose. The increasing adult usage of benzodiazepines is particularly noteworthy, as increased prescription drug use in adults has been demonstrated to lead to increases in pediatric poisonings. Furthermore, given the increasing availability of benzodiazepines, intentional misuse and abuse of benzodiazepines in children of adolescent age is also an area of concern. The purpose of this study was to describe national trends in pediatric benzodiazepine exposures over time.

Methods: A retrospective database analysis was conducted. Data pertaining to benzodiazepine exposures in children ages 0–19 years reported to US poison centers from January 1, 2000 to December 31, 2015 were obtained from the National Poison Data System (NPDS). Data were collected from all participating US poison centers. Exposure data were documented by specialists in poison information (SPIs) using standardized data fields and definitions. Given the pediatric focus of this study, 18 and 19-year-old patients were ultimately excluded. In order to generate the rate of benzodiazepine exposures per 100,000 US children, population data was obtained from the US Census Bureau's 2000 and July 1, 2010 population estimates for the years 2000–2015. Data were analyzed using chi-squared tests, and a *p*-value of less than 0.05 was considered significant.

Results: 296,838 pediatric benzodiazepine exposures were identified during the study period. The rate of pediatric benzodiazepine exposure reported to US poison centers increased 54% between 2000 and 2015, from 17.72 exposures per 100,000 children in the year 2000, to 27.30 exposures per 100,000 children in 2015 (Figure 1). Furthermore, the severity of medical outcome for such exposures is increasing on an annual basis [$p < 001$], with 24% of exposures in the year 2015 resulting in a major or moderate effect (Table 1). Also noted was an increased prevalence polysubstance abuse, especially with children ages 12–17 [$p < 001$], as 79% of reported benzodiazepine exposures in children aged 12–17 in the year 2015 involved co-ingestion of one or more additional substances. Furthermore, by 2015, nearly half of all pediatric benzodiazepine exposures were intentional in nature, representing abuse, intentional misuse, or attempted suicide. This reflects a significant national trend of increasing



Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Total Annual Pediatric Benzodiazepine Exposures	12,827	14,001	15,194	15,768	17,408	17,830	18,687	20,235	21,126	21,736	21,389	20,880	20,139	19,552	19,960	20,106
Benzodiazepine Exposures per 100,000 Children	17.72	19.27	20.83	21.57	23.75	24.25	25.34	27.34	28.51	29.32	28.86	28.25	27.32	26.57	27.12	27.30

Figure 1.

Table 1. Changes in NPDS outcome for benzodiazepine exposure, by year [$p < 001$].

Outcome	2000	2005	2010	2015
Death	5 (0%)	10 (0%)	27 (0%)	23 (0%)
Major or moderate effect	1728 (13%)	2612 (16%)	3730 (17%)	4780 (24%)
Potentially toxic exposure	1075 (8%)	1447 (7%)	1529 (7%)	1046 (5%)
Minor effect or no effect	9838 (77%)	13,616 (75%)	15,872 (74%)	14,019 (70%)
Unrelated effect	181 (1%)	145 (1%)	231 (1%)	238 (1%)

Table 2. Listed reason for benzodiazepine exposure, by year [$p < 001$].

Reason	2000	2005	2010	2015
Intentional (i.e., overdose, abuse, suicide)	4752 (37%)	6676 (37%)	7795 (36%)	9590 (48%)
Unintentional (accidental ingestion, incorrect dose)	7787 (61%)	10,762 (60%)	13,109 (61%)	10,008 (50%)
Adverse Reaction	103 (1%)	154 (1%)	146 (1%)	184 (1%)
Other	72 (1%)	80 (0%)	79 (0%)	86 (0%)
Unknown reason	113 (1%)	158 (1%)	260 (1%)	238 (1%)

intentional benzodiazepine exposure annually [$p < 001$], (Table 2). Finally, of the 296,838 exposures analyzed, the three most commonly identified benzodiazepines of exposure were alprazolam, clonazepam, and lorazepam, with 59,117 (19.9%), 54,303 (18.3%), and 28,397 (9.57%), exposures recorded, respectively.

Conclusion: (1) The rate of pediatric benzodiazepine exposure is increasing, (2) medical outcomes of such exposures are increasing in severity, and (3) 79% of adolescent benzodiazepine exposures involve co-ingestion of one or more substances. Providers in primary care and emergency care settings must be educated about this growing epidemic of pediatric benzodiazepine exposure in order to screen effectively for abuse and to avoid preventable harms to adolescents, young children, and infants.

KEYWORDS Benzodiazepine; pediatric; overdose

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259. Safety intervention effects on exposures to liquid laundry detergent packets among US children

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Objective: To investigate exposures to liquid laundry detergent packets among children <6-years-old in the United States and evaluate the impact of the ASTM voluntary product safety standard.

Methods: Data from the National Poison Data System involving exposures to liquid laundry detergent packets from 2012 to 2017 for all ages were analyzed.

Results: From January 2012 to December 2017, there were 72,947 single and polysubstance exposures to laundry detergent packets. Most exposures (91.7%) were documented among children <6-years-old. Exposures among children <6-years-old increased 110.4% from 2012 to 2015 before decreasing 18.0% through 2017, while the number of exposures among individuals 6 years and older increased throughout the study period. The proportion of children <6-years-old admitted to a hospital in a given year decreased from 4.8% in 2012 to 2.0% in 2017. The proportion of children <6-years-old utilizing a healthcare facility within a given year decreased from 41.0% in 2012 to 33.1% in 2017. Ocular exposures were reported as a route of exposure in 32.2% of individuals 6 years and older compared to children <6-years-old (8.7%). Vomiting (39.4%) and ocular irritation/pain (15.1%) were common clinical effects reported among single substance exposures. Significant clinical effects, such as coma (36 cases) and respiratory arrest (12 cases), were seen primarily among children <6-years-old and older adults.

Conclusion: Both the number and severity of laundry detergent packet exposures have begun to decrease in recent years among children <6-years-old, likely attributable, in part, to the voluntary product safety standard and public awareness efforts about the hazards of laundry detergent packets. However, exposures among older children and adults are increasing. Opportunities exist to strengthen the current product safety standard to further reduce laundry detergent packet exposures.

KEYWORDS Laundry detergent packet; pediatrics; unintentional poisoning

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260. Acute high body burden of lead due to delayed removal of an ingested foreign body

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Background: Foreign body ingestion is a common event in children. Depending on the foreign body ingested, management may be expectant or may be urgent removal. When the foreign body is lead-containing, lead absorption can occur at different rates impacted by gastrointestinal transit time as well as object size, shape, and lead content. We describe a case of acute high blood lead concentration, as well as high body burden of lead, in a child with a lead-containing foreign body in their gastrointestinal tract for a short period of time.

Case report: A previously healthy 6-year-old boy presented to an emergency department (ED) after he swallowed an antique fishing weight. An abdominal x-ray identified the object in his stomach and expectant management was recommended. The following day, he developed abdominal pain. In a second ED, a repeat x-ray again identified the object (3.6 cm oval) in his stomach and no signs of obstruction. His vital signs were stable; he had no vomiting, diarrhea, bloody stool, difficulty swallowing, or changes in neurologic function. Expectant management was recommended by gastroenterology. Toxicology was also consulted and recommended a blood lead as well as removal via endoscopy. The blood lead was 95 mcg/dl at 16.5 h post ingestion. A complete metabolic panel was unremarkable; hemoglobin was 13 g/dl. Endoscopic removal of the fishing weight was successfully performed at 19 h post ingestion. The patient's blood lead was repeated at 19.5 h post ingestion and was 84 mcg/dl. Whole bowel irrigation (250 cc/h for 6 h) and intravenous hydration were done. The blood lead remained elevated to 65 mcg/dl at 30.5 h post ingestion. Chelation with oral succimer was started at 10 mg/kg/dose every 8 h for 5 d and then every 12 h for 14 d. A 24-h urine collected 2 to 3 d post ingestion and 0.5 to 1.5 d post initiation of chelation, had 1055 mcg of lead/l. At 54 h post

ingestion, the blood lead concentration had decreased but remained abnormal at 38 mcg/dl; the patient was asymptomatic. At 3 weeks post ingestion, the patient had a blood lead concentration of 8 mcg/dl.
Discussion: Lead toxicity secondary to lead-containing foreign body ingestion is a known issue. After lead-containing foreign body ingestion, blood lead increases with time in the gastrointestinal tract as well as specific characteristics of the object(s). In addition, children absorb lead at a rate of 30–40%, which is double the rate (15–20%) in adults. Case reports of resultant lead toxicity have described situations of multiple objects or lead-contaminated material as well as often prolonged or uncertain duration since ingestion. In this case, there was a single foreign body and the time from ingestion to removal was known and short (19 h). Within that time, however, the amount of lead absorbed resulted in a high body burden, not just a transiently high blood concentration.
Conclusion: Time-sensitive removal of a lead-containing foreign body is necessary to avoid high body burden of lead, subsequent chelation, and risks of adverse effects of lead and/or chelation.

KEYWORDS Lead; foreign body; ingestion

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261. Predictors of poison control center utilization for pediatric poison cases managed in a health care facility

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Background: In 2016, the American Association of Poison Control Centers (AAPCC) recorded over one million exposure calls for children under 6-years-old, with 12.8% requiring management in a healthcare facility. Despite poisoning being a mandatory reportable condition in our jurisdiction, underreporting to our PCC persists.
Objectives: The aim of this study was to determine the factors associated with healthcare facility (HCF) reporting of childhood poisoning cases to our PCC.
Methods: This study is a retrospective database review using 2010–2014 poisoning visit information from two databases: PCC Toxicall and the Statewide Planning and Research Cooperative System (SPARCS). SPARCS is an all payer database that collects patient demographics, diagnoses, treatments, and charges for all inpatient hospital services and emergency department (ED) visits. Children under 6-years-old presenting to a HCF in the PCC primary catchment region with ICD9 diagnosis codes 960–979, 981–987, or 989 were identified in SPARCS. These cases were then uniquely matched to the PCC Toxicall data based on patient age, sex, HCF, name, and admission date. Matched cases were then classified as poisoning visits reported to PCC. Chi-square statistics were used to assess the univariate association between PCC reporting and age, sex, poverty level, county, private insurance, hospital type (with or without a pediatric intensive care unit – PICU), presenting location (ED versus inpatient), disposition (admit to ICU, admit to floor, or discharge), length of stay, or poison category (drug/pharmaceutical versus non-medicinal/environmental). We then used stepwise logistic regression to model the relationship between these covariates and PCC reporting. Relative risks with corresponding 95% confidence intervals were then approximated from the adjusted odds ratios.
Results: We identified 11,620 children in SPARCS under the age of six years treated in a local HCF with at least one poisoning diagnosis code. Only 59.8% of these patients were matched to a unique PCC Toxicall case, indicating underreporting by 40.2%. Young age, having private insurance, presenting to the ED, being treated at a hospital with a PICU, admission to ICU, length of stay longer than 24 h, being treated for a drug/pharmaceutical poison and treatment within the same county where the PCC is located were all associated with increased reporting to the PCC. After controlling for age, county, insurance type, poison type, disposition, location of presentation, and length of stay, younger children (age <1 years; RR = 1.35, 95%CI 1.28–1.41) and those with drug/medicinal exposures (RR 1.62, 95%CI 1.58–1.65) were more likely to be reported to PCC. Additionally, patients transferred for care with a resultant length of stay longer than 24 h were more likely to be reported to PCC (RR = 2.86; 95%CI 1.6–4.01).
Conclusions: Only 60% of pediatric poison exposures were reported to our PCC by healthcare facilities. While, the youngest patients and those that require transfer for longer care are more likely to involve the PCC for consultation, additional outreach and education is required to improve PCC penetrance.

KEYWORDS Poison control center; pediatric; utilization

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262. Healthcare facilities that treat pediatric poisoning victims consistently underreport environmental exposures to poison control centers

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Background: In 2016, the American Association of Poison Control Centers/National Poison Data System (AAPCC/NPDS) recorded over one million exposure calls for children under 6-years-old with 12.8% requiring management in a healthcare facility. While widely used as a method of poisoning surveillance and epidemiologic information, the AAPCC/NPDS requires active reporting and is subject to significant underreporting of cases.
Objective: The aim of this study was to assess the reporting of pediatric poisoning cases treated at healthcare facilities (HCF) to our regional poison control center (PCC) based on poison exposure category.
Methods: This analysis builds on a previously unpublished retrospective review assessing factors associated with PCC reporting. We obtained poisoning visit information from two databases:

PCC Toxicall and the Statewide Planning and Research Cooperative System (SPARCS) over a 4-year period (2010–2014). SPARCS is an all payer database that collects patient demographics, diagnoses, treatments, and charges for all inpatient hospital services and emergency department visits. Children under 6-years-old treated at a HCF located within the PCC primary catchment area with ICD9 diagnosis codes 960–979, 981–987, or 989 were identified in SPARCS. These cases were then uniquely matched to PCC Toxicall on patient age, sex, healthcare facility, name, and admission date. The resulting matched dataset was used to describe PCC reporting for visits within each poison category. ICD9 diagnosis codes were grouped into poison categories consistent with AAPCC/NPDS major categories. We calculated the proportions of each poison category reported to the PCC and determined which poison categories had highest and lowest percentages of reporting. We used descriptive statistics to characterize the data.

Results: We identified 11,620 children in SPARCS under the age of six years treated in a local HCF with a poisoning diagnosis code; 59.8% ($N = 6951$) of these patients were matched to a reported PCC Toxicall case. The poison categories with the largest percentage of cases reported to PCC included: anticonvulsants ($N = 73$, 84.9% reported; RR 1.45, $p < 001$), cardiovascular drugs ($N = 420$, 80.7% reported; RR 1.40, $p < 001$), antihistamines ($N = 336$, 79.8% reported; RR 1.37, $p < 001$)), antidepressants ($N = 115$, 79.1% reported; RR 1.35, $p < 001$), and sedatives/hypnotics ($N = 405$, 77.8% reported; RR 1.34, $p < 001$). Of the unreported cases ($N = 4669$), the poison categories with the smallest percentage of cases reported to PCC included: venom ($N = 755$, 0.3% reported; RR 0.004, $p < 001$), heavy metals/lead ($N = 117$, 1.7% reported; RR 0.03, $p < 001$), CO/gases ($N = 972$, 15.4% reported; RR 0.25, $p < 001$), plants/mushrooms ($N = 84$, 16.7% reported; RR 0.28, $p < 001$), and antimicrobials ($N = 183$, 56.3% reported; RR 0.97, $p = .62$).

Conclusions: Environmental exposures, including heavy metals/lead and carbon monoxide, were associated with a high percentage of underreporting to our regional PCC. These findings suggest an area for focused outreach and education regarding the availability of the PCC in the consultation and treatment of all types of pediatric poisoning exposures, specifically including non-medicinal/environmental exposures.

KEYWORDS Poison control centers; pediatrics; utilization

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263. Chronic lead poisoning in an adult with signs of encephalopathy

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Background: Most common causes of lead poisoning in adults are occupational exposure and traditional medicine usage, and hereby encephalopathy is an uncommon presentation [1]. We report a case of lead poisoning with central nervous symptoms of primarily unclear etiology.

Case report: A 53-year-old Swiss resident of oriental origin presented for investigation of severe anemia (61 g/l) associated with abdominal pain, myalgia of lower limbs, and impaired concentration, from which he had suffered during the previous weeks. Common causes of anemia such as iron or vitamin B22 deficiency, and gastrointestinal bleeding were previously ruled out. At hospital admission, the patient showed intention tremor, symmetric hyperreflexia, and word finding difficulties (anomia). The urine toxicology screen was positive for benzodiazepines and opiates, and a search in urine for a wide variety of medications and drugs of abuse identified additional codeine and its metabolites, morphin-3 glucuronide, noscapine, papaverine, thebaine, and hydrocodone. The patient received one pack of concentrated erythrocytes. On the day after admission, the patient developed disorientation, confusion, hyperactivity and fever. Therefore, he was sedated and transferred to the ICU. The EEG was normal, except slight deceleration. The cerebrospinal fluid showed no signs of infection, but the pressure was 27 mmHg (normal 5–15). The CT scan of the brain displayed widened ventricles, probably in the context of a chronic hydrocephalus. The blood film revealed poikilocytosis, polychromasia, anisocytosis and basophilic stippling. The tentative diagnosis of plumbism was confirmed by a blood lead concentration of 4.2 μmol/l (normal <0.48 μmol/l), and the central nervous symptoms were suggestive for lead encephalopathy. Since all neurological and abdominal symptoms resolved spontaneously within 48 h and the patient admitted at this point to consume opium regularly, opiate withdrawal was assumed to be the likely cause of his central nervous symptoms. Opium as potential lead source was discussed, as poisoning with lead contaminated opium is described in Iranian medical literature [2], and ingredients of opium were found in the urine. Furthermore, there was no history of recent dietary, environmental or occupational lead exposure. The patient underwent chelation therapy with succimer without appearance of side effects. He was discharged after 10 d of hospitalization after receiving another 2 bags of concentrated erythrocytes. Later, a high concentration of lead was found in a sample of the patient's opium (11,500 ng lead/mg opium). The patient was urgently advised to abstain from further opium use.

Case discussion: Lead poisoning is an important element of differential diagnosis of anemia in combination with abdominal pain, and opium can be a source of lead exposure, even in western countries [3].

Conclusion: In patients with plumbism and illicit drug abuse experiencing transient encephalopathy, opiate withdrawal rather than lead encephalopathy should be considered.

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KEYWORDS Plumbism; opium; drug adulterants

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264. Quetiapine ingestions in the pediatric population: a descriptive analysis of cases from four regional poison centers

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Background: Quetiapine fumarate (Seroquel®, Seroquel XR®; AstraZeneca) works by blocking several receptors including serotonin and dopamine, for the treatment of psychiatric disorders. It has been reported that a dose of more than 100 mg could be toxic in a drug-naïve child <12-years-old. Safety and efficacy in children <10 years have not been established. Our aim was to compare acute ingestions of quetiapine exposure outcomes and describe symptoms experienced at various doses ingested.
Method: This IRB approved retrospective chart review of four regional poison centers (RPC) involved children <6 years with a single acute exposure to quetiapine from January 2000 to December 2017. Basic descriptive statistics were performed to analyze the data.
Results: Over this 18-year period, 627 cases of quetiapine-only ingestions in children <6 years were received by 4 RPCs; 501 (80%) were 3 years and younger. Males accounted for 54%. Accidental ingestion accounted for 94% of all cases. There were 266 (42%) patients in the ED when the RPC was contacted, 168 (27%) were referred to the ED by the RPC, and 29% were managed outside a HCF. Of the 83 cases admitted, 50 went to the ICU. Of the 434 patients treated in the ED, 278 (64%) were released from the ED. The exact amount was known in 166 (28%), of which 108 patients were followed to a known outcome. Of these, 22 had minor effects (0.9–34.9 mg/kg) including 18 drowsiness, 3 ataxia and 1 tachycardia; 6 had moderate effects (3.1–57.1 mg/kg) including 5 drowsiness, 4 tachycardia, 3 agitation, 2 hypertension and 1 dystonia. No major effects were reported in "exact amount" cases and 75% of all ingestions up to 100 mg remained asymptomatic. Cases were followed to a known outcome in 67% of all cases. No effects were reported in 290 (69.5%) of cases followed to a known outcome with reported ingestions of 0.8–419.6 mg/kg; 125 (30%) had minor to moderate effects with amounts of 0.9–85.7 and 0.8–88.5 mg/kg respectively. Only 2 cases reported a major effect; one of these cases involved a 14.7 mg/kg maximum amount per history exhibiting drowsiness, hypertension, tachycardia, and respiratory depression. The second case involved an unknown amount per history experiencing drowsiness, muscular rigidity and seizure activity. CNS effects predominated in all symptomatic cases: 119 reported sedation; 18 agitation; 12 ataxia. Tachycardia and vomiting were also noted (23 and 9 cases, respectively).
Discussion: A majority of pediatric accidental quetiapine exposures resulted in no effects when followed to an outcome. In cases where symptoms were reported, the majority exhibited minor sedation. Ingestions up to 100–200 mg exhibited minor to moderate effects at worst. Our review suggests that accidental quetiapine ingestions in children <6-years-old are generally well tolerated.

KEYWORDS Quetiapine; pediatric; toxicity

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265. Administration of IV N-acetylcysteine in a premature infant weighing 895 g

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Background: In maternal overdoses, acetaminophen has been associated with increased fetal death and spontaneous abortion. Special considerations are needed for the treatment of acetaminophen overdoses in the premature infant population. Clinicians need to be cognizant of the maximum concentrated dose of IV N-Acetylcysteine (NAC) and the total volume allowed to be administered, to prevent potential fluid overload and severe hyponatremia in this population. A premature infant weighing under one kilogram born with acetaminophen toxicity was successfully treated with NAC IV.
Case report: A 26 week, 1 d-old-male infant weighing 895 g was born via emergency C-section due to breach positioning and premature labor. Initial APGAR scores were 2 and 5. Mother was on methadone and had positive urine toxicology for oxycodone (unknown preparation), phencyclidine, and a plasma acetaminophen concentration (APAP) of 287 mcg/ml. Neonate was intubated due to APGAR scores and premature lungs. APAP in infant was 114 mcg/ml 8 h post-delivery, AST 125 U/l, ALT 14 U/l, PT 25.2 s, PTT 68 s, Fibrinogen 120 mg/dl, INR 2.1 and Na 136 mEq/l. Urine toxicology was negative but meconium stool toxicology was positive for opioids. Infant was treated with FFP, PRBC, Vitamin K, lorazepam, fentanyl, and morphine for sedation and opioid withdrawal, and sodium bicarbonate for acidosis. NAC IV loading dose of 150 mg/kg (134.5 mg mixed in 2.7 ml of D5W) over an hour, 50 mg/kg (44.75 mg mixed in 0.895 ml D5W) over 4 h, and 100 mg/kg (89.5 mg mixed in 1.79 ml of D5W) over 16 h were administered. Repeat laboratory
Results: APAP was 72 mcg/ml 19 h post-delivery, AST 121 U/l, ALT 29 U/l, Fibrinogen 158 mg/dl, INR 1.9, PT 22.3 s, PTT 44s, and HCT 34%. APAP decreased to 22 mcg/ml 37 h post-delivery, AST 85 U/l, ALT 28 U/l, INR 1.9, and Na was 144 mEq/l. Patient received a fourth dose of IV NAC at 6.25 mg/kg/h mixed in D5W for 16 h. At 74 h post-delivery, APAP was undetectable, AST 74 U/l, ALT 23 U/l, Na 144 mEq/l, opioid withdrawal was managed, and infant improving. IV NAC was discontinued, a total of 400 mg/kg of NAC IV was administered over 37 h. The observed half life of elimination of acetaminophen was 15 h. AST 12 U/l, ALT 33 U/l, HCT 35%, and Na 144 mEq/l, were resulted day 6th of life. By 11th day, infant was overall improving, trickle tube feeds were started, still intubated weaning ventilator settings but pulmonary edema resolved, patient was producing his own bowel movements, and opioid withdrawal was being managed with phenobarbital and morphine. Pt was discharged 91 d post birth.
Conclusion: Premature infants are at risk for fluid overload, hyponatremia, and blood loss with frequent blood draws, when administered NAC IV for acetaminophen toxicity. Careful dosing and monitoring can mitigate these potential complications.

KEYWORDS Premature infant; acetaminophen overdose; concentrated N-acetylcysteine

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266. Accidental chlorine gas exposure in a pediatric patient

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Background: Chlorine gas exposure can occur from multiple sources including in-home cleaning products, swimming pool chlorination reactions, industrial accidents, and intentional exposures with intent to harm as a chemical weapon. Toxic effects are mediated by the chlorine's reaction with water on the mucus membranes to form hypochlorous and hydrochloric acids. As this chlorine exposure can lead to serious pulmonary edema and ARDS, treatments leading to symptomatic relief and prevention of further complications are paramount.
Case report: A 9-year-old male presented to the ED after smelling a canister of chlorinated tablets by their pool approximately

30 min prior to arrival. He reported difficulty breathing and a persistent dry cough with dry heaving. He had a history of asthma and used albuterol as needed. His mother gave the patient an albuterol nebulizer treatment at home without improvement. On exam in the ED, the patient had difficulty speaking with intermittent coughing (oxygen saturation was 92% on room air). He had chest pain and was tachypneic without retractions. No wheezing was noted but he had coarse upper airway breath sounds. The patient had two episodes of desaturation to 89% and he was placed on 1 l supplemental oxygen via nasal cannula with improvement to 98%. He was given 4 ml of 3.75% sodium bicarbonate in nebulized solution over 15 min. Chest radiographs were unremarkable. His symptoms significantly improved after administration of the sodium bicarbonate nebulizer treatment and he no longer complained of pain or cough and was weaned to room air with oxygen saturations in the upper 90s. The child was admitted and continued to improve without any further interventions and remained on room air. He was discharged within 24 h without any further complication.

Discussion: Inhaled chlorine gas acts as a mucous membrane irritant. Its respiratory effects may produce shortness of breath, coughing, wheezing, and tachypnea. When the patient hyperventilates, an increased amount of chlorine is inhaled into the lungs, thereby causing more lung damage. Symptoms and findings are related to the concentration of chlorine in the air and to the duration of exposure, and usually begin within minutes or hours. Standard therapy for chlorine inhalation is largely supportive and consists of decontamination, humidified supplemental oxygen, and nebulized β-agonists for bronchospasm. Inhaled nebulized sodium bicarbonate has been suggested as a therapy for chlorine exposure. The proposed mechanism of the action is the neutralization of the formed acids in the respiratory tissues. Recommended dose concentrations are between 3.75% and 5%. Several observational studies and one prospective study has evaluated the utility of nebulized sodium bicarbonate for chlorine inhalation with conflicting results.

Conclusions: We describe the use of nebulized sodium bicarbonate for the treatment of chlorine inhalation injury in a young child. The patient's respiratory symptoms quickly resolved after 4 ml of 3.75% sodium bicarbonate solution. As chlorine inhalation remains a relatively common toxicological emergency, further long-term prospective clinical trials are needed to add support and evidence of safety to this treatment modality.

KEYWORDS Chlorine gas; pediatric; sodium bicarbonate

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267. The granny syndrome and severity of outcomes in pediatric poisonings

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Background: Studies have demonstrated that being under the care of grandparents—also known as "the granny syndrome"—can be potential risk factors for pediatric poisonings. Little is known on the severity of outcomes of pediatric patients with these risk factors. We hypothesize that such patients would be at a higher risk for more severe outcomes. The aim of this study is to compare outcomes in poisoned pediatric patients reported to our regional poison center (RPC) who are under the care of a grandparent compared to those who are not.

Methods: All pediatric (£6 years) poisonings reported to our RPC requiring admission to the hospital over a 2-year period (2016–2017) were retrospectively queried. Cases lost to follow up were excluded. Patients were divided into two groups: Group 1 were patients in whom grandparents were involved in their care at the time of exposure, and Group 2 were patients without grandparent involvement. A trained and monitored reviewer abstracted the following information: age, type of medication or product the patient was exposed to, what kind of container the xenobiotic was in at the time of exposure, length of stay (LOS), outcome, intensive care unit (ICU) admissions, rates of hypoglycemia (<60 mg/dl), intubations, and development of seizures.

Results: A total of 607 patients were included in this study (126 in Group 1; 482 in Group 2). Kappa was 0.8. The average age of patients in both groups was 2.1 years. When patients were under the care of grandparents a greater proportion of exposures involved a medicinal agent (94% in Group 1 versus63% in Group 2). Blood pressure medications were the most common type of medication exposure in both groups, but the percentage of exposures was higher in Group 1 (48% versus 15% in Group 2). Pill organizers were the most common source of exposure in Group 1 (25%) compared to pill bottles in Group 2 (15%). The average LOS was similar for each Group (1.3 versus 1.4 d). Outcome effects in Group 1 versus Group 2 were: none 52% versus 31%, minor 20% versus 27%, moderate 26% versus 39%, major 2% versus 3%, death 2% versus 0.2% respectively. Other objective comparisons between Group 1 and Group 2 were ICU admissions (60% versus 47%), hypoglycemia (8% versus 3%), intubations (3% versus 3%), and seizures (1% versus 1%) respectively.

Conclusions: While there were more medicinal (specifically antihypertensive medication) exposures in patients associated with grandparents, these patients had slightly better outcomes. However, ICU admission rate was 22% greater, and death rate was 5 times greater in Group 1 versus Group 2. Limitations of this study include its retrospective design, incomplete poison center records, potential inconsistent coding of outcomes severity, and the small sample size. Further and larger studies are required to fully understand the risk of severe outcomes in pediatric patients under the care of their grandparents.

KEYWORDS Pediatric poisoning; granny syndrome; severity of outcomes

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268. Let's Iron Out® What is Toxic in Here

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Background: Fluorosilicic acid is commonly used in low concentrations in water fluoridation, as well as in the tanning of animal hides, glass etching, in paints, oil well acidizing, wood preservation, hardening masonry, sterilizing equipment and for removal of mold, rust and stains. Exposure in workplaces that manufacture fluorosilicic acid can be expected, though use in the home is relatively low. We present a case in which the ingestion of a commercially available rust remover containing fluorosilicic acid caused life-threatening outcomes.

Case report: A 62-year-old male arrived at the emergency room after accidentally drinking Iron Out® that was stored in a

beverage container. He had pink-tinged emesis and was given intravenous fluids and ondansetron 8 mg. Although the original container had been disposed of, the nurse was able to verify that the product purchased contained fluorosilicic acid (unknown concentration) and oxalic acid 7–13% with a pH < 1. Over the next 3 h, his serum calcium level decreased from 8.7 mg/dl to 7.5 mg/dl and magnesium decreased from 1.6 mg/dl to 1.3 mg/dl. Poison control recommended giving 1 gram of calcium gluconate and replacing magnesium to 1.8 mg/dl, as well as following calcium and magnesium every 4 h and serial electrocardiograms (ECGs), though patient had a pacemaker. After supplementation, calcium and magnesium were within normal limits by hospital day 2, not requiring further repletion. On hospital day 2, calcium crystals were seen in the urine and blood oxalate levels were 8.8 mmol/l. Throughout the hospital course, his serum creatinine increased from 1.15 mg/dl to 7.5 mg/dl with anuria developing on hospital day 3. He received daily hemodialysis on hospital days 4–12, in which the last follow up was obtained. In addition, esophagogastroduodenoscopy on day 2 revealed gastritis with moderate to severe esophageal burns and hemorrhagic gastropathy (ungraded and patient complained of minimal pain), as well as vocal cord edema. On final follow up, patient was not able to be located and was assumed discharged to home.

Discussion: Fluorosilicic acid is a moderately strong acid (pH 1.2 for a 1% solution) that undergoes essentially 100% hydrolysis at the pH of drinking water to hydrofluoric acid and silica. Corrosive injury to mucous membranes, possibly delayed, and hypocalcemia and hypomagnesemia can be expected from hydrofluoric acid ingestion. In this product, fluorosilicic acid is not listed in the composition on the safety data sheet and no guidance is offered for exposure to this chemical. This case is complicated by the presence of oxalic acid, which also causes corrosive injuries, hypocalcemia and renal failure. Management of fluorosilicic acid and oxalic acid ingestions are similar, including monitoring ECGs, renal function, presence of oral burns and repleting electrolytes, specifically calcium and magnesium.

Conclusion: By raising awareness about fluorosilicic acid, aggressive management can be initiated as soon as poison control is aware of an exposure. Calcium repletion and ECG monitoring can begin either in transit or promptly after arriving at a health care facility and close monitoring could help mitigate complications.

KEYWORDS Fluorosilicic acid;hydrofluoric acid; oxalic acid

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269. Clinical manifestations and treatment of methamphetamine toxicity in children

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Background: Methamphetamine exposure is a common cause of stimulant toxicity in pediatric patients in the Phoenix metropolitan area. Our experience is that clinical signs of pediatric methamphetamine toxicity, including repetitive stereotypical movements, may be refractory to initial benzodiazepine therapy yet respond well to dopamine antagonists. There is little in the medical literature addressing the use of antipsychotics in the management of pediatric patients with sympathomimetic toxicity. Some authors caution against their use citing concern for adverse effects but offer little quantification of this risk. The aim of this study was to describe clinical manifestations and treatment of methamphetamine toxicity in pediatric patients including use of antipsychotics.

Methods: This is a retrospective review of patients age >2 months and ≤18 years admitted to a single tertiary care children's hospital with ICD-9 or ICD-10 codes suggestive of stimulant exposure between September 1, 2010 and July 31, 2017. Patients with clinical manifestations of sympathomimetic toxicity (defined as one of the following: hyperthermia >38 °C, tachycardia, hypertension, agitation, rhabdomyolysis (CK > 1000 IU/l), mydriasis or seizure) and confirmation of methamphetamine/amphetamine identified on comprehensive urine drug testing via GC/MS were included. Occurrence of complications after receiving antipsychotics, specifically hyperthermia, seizures, dystonic reactions, QTc prolongation >440 ms and Torsade de Pointes (TdP), were determined. Continuous variables were reported as medians and IQRs and categorical variables as percentages. Continuous variables were compared using Mann-Whitney U tests, and categorical variables were compared using Fisher exact tests.

Results: Seventy-nine patients were included. Route, nature and source of exposure are shown in Table 1. Clinical manifestations and presenting neurologic examination are summarized in Tables

Table 1. Route, nature, and source of exposure.

Route of exposure	Percent
Ingestion	46.1%
Unknown/not documented	43.4%
Insufflation	10.5%
Nature of Exposure	
Exploratory/accidental	44.0%
Unknown/not documented	33.3%
Intentional misuse/abuse	13.3%
Intentional self-harm	9.3%
Source	
Unknown	44.0%
Prescription	29.3%
Not patient's prescription	59.1%
Patient's prescription	40.9%
Illicit/drug of abuse	26.7%

Table 2. Clinical manifestations.

Clinical manifestation	Percent
Hypertension (age-based)	93.4%
Tachycardia (age-based)	85.7%
Abnormal motor activity	55.8%
Mydriasis	44.9%
Gastrointestinal symptoms	26.3%
Rhabdomyolysis (CK > 1000 U/l)	16.7%
Metabolic acidosis	14.3%
Hyperthermia (temperature > 38 °C)	11.5%
Diaphoresis	5.2%
Acute kidney injury	0.0%

Table 3. Presenting neurologic exam.

Neurologic exam	Percent
Alert/agitated	79.7%
Alert/not agitated	11.4%
Somnolent or comatose	7.6%
Hallucinations	5.1%
Other	2.5%

2 and 3, respectively. Median length of stay (LOS) was 45.4 (23.0–71.0) h. Patient disposition was as follows: 67.9% (53/78) discharged home, 16.7% (13/78) to inpatient psychiatry, 15.4% (12/78) other (i.e. child protective services custody), and no patients died. The most common treatments used were IVFs (96.1%) and benzodiazepines (77.9%). Antipsychotics were administered to 41% (32/78) of patients, with haloperidol being used in the vast majority 97% (31/32). No patients developed seizures, dystonia, TdP or required cooling after antipsychotic administration. QTc prolongation was noted in 38.6% of all patients with a median (IQR) QTc of 460 (448–475)ms. Of 5 patients with an EKG/rhythm strip after antipsychotics, two had QTc prolongation: one 442 ms and the other, 478 ms. In subgroup analysis, abnormal motor activity was more prevalent in the youngest group (<3 years) at 73.2% versus 16.2% in the oldest group (12–18 years) ($p < 01$). Antipsychotics were administered more often in the youngest group (47.6%) compared to the oldest group (20.8%) ($p = .038$).
Conclusions: This population of children with methamphetamine toxicity displayed many typical clinical manifestations of sympathomimetic toxicity with tachycardia (93.4%), hypertension (85.7%), agitation (79.7%) and abnormal motor activity (55.8%) occurring frequently. While we continue to use supportive care and benzodiazepines as first line therapy, antipsychotics are valuable adjuncts in the treatment of methamphetamine toxicity and were used without any adverse effects. Clinicians should consider antipsychotics in the treatment of methamphetamine toxicity in children.

KEYWORDS Methamphetamine; pediatric; exploratory

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270. "Paraquat tongue" in a child after a taste exposure to paraquat concentrate

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Background: Paraquat is a highly effective contact herbicide that displays dramatic toxicity. In the US, its sale and use are highly restricted, with use for residential purposes strictly prohibited. However, illegal transfer of paraquat into unlabeled containers for home use continues to cause poisoning, not only systemic toxicity but also lesser-known local tissue corrosion. We report a case of a month-long "paraquat tongue" in a toddler after a taste exposure to paraquat dichloride 30.1% contained in a cup.
Case report: A 23 month-old boy tasted residue from a cup that had held an unknown, concentrated hunter-green herbicide obtained from a family member. He immediately began spitting and his parents rinsed his mouth. Initial ED exam showed a green tongue, but he was otherwise asymptomatic during observation. The herbicide was later identified only as a Gramoxone formulation with the concentration of paraquat unspecified. At physician evaluation 24-hrs after exposure, he had only a runny nose, normal labs, and good food intake. However, later that evening he vomited once, and then awoke from sleep to spit out "green phlegm." At the 48-hr physician evaluation, repeat renal labs were normal, otitis media was diagnosed, and antibiotics given. Irritation of the inner lip and drooling were noted. Over the next day, he developed ulcerations on the inner lip and tongue and refused food except for pudding consistency, which was attributed by his pediatrician to a virus. On the next physician evaluation, 8 d after paraquat exposure, the anterior two-thirds of the tongue was markedly erythematous with a layer of necrotic tissue that stripped off to reveal a raw bleeding surface. He was still eating only soft food. It was finally determined that the child had developed "paraquat tongue" which is a manifestation of paraquat-induced local tissue injury that has delayed onset and healing. At this time the paraquat formulation in the cup was identified as Gramoxone Inteon® which contains 30.1% paraquat HCl, a dye, stenchant, emetic and purgative. Over the next 3 weeks the tongue gradually healed so that he was asymptomatic and back on a normal diet. Renal and pulmonary status remained normal.
Case discussion: Paraquat induces a self-sustaining production of oxygen radicals which harm lipid membranes. There is no known substance that can stop the damage once it begins. Systemic poisoning targets the lungs and can ultimately end in death weeks later. In localized oral injury, by day 5–7 the cascade of radicals produces necrotic sloughing with tender, bleeding, and bright red tissue underneath.
Conclusion: Illegal transfer into unlabeled containers is an exceedingly dangerous practice. Even trivial oral contact exposure to concentrated paraquat can cause significant injury to the oral mucosa. Ingestion of more than a taste puts the patient at risk of esophageal involvement as well as potentially fatal systemic toxicity. Poison centers and pediatricians need to be aware of delayed and poorly healing local damage such as "paraquat tongue" from a taste of a concentrated solution.

KEYWORDS Paraquat tongue; container transfer; pediatric

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271. The impact of an updated nicotine triage guideline on ED referral

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Background: Nicotine is not as potent as we have been led to believe. An editorial in Arch Toxicol (Mayer 2014) trace the origin of purported extreme nicotine toxicity to 1856; it has persisted unchallenged into current day literature. The poison center noted there was no significant toxicity in accidental pediatric nicotine exposure despite the purported 40–60 mg lethal dose. To reflect this reduced risk, we updated our maximum tolerated nicotine dose for home observation from 15 mg total ingestion in the former triage guideline (TG) to 2–3 mg/kg in the updated TG. We evaluated appropriateness and safety by comparing ED referral patterns and outcomes before and after instituting the updated TG.
Methods: We searched archived Toxicall® records for pediatric (0–5 years) nicotine cases over 12-month periods both before and after instituting the TG update. Multi-substance, non-oral, unknown outcome, and cases already-in-HCF were excluded. We abstracted each case data set to obtain the management site recommended by the SPI based on the TG in effect at the time, the actual management site, and the outcome. Triage failure was defined as moderate/severe outcome for a patient triaged to home observation. Data abstractors applied the same TG as did the SPI who triaged the case (audit); then the alternate TG not in effect at the time (cross-triage). We determined odds ratios for ED referral rates under both TG.

Cases using former TG ($n = 330$)							
Prospective triage by former TG		Cross-triage by updated TG		SPI recommendation using former TG		Actual management site	
Home	ED	Home	ED	Home	ED	Home	ED
297	33 (10%)	324	6 (1.8%)	297	33 (10%)	298	32 (9.7%)
Cases using updated TG ($n = 348$)							
Prospective triage by updated TG		Cross-triage by former TG		SPI recommendation using updated TG		Actual management site	
Home	ED	Home	ED	Home	ED	Home	ED
334	14 (4%)	292	56 (16%)	334	14 (4%)	329	19 (5.5%)

Results: After exclusions, there were 330 cases before TG update and 348 after. Of the cases before TG update, 33 (10%) were referred to ED. When the updated TG was applied to these same cases, only 6 (1.8%) warranted ED referral (OR 6, CI 2.5–14.5). Of cases after TG update, 14 (4%) warranted ED referral; while cross-triage using the former TG predicted that 56 (16%) would have been referred to ED (OR 4.5, CI 2.5–8.4). Patient safety was equal under both TG (before versus after TG update): No effect 230 versus 243 cases, $p = .98$; minor 100 versus 102, $p = .78$; moderate 0 versus 3, $p = .26$. There were no major outcomes or triage failures in either data set. When comparing referral patterns before and after TG update, 27 ED referrals would have been avoided had the updated TG been in place; while 42 ED referrals were avoided after instituting the updated TG.
Conclusions: Updates to the TG enabled SPIs to observe higher amounts of nicotine at home in young children, thus resulting in fewer ED referrals while maintaining patient safety. Such changes optimize healthcare resource utilization. Regardless of management site, the risk for serious nicotine toxicity in pediatric exposures appears low, thus supporting the assessment that nicotine toxicity has been overstated.

KEYWORDS Nicotine; pediatric; ingestion

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272. Symptomatic single-tablet propafenone ingestion in a 17-month-old

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Background: Propafenone is a type-IC anti-arrhythmic medication which exerts its effects via sodium channel blockade in the cardiac myocytes, slowing sodium ion influx and decreasing cell excitability. Conduction and refractoriness is prolonged across the myocardium, and spontaneous automaticity is reduced. It also exerts weak, non-selective beta-adrenergic receptor blockade. Case reports of propafenone toxicity are few in the literary corpus, and there is only one report of significant toxicity with single-tablet exposure. It is not commonly included on lists of medications that can cause toxicity in single-tablet pediatric exposures; however, it can cause significant hemodynamic effects in such settings. We describe here the unintentional, symptomatic exposure of a 17-month-old patient with a single tablet of propafenone.
Case report: A 17-month-old male ingested one tablet of propafenone 300 mg at approximately 1300. Two hours later, he became lethargic, irritable, and less interactive. Upon presentation to the emergency department, his heart rate and blood pressure were within age-appropriate ranges. Electrocardiography (ECG) revealed QRS widening to 163 msec and QTc prolongation to 552 msec. Repeat ECG revealed sustained prolongation of the QTc at 593 msec. He was given sodium bicarbonate and magnesium sulfate intravenously and transferred to another facility for pediatric intensive care admission. After 19 h of observation, his ECG intervals had returned to normal ranges and he was discharged in good condition with no long-term sequelae.

Table 1. Substances related to ED visit, by age group.

Substance	0–18 Years (200)	0–5 Years (63)	13–18 Years (130)
Oxycodone	29%	33%	27%
Hydrocodone	25%	10%	33%
Heroin	17%	–	27%
Buprenorphine	10%	32%	–
Tramadol	6%	11%	3%
Methadone	3%	6%	2%
Codeine	3%	3%	3%
Unknown opioid	3%	2%	4%
Morphine	2%	–	3%
Oxymorphone	1%	3%	–

Discussion: The usual pediatric dose of propafenone is 10–20 mg/kg/day in two or three divided doses. Our patient ingested approximately 28 mg/kg as a single intake and became symptomatic, though he required only appropriate supportive care. Previous reports of severe, life-threatening toxicity with propafenone range from 15 mg/kg to 133 mg/kg; this variability may be due to polymorphism in the enzymes responsible for metabolism of propafenone, as well as extensive, though saturable, first-pass metabolism affecting serum levels.
Conclusions: All patients presenting with suspected propafenone toxicity should be placed on continuous cardiac telemetry with frequent assessments of EKGs, vital signs, and neurological status. Gastrointestinal decontamination is generally not recommended; however, activated charcoal may be considered if presentation is early after ingestion and the patient's airway is controlled. There is no antidote or method to enhance elimination. Treatment is largely supportive and consists of fluids and vasopressors for hypotension, benzodiazepines for seizures, sodium bicarbonate and magnesium sulfate for QRS and QT interval changes, and electrical cardioversion as necessary. Consideration should be given to inclusion on pediatric single-tablet exposure lists.

KEYWORDS Pediatric; propafenone; toxicity

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273. The youngest victims of the opiate crisis: one healthcare system's pediatric Emergency Department opiate related encounters

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Background: Overdose is the leading cause of injury death in the United States (U.S.) and in this state which is now 7th in the nation for overdose deaths. Toxicologic ingestions are common in children and opiates are among the most dangerous ingestions. Recent national data showed that pediatric hospitalizations for opioid poisonings nearly doubled from 1997 to 2012.
Objective: To describe the characteristics of children seen for opiate-related events or conditions in the Emergency Departments (EDs) of a large U.S. health care system
Methods: We systematically collected demographic and clinical data from the electronic records of patients 0–18 years seen in any of 16 EDs in one healthcare system with ICD9 coding for opioid poisoning, opioid abuse, or opioid dependence from October 2013 to September 2015. This system accounts for 55% of the ED care in this state.
Results: Three hundred and twenty-five patients were identified by ICD code and 62% (200) of those were confirmed by chart review as experiencing an opiate-related event. The age distribution is bimodal, 32% 0–5 years, 65% 13–18 years (Image 1). Fifty-two percent were female. Ninety-two percent of exposures occurred in the home and none were at school. Events were concentrated in the state's urban and suburban population center. For medication exposures, 79% of substances were not the patient's: 61% parent/sibling, 17% other family. Substance breakdown is in Table 1. In 33%, the exposure was a self-harm attempt. Naloxone was administered en route to or while in the ED in 27%. Fifteen percent were admitted for behavioral health treatment and 24% were hospitalized for medical stabilization. Fifty percent of those admitted to a medical service required ICU-level care. There was 1 fatality. Fifty-one (26%) patients presented requesting detoxification, recovery treatment, and/or with opiate withdrawal symptoms; all were 14–18 years and 65% were discharged from the ED without placement in detox or treatment.
Conclusions: Children with opiate related ED visits in this healthcare system had a bimodal age distribution, mostly ingested medications belonging to family members, and 39% were admitted for further medical or behavioral health care. These results support redirecting anticipatory guidance to include screening for opioids in the home, education on the risks of opioid exposure in children, and access to naloxone rescue kits in homes with opioids and children present. Increased access to recovery services are also needed. Further evaluation of how current overdose prevention and treatment access strategies can target those at risk is necessary.

KEYWORDS Opiate overdose; pediatric; unintentional exposure

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274. Phenol toxicity from misuse of household products in a Latin American Community

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Background: Phenols (carbolic acid) are aromatic hydrocarbons found in household disinfectant products with potential for local caustic injury and systemic central nervous system, pulmonary, and cardiac toxicity. We report three cases within a Latin American community in NYC presenting with varying manifestations of phenol toxicity secondary to misuse of household products.
Case reports: An 82-year-old man with dementia presented to the ED after unintentionally biting into a bar of carbolic acid soap (concentration not specified) mistaken for food. He immediately spit out the product and irrigated with copious amounts of water. He developed edema of the lips and several shallow white ulcers on the tongue without drooling, stridor, or vomiting. The remainder of physical exam, vitals, ECG, venous blood gas, chemistry, CBC, chest x-ray, and flexible laryngoscopy were normal. He received methylprednisolone 125 mg IV and was discharged after 24 h of observation tolerating an advanced diet. A 76-year-old man without any known medical history, employed as a building superintendent, presented to the ED with altered mental status after using Creolin® (50% carbolic oil, 10% Xylenol, and 10% mixed chloroxylenol) as a cleaning agent. He had a strong chemical odor and was combative, requiring Haldol 5 mg IM, Ativan 2 mg IM, and physical restraints. He was hypoxic to 92% on room air, with scattered rales on lung exam, and bilateral fluffy infiltrates on chest x-ray. He had been working in a poorly aerated space, without protective gloves, mask, or goggles, and had not diluted the solution. He was showered in the decontamination unit and QT prolonging drugs were discontinued. Supplemental nasal cannula oxygen and cardiac monitoring was provided. Remaining vital signs, physical exam, ECG, venous blood gas, chemistry, CBC, carboxyhemoglobin, ethanol, acetaminophen, salicylates, urine toxicology, and head CT were normal. He was discharged within 48 h after return to normal mental status, resolution of pulmonary edema on serial x-rays, and normalization of oxygen saturation. An 11-year-old boy with asthma presented to the ED with shortness of breath, chest pain, and dysphagia after ingesting a teaspoon of Creolin®, misused as a cough syrup by his grandmother. He was tachypneic with a respiratory rate of 30 breaths per min, oxygen saturation 97%, and diffuse wheezes on lung exam. There was no drooling, stridor, vomiting, or ulcerations on oropharyngeal exam. Laboratory studies and CXR were unremarkable. He was provided with albuterol intermittently and discharged after 24 h of observation tolerating an advanced diet.
Discussion: Household use of phenols may be uncommon due to availability of safer products with less potential for CNS toxicity, cardiac dysrhythmias, caustic injury, and lung toxicity such as pneumonitis. The Latin American community in NYC may be accustomed to using phenols for household cleaning, and as purported remedies for hair lice, hair loss, impetigo, acne, and scabies among other ailments.

Conclusion: Phenol toxicity can occur from inhalation, ingestion, and dermal exposure. Misinformation about their utility, inappropriate application, and unsafe storage may lead to toxicity.

KEYWORDS Phenol; toxicity; hydrocarbon

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275. Naloxone Use in the Pediatric Population Reported to the U.S. Poison Centers

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Background: Between 1997 and 2012, the annual incidence of hospitalizations for opioid poisonings among children 1 to 4 years of age increased by 205% according to Healthcare Cost and Utilization Project. Naloxone reverses the effects of an opioids. Due to a lack of literature regarding naloxone use in children, the goal of this study was to evaluate the trends in naloxone reports in young children from acute care hospitals and EDs (ACH) using the National Poison Data System (NPDS).
Methods: Exposures among children under 6 years of age where naloxone therapy was "Recommended and/or Performed" from 2003 to 2016 were included for the analyses. Patterns of naloxone use in this population reported by ACH was evaluated in a sub-analysis. Descriptive statistics were used to analyze the characteristics of naloxone reports. Poisson regression models were used to evaluate the trends in the rates of naloxone reports (per 100,000 exposures in $<=5$ years). The percentage changes and corresponding 95% confidence intervals (95%CI) during the study period were reported.
Results: Overall, there were 18,604 cases of children under 6 years of age that reported naloxone therapy to the U.S. PCs during the study period. The number of naloxone reports increased from 567 cases in the year 2003 to 1445 cases in 2016. Among these cases, 60.7% were reported from ACH, with these cases also demonstrating and increase from 466 to 1008 calls during the study period. The proportion of cases from ACH among the overall calls increased from 55.7% to 69.7% during the study period. The proportion of cases where naloxone was utilized prior to PC recommendation was higher than cases where naloxone use occurred by recommendation in both total cases and cases from ACH (37.3% versus 30.2% and 43.6% versus 32.4%, respectively). Males accounted for 54.1% of the cases. Single substance exposures (84.1%) accounted for majority of the cases. The most frequent reason for exposure among this population was unintentional (91.4%), with therapeutic errors causing 761 exposures. Moderate clinical effects were seen in 40.6% cases, while major clinical effects accounted for 10.2% of the sample. Minor outcomes were reported for 30.2% cases. There were 50 deaths in this group during the study period. Characteristics of patients and exposures reported from ACH demonstrated similar patterns. The most frequent opioid reported for exposures overall and from ACH was oxycodone (10.6% and 11.4%, respectively), while clonidine (28.4% and 30.9%, respectively) was the most common non-opioid substance causing toxic exposures. The rate of naloxone reports overall (113.2%, 95% CI: 59.6%–184.7%, $p < .001$) and from ACH (69.8%, 95% CI: 55.7%–85.2%, $p < .001$) increased significantly.
Conclusions: Naloxone use among cases less than 6 years of age increased. The majority of pediatric cases demonstrated moderate and major clinical effects; however, naloxone was used in 30.2% of cases with minor only effects which raises the question of why naloxone was administered. As would be expected, the most commonly reported final exposure substance was an "opioid" and the most common reason for exposure was "unintentional".

KEYWORDS Naloxone; pediatrics; poison centers

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276. Exploratory Pediatric Ingestion of Dimethyl Fumarate

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Introduction: Dimethyl fumarate (Tecfidera®) was approved in 2013 to treat adult patients with relapsing/remitting multiple sclerosis. The exact mechanism underlying its therapeutic effect remains unknown. Both dimethyl fumarate (DMF) and its active metabolite, monomethyl fumarate, are theorized to provide anti-inflammatory and cytoprotective therapy via activation of a specific nuclear factor pathway, Nrf2. DMF is manufactured as 120 mg and 240 mg delayed release capsules To the best of our knowledge, no case reports of unintentional pediatric DMF overdose have been published. Here we present a case of a 16-month-old who ingested a capsule of DMF 240 mg.
Case report: A local urgent care provider contacted the regional Poison Center (PC) 30 min after a 16 month-old boy who was found holding his father's pill box. The only medication missing was a single DMF 240 mg capsule. The child's mother had immediately induced vomiting, and retrieved the bottom half of the capsule shell. The child developed facial flushing 1 h after the incident; this spontaneously subsided. Per the provider's assessment, the child was acting normally, and in an age-appropriate manner. Based on the pharmacokinetic profile of DMF, the PC recommended a 3-h observation period at the urgent care center; the child was discharged home with the PC continuing to follow the patient's progression at home. A 1-week follow-up appointment with the pediatrician was scheduled to verify cell counts following the exposure. At 3 h post ingestion, the child showed no symptoms, including gastrointestinal effects. No abnormal muscle movement or abnormal tone developed. At 24 h post ingestion, the child developed what his mother described as "a little bit" of diarrhea, but was otherwise without symptoms, and with normal urine output. Flushing did not recur. At 1 week post-ingestion, the child remained asymptomatic; the pediatrician decided against recommended follow-up laboratory work-up.
Discussion: Little is known about the effects of acute exposure to DMF in young children. The pharmacokinetic and pharmacodynamic profile of DMF suggest a time to peak effect of 2 to 2.5 h, with a delay to 5.5 h if ingested with food. Approximately 60% is excreted via exhalation as carbon dioxide; 16% is eliminated in the urine as the metabolite, monomethyl fumarate. DMF undergoes extensive hydrolysis to its active metabolite, which is then further metabolized via tricarboxylic acid cycle into fumaric acid, citric acid, and glucose. While common side effects include flushing and gastrointestinal symptoms, cases of progressive multifocal leukoencephalopathy and significant post-marketing cases of hepatic injury are reported; lymphopenia and proteinuria are also reported following chronic DMF therapy.

Conclusion: No reports of acute DMF overdose in children have been published. Our experience suggests that known side effects common to therapeutic treatment in adults – flushing and gastrointestinal upset – are likely in acute unintentional overdose, as well. It remains unclear if intentional ingestions of larger DMF doses will precipitate further toxicity, however this case suggests that concerns regarding acute toxicity in a low dose, exploratory setting are limited to symptoms treated easily with supportive cares alone.

KEYWORDS Pediatrics; dimethyl fumurate; multiple sclerosis

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277. Asystole complicating a pediatric cannabinoid exposure

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Background: Marijuana and other cannabinoids are well known to cause psychological effects. While tachycardia is reported following acute marijuana exposure, chronic exposures can result in bradycardia. We report a case of asystole associated with an acute ingestion of a marijuana edible product.
Case report: A 4-year-old child without any significant past medical history presented to an outside hospital with altered mental status. That eventing the family went to a relative's house for a Christmas party. As they were about to leave, his parents noticed that his behavior was different. His speech and his gait were altered and his reactions and responses were slowed. Aside from an upper respiratory illness that had resolved 2 weeks ago, he was in good health and acting normally prior to the party. Upon further questioning, he admitted to reaching into the trash to eat a cookie, which was a marijuana edible. No other medications were present or missing and he did not have a history of other accidental ingestions or exploratory behavior. At a local hospital, his labs including a serum ethanol and metabolic panel were unremarkable aside from a urine drug screen (UDS) that was positive for cannabinoids. Because he was altered, he was transferred to our tertiary care center. In our emergency department, he was evaluated by social work with a plan to discharge him once his mental status returned to normal. He was improving when he suddenly went unresponsive and a 15 s asystolic event was captured on the monitor. He was noticed to be slightly rigid and was apneic. He did not have any clonic or other seizure-like activity but was incontinent after the event. He spontaneously returned to normal without a postictal period. Prior to the event, his heart rate ranged from 70 to 110 bpm with a normal blood pressure. Repeat laboratory investigation was normal. A repeat UDS was not obtained. Electrocardiograms (EKGs) before and after the event were also unremarkable. He was evaluated by cardiology who confirmed the asystolic event and admitted him to their service. No other arrhythmias were captured overnight. A follow up EKG the next morning was normal and he was no longer altered. A transthoracic echocardiogram obtained that morning was also normal. No other etiology was found. No other arrhythmias occurred over the following 4 months.
Case discussion: Cardiac arrhythmias are associated with cannabinoid exposures. Rarely, asystolic events are reported in older individuals following recreational use of marijuana and other cannabinoids. The amount of marijuana and other cannabinoids in edible products continues to increase. Additionally, these products continue to be become increasingly more potent which leads to increasing toxicity. Given the increasing number of states that are legalizing either recreational or medicinal marijuana, it is important to remember that these products are far from harmless. This is especially important as opinions regarding their safety continue to change as legalization increases.
Conclusion: We describe a child with asystole following consumption of a marijuana edible product.

KEYWORDS Marijuana; cannabinoids; arrhythmia

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278. Not just malignant: an insidious presentation of malignant hyperthermia crisis in a patient with a KCNA1 mitochondrial myopathy

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Background: Malignant hyperthermia is a hypermetabolic reaction to volatile anesthetics, succinylcholine, heat or vigorous exercise. Malignant hyperthermia crisis can occur immediately following anesthetic induction, during administration or within minutes of stopping the anesthetic. Early findings include hypercarbia >55 mmHg, sinus tachycardia and rigidity, with late findings comprised of hyperthermia, rhabdomyolysis, and possible multi-organ system failure. Due to variable penetrance of the inherited trait and contemporary changes in anesthetic techniques, diagnosis may be delayed or missed. Patients with mitochondrial myopathies can have worsening of their baseline myopathies under any stress, so the connection between these conditions and malignant hyperthermia remains controversial, though a handful of case reports suggest an association. Finally, genetic testing is specific, but not sensitive, with the caffeine-halothane contracture test being the gold standard for diagnosis.
Case report: An 8-year-old girl with medical history notable for mitochondrial deletion syndrome and episodic ataxia (mutation KCNA1) presented to the ED for altered mental status and muscle rigidity, 12 h after discharge from the PACU. She had undergone an elbow arthrogram the prior day, receiving sevoflurane 26.32 ml, propofol 40 mg, rocuronium 20 mg, and neostigmine 1 mg during the 13-min procedure. Intraprocedurally, her pCO_2 peaked at 55 mmHg with peak HR 140/min, peak RR 34/min and peak temperature 37.1C. Postprocedurally, her tachycardia resolved, but she was rigid; however, this was attributed to her baseline spasticity and she was discharged. On awakening the next day, she had lead pipe rigidity and somnolence. Presenting ED vitals were T 36.4C, HR 173/min, RR 52/min, BP 127/90 mmHg, SpO_2 99%. Within 2 h, her temperature had increased to 38.5C. Dantrolene 1 mg/kg was given with resolution of rigidity and normalization of vital signs. Withdrawal of dantrolene at 24 h was attempted, but tachycardia and rigidity returned so it was continued for another 24 h. The patient was discharged at baseline on hospital day 3, with malignant hyperthermia confirmatory testing pending.
Case discussion: Patients with underlying spastic myopathies present a challenge to providers when detecting malignant hyperthermia, especially when signs and symptoms develop insidiously. In this patient's case, her hypercarbia was not trended and rigidity was attributed to baseline spasticity. The fact that she did not become hyperthermic until nearly 16 h post-anesthesia was also deceptive. General anesthesia has progressed since the era of halothane. Newer agents, like sevoflurane, are known to trigger relatively late in administration, and early withdrawal of the offending

agent leads to symptom abatement. Moreover, neuromuscular blockade is also mitigating. Mitochondrial myopathies are a diverse collection of pathologies and stress is known to worsen symptoms. However, some appear more susceptible to malignant hyperthermia, sometimes through mutations not involving known malignant hyperthermia genes (RYR1 and CACNA1S). KCNA1 was implicated as one of those genes in a 2016 paper.
Conclusions: We describe an insidious presentation of malignant hyperthermia crisis in a patient with a KCNA1 mitochondrial myopathy. Providers should be sensitive to subtle diagnostic markers such as hypercarbia and consider malignant hyperthermia even when triggering agent exposure appears relatively remote. Certain mitochondrial myopathies may confer additional susceptibility.

KEYWORDS Malignant; hyperthermia; mitochondrial

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279. Sustained stimulation? pediatric modified release stimulant exposures reported to the NPDS

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Background: Modified release stimulants (MRS) are commonly used in the treatment of attention-deficit/hyperactivity disorder (ADHD). The numbers of these products have increased over the last decade. Due to their prevalence and modified release properties they may pose a significant toxicity risk in the pediatric population. We sought to characterize pediatric single agent MRS exposures reported to the National Poison Data System (NPDS).
Methods: The modified release stimulant product codes for this dataset were gathered through an analysis of Micromedex product codes that fall under the amphetamines and related compounds and methylphenidate generic codes. Using the identified set of product codes, SQL queries were written to extract data from the NPDS database for cases from December 1, 2007 to December 31, 2017. The result set was validated by two separate data analysts – one external to the AAPCC Central Office and one within the Central Office. Cases involving single agent MRS exposures in patients less than 19 years of age were selected. All data entered into NPDS was collected and analyzed using Microsoft Excel (Microsoft Corp., Redmond, Washington, 2010).
Results: A total of 28,544 cases of single agent MRS exposures were identified. The average age was 1.43 years (range 1 month–18 years, SD 1.54) and 64% of cases were male ($n = 18,389$). The highest number of cases were reported in 2008 ($n = 3160$). There were 2853 exposures reported in 2017. Sixty-seven percent of cases ($n = 19,156$) involved an acute exposure. Unintentional therapeutic error was the single most common reason for exposure ($n = 12,814$). Overall unintentional exposures accounted for 85% ($n = 24,170$) of exposures. Ingestion of the MRS was reported in 28,445 (99%) exposure but there were 152 cases (0.5%) where exposure was via inhalation/nasal route. Focalin (dexmethylphenidate) XR was the most common single agent identified ($n = 7732$). Table 1 lists the top five MRS reported. Ninety-two percent ($N = 26,222$) of exposures occurred at the caller's residence and 65% ($n = 18,690$) of calls originated from own residence. Thirty-nine percent ($n = 11,166$) of cases were either referred to or managed in a health care facility (HCF). Of symptoms documented as being related, tachycardia ($N = 3546$) was the most common. Agitation was documented as related in 2808 cases while drowsiness/lethargy was documented as related in 1050 cases.

Table 1. Top five most common modified release stimulants products reported to NPDS for pediatric exposures.

MRS product	# of Exposures reported
Focalin XR	7732
Adderall XR – 20 mg capsule	3347
Adderall XR – 30 mg capsule	3009
Ritalin LA	2542
Quillivant XR	2371

Benzodiazepines were given in 1374 cases. The most common disposition for those referred/treated at a HCF was treated and release ($n = 6985$). Nineteen percent ($n = 2082$ cases) were admitted to either a noncritical care unit ($n = 1209$) or critical care unit ($n = 873$). Of the 15,683 cases that were followed to a known medical outcome there were 90 major effect, 2776 moderate effect and 4370 minor effect. There were no deaths reported.
Conclusions: Pediatric single agent MRS exposures were typically unintentional and not associated with major effects or death.

KEYWORDS Stimulant; modified release; amphetamine

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280. Iatrogenic methylergonovine exposure in a 2-h-old infant

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Background: Methylergonovine (MEV) is a semi-synthetic ergot amine alkaloid used to control postpartum hemorrhage through direct stimulation of uterine and vascular smooth muscles. MEV interacts with alpha-adrenergic, dopaminergic and serotonergic receptors resulting in vascular, central nervous system and smooth muscle effects. Multi-organ ischemia may result from alpha-adrenergic agonism; respiratory failure, seizures and hypotension are described in newborns administered MEV.
Case report: A 3840-g, full-term male was born in an outpatient birthing center via vaginal delivery to a 32-year-old gravida 1, para 0 mother. Apgar scores were 8 and 9 at 1 and 5 min. The infant was uneventfully discharged home with parents 4 h after birth, a common practice for this birthing center. At 7 h postpartum, the practitioner discovered that 0.2 mg (0.2 mg/ml) MEV was administered intramuscularly 2 h after birth instead of vitamin K. The family was alerted and directed to present to a children's emergency department. Initial vital signs were HR 127 bpm, BP 89/62 mmHg, SpO_2 97% on room air, respiratory rate 40 and temperature 36.5 °C. Physical exam was unremarkable. Initial labs revealed sodium 133 mEq/l, glucose 64 mg/dl, creatinine 0.62 mg/dl and lactate 33.4 mg/dl. Venous blood gas showed pH 7.22, pCO_2 67 mmHg and pO_2 35 mmHg. Intravenous 0.9% sodium chloride was started at 5 ml/kg/h. After episodes of diminished air entry, decreased respiratory rate (27bpm) and hypoxia (SpO_2 89%), oxygen (4L) was started via high-flow nasal cannula and he was transferred to neonatal intensive care (NICU). Six hours later oxygen was discontinued after capillary blood gases showed pH 7.33 and pCO_2 48 mmHg. Systolic and diastolic blood pressure ranged from 65 to 95 mmHg and 45–64 mmHg throughout the 16 h after admission. Heart rate ranged between 118 and 159 through the hospital stay. Serum lactate decreased to 24 mg/dl and 19 mg/dl 12 and 24 h after admission. Two days post-exposure the neonate discharged from the hospital.

Table 1. CPAP – continuous positive airway pressure, CNS – central nervous system, ABG – arterial blood gas, PCC – poison control center

Reported methylergonovine (MEV) exposures to a regional poison center, 2002–2018

Case number	1	2	3	4	5
Age at hospital admission (hours)	7	Less than 9	3	2	–
Gestational age	Full term	Full term	35 weeks	–	–
Birth weight (g)	3840	–	–	–	–
Gender (M/F)	M	M	F	F	F
Methylergonovine dose (mg)	0.2	0.18	0.1	0.2	0.2
Signs and symptoms					
Respiratory depression	Y	Y	–	Y	–
Hypertension (mmHg)	Y (94/64)	–	–	–	Y
Hypotension (mmHg)	N	–	Y (70/19)	–	–
Interventions					
Oxygen requirement	Y	Y	Y	Y	Y
CPAP	–	–	Y	–	–
Intubation	N	Y	N	N	Y
Duration (d)	–	1	–	–	1
Nitroprusside intravenous	N	Y	N	N	Y
Maximum dose (mcg/kg/min)	–	1.2	–	–	–
Duration (d)	–	1	–	–	2
Fluids	Y	N	N	N	N
Clinical features					
CNS	–	Hyperirritable, exaggerated startle reflex	Posturing	–	Posturing, questionable seizure-like activity requiring lorazepam
ABG	Hypercarbia, acidosis	Hypercarbia (pCO_2 94 mmHg)	Hypercarbia	–	–
Oliguria	N	Y	N	N	N
Serum creatinine (mg/dl)	0.62	1.2	–	–	–
Elevated lactates (mg/dl)	Y	–	–	–	–
PCC follow-up (d)	2	5	1	1	3
Outcome	Recovery	Recovery	Recovery	Recovery	Recovery

Case discussion: Previous case series have described iatrogenic MEV exposures in neonates mimicking sepsis, with common symptoms of lethargy, feeding intolerance, hypoventilation and seizures. In the past 16 years, our regional poison center was alerted to 4 additional iatrogenic MEV cases (see Table 1). Exposures ranged from 0.1 to 0.2 mg, with three cases of respiratory depression and hypercarbia. All received supplemental oxygen and two required mechanical ventilation. Other interventions included: intravenous sodium nitroprusside, benzodiazepines for suspected seizure-like activity, and furosemide for oliguria. All cases were managed in NICU and fully recovered with poison center follow up at 1 to 5 d. Symptoms of MEV toxicity in the first few days of life might easily be missed in infants discharged from birthing centers immediately post-partum.
Conclusion: We report respiratory depression, hyponatremia and lactatemia after iatrogenic administration of MEV to a 7-h-old neonate. Previous local and national cases highlight the significant adverse effects and potentially fatal outcomes surrounding iatrogenic MEV exposure; NICU monitoring is thus advised following exposures. Heightened medication safety practices, including isolation of medications for maternal post-partum care, are recommended in delivery centers, particularly in light of their popularity as an alternative to traditional in-hospital labor and delivery units.

KEYWORDS Methylergonovine; iatrogenic; neonatal

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281. Benign outcomes among unintentional exposures to pimobendan

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Background: Vetmedin® is the brand name for pimobendan, a veterinary pharmaceutical marketed to treat congestive heart failure in dogs. According to the prescribing information, "Pimobendan exerts a stimulatory myocardial effect by a dual mechanism of action consisting of an increase in calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase (Type III). Pimobendan exhibits vasodilating activity by inhibiting phosphodiesterase III activity." This is similar in mechanism to milrinone[OTD1] (somewhat also to that of levosimendan), which is known to cause hypotension in overdose. Pimobendan was approved for use in dogs by the US Food and Drug Administration (FDA) in April 2007. It is also approved for use in humans in Japan. It is rapidly absorbed; the oral bioavailability in dogs is 60–63% and is significantly reduced when ingested with food. We report a summary of 9 unintentional exposures to pimobendan and their outcomes.
Case series: Nine cases are reported, spanning the years 2011–2017. Age distribution was bimodal: three cases involved children ≤2-years-old (11 months–2 years); the remaining six cases were of adults 44–75 years of age. Females comprised 56% (5/9) of the cases. All exposures were coded "unintentional". Estimated exposure doses ranged from 0.125 to 15 mg, however 8 of the 9 cases involved exposures of 2.5 mg or less. The single case of 15 mg exposure was in a 2-year-old boy, for which the quantity was estimated as a maximum. Only 2 of the victims were referred to healthcare facilities, both of them 2-year-old boys. Seven of the nine cases were coded as "No Effect"; the other 2 as "Minor Effect". The cases coded as "Minor Effect" were 59-year-old and 75-year-old women. Documented effects were "brief lightheadedness" and belching, both resolving spontaneously.
Discussion: Among 9 cases of unintentional exposure to pimobendan, three were children under the age of 3 years. Minimal symptoms were reported, and there were no hospital admissions or medical therapies. Absent hypotension in these cases may have resulted from low-dose unintentional exposures or from the competing inotropic and vasodilatory effects of pimobendan.

Conclusions: Despite the possibility of hypotension from pimobendan exposure, it appears that unintentional exposures result in minimal to no toxicity, and likely can be safely managed at home by Poison Control Centers.

KEYWORDS Pimobendan; vetmedin; levosimendan

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282. The clinical course after extreme inhalational overdose of a long-acting betaagonist

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Background: Inhaled β2 receptor agonists reduce bronchoconstriction and improve laminar airflow through bronchioles. These commonly prescribed medications have well-known adverse effects in overdose, including tremulousness, tachycardia and hypokalemia. Long-acting β2 agonists (LABA) such as formoterol are used to treat asthma and chronic obstructive pulmonary disease, and to prevent wheezing caused by exercise. In asthma, LABAs must be used in combination with a long-term asthma control medication, and are most often prescribed in combination inhalers with corticosteroids. Large inhalational overdoses of LABA may result in prolonged pronounced systemic effects partially due to oral drug deposition, ingestion and gastrointestinal absorption. Very few cases of extremely large inhalational LABA overdoses exist, particularly in children.
Case report: A 10-year-old boy with asthma intentionally inhaled 94 puffs of his prescribed Dulera® (formoterol fumarate dihydrate 5 mcg/mometasone furoate 100 mcg) in rapid succession out of his own curiosity. Sertraline and guanfacine were taken as prescribed. The patient presented to the emergency department less than 45 min after exposure with tachycardia (HR 151), tachypnea (RR 30), agitation and diaphoresis. EKG on presentation revealed sinus tachycardia with QRS 102 msec and QTc 502 msec. Electrolyte derangements were seen, including hypokalemia (K 2.2 mEq/l), hyperglycemia (201 mg/dl) and total CO_2 19 mEq/l. Blood pressure dropped from 103/51 to 73/41 mm Hg shortly after presentation, and the patient experienced nausea and vomiting. BP improved after intravenous fluid administration. Agitation was treated with lorazepam 1 mg. Potassium was replaced and improved to 3.6 mEq/l but QTc remained prolonged at 529 msec. QTc gradually normalized to <500 msec by 8 h post-exposure, but tachycardia persisted for 12 h and tremor for nearly 24 h. The patient was discharged on hospital day three.
Discussion: This case describes the time course of clinical effects after an extremely large LABA inhalational exposure. Hypokalemia and significant sympathomimetic effects developed, as expected. Our patient also became hypotensive and had persistent prolongation of the QTc interval on EKG, likely secondary to his electrolyte disturbances. The use of guanfacine in our patient may have blunted some of the cardiovascular effects of the LABA overdose. Due to the long duration of action of formoterol, the patient remained symptomatic for nearly 24 h and required prolonged observation and supportive care.
Conclusion: After an excessive inhalational exposure to a LABA, our patient experienced prolonged tachycardia and tremulousness in addition to hypotension, hypokalemia, and prolongation of the QTc interval. Providers should be aware that large LABA exposures may require a prolonged observation period.

KEYWORDS LABA; pediatric; asthma

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283. Sustained low-efficiency dialysis (SLED) therapy following Ingestion of Isopropanol in a pediatric patient

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Background: Cardiovascular collapse due to large ingestions of isopropanol is rare. Usually supportive care with IV fluids and airway support are the mainstay of treatment. Dialysis is usually only recommended with a severely symptomatic patient or an isopropanol level ≥500 mg/dl.
Case report: A 14-year-old 50 kg male was initially reported to have ingested an unknown amount of HEET® gas line antifreeze about 1 h prior to emergency department (ED) arrival. The patient was falling asleep within 30 min of ingestion and was being intubated when the local poison center was contacted. Suspecting a toxic alcohol ingestion, the poison center specialist recommended giving a dose of fomepizole and transporting the patient to a facility where dialysis could be performed. Upon arrival to a pediatric intensive care unit (PICU), the patient went in to cardiac arrest and pediatric advanced life support (PALS) was performed. Upon the establishment of a cardiac rhythm, his HR was 67 and BP 52/24 mmHg. After titrating dopamine (20 mcg/kg/min), epinephrine (0.3 mcg/kg/min), and phenylephrine (0.5 mcg/kg/min) the patient's blood pressure came up to 96/56 mmHg.
Despite severe CNS, respiratory depression and cardiovascular collapse, the patient was not initially acidotic. The patient did have an elevated osmolar gap. Approximately 6 h post ingestion relatives updated the history to reflect that the product was in fact called ISO-HEET® which contains 99% isopropanol. Based on these concerns, a serum isopropanol and acetone levels were obtained that resulted at 475 mg/dl and 75 mg/dl respectively. The patient's lactate increased from 3 mg/dl to 8.2 mg/dl at 4-h and 12-h post ingestion respectively.
Due to the patient's cardiovascular collapse, hemodialysis was not a viable option. The patient was started on sustained low-efficiency dialysis (SLED) which commenced 11 h post-ingestion. Serum and ultrafiltrate concentrations for isopropanol and acetone decreased to normal range over the course of SLED therapy. The patient's pre-dialysis clearance was calculated as 39.81 ml/min based on measured t1/2 and estimated Vd. During SLED therapy the machine alone was able to clear isopropanol and acetone at 41.21 ml/min and 32.80 ml/min respectively. The patient recovered over time without neurologic sequela.
Discussion: Critically ill patients can often require renal replacement therapy or hemodialysis. SLED therapy is a lower volume renal replacement therapy and the goal of therapy is to provide the patient with a normal renal function in a time when the kidneys are not adequately removing the drug or toxin from systemic circulation. In the hemodynamically unstable patient with acute renal failure (ARF), blood flow often cannot be maintained that would allow adequate drug/toxin clearance. SLED was instituted in this patient primarily for treatment of elevated serum lactate, isopropanol, and acetone concentrations. This therapy was able to provide our patient with a clearance equivalent to his systemic clearance during a time of hemodynamic instability. This effectively doubled his drug removal.
Conclusion: SLED therapy is a viable treatment option when a patient is hemodynamically unstable and hemodialysis is not an option.

KEYWORDS Sustained low-efficiency dialysis (SLED); isopropanol; pediatric patient

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284. Neonatal resistance to transplacental acetaminophen hepatotoxicity

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Background: Premature newborns have diminished cytochrome metabolism and should have less risk of hepatotoxicity from acetaminophen (APAP). We describe a materno/fetal dyad with maternal APAP exposure with significant maternal toxicity and no apparent neonatal hepatotoxicity despite similar treatment with N-acetylcysteine.
Case reports: A 1.7 kg 30 week pre-term infant was born to a 27-year-old mother. At birth the mother had an acetaminophen level of 134 mcg/ml. The mother admitted to taking a full bottle (bottle size unknown) of acetaminophen the day and night preceding the birth of the baby for a toothache. A serum acetaminophen concentration was performed on the baby and confirmed the presence of a high serum acetaminophen level at 122 mcg/ml. The child had bleeding issues around the central line and indications of coagulopathy. Platelets were initially 140,000 but dropped to 97,000. PT and PTT were abnormal and treated with fresh frozen plasma and packed red blood cells. The infant's liver enzymes indicated very little evidence of hepatotoxicity (AST 51, ALT 10, alkaline phosphatase 124 and total bilirubin of 3). At admission, intravenous N-acetylcysteine was given according to the following protocol: 150 mg/kg over 1 h, then 50 mg/kg over 4 h, then 100 mg/kg over 16 h. The APAP level decreased to 48 mcg/ml, and NAC was continued until the acetaminophen level was less than 10 mcg/ml. Labs performed at the end of NAC therapy indicated AST 21, ALT 10, INR 1.3, and platelets 141. In contrast, the mother's liver enzymes and coagulation profile were both abnormal: ALT 2657, AST 3837, PT 32.7, INR 3.4. Intravenous N-acetylcysteine was given: 150 mg/kg over 1 h, then 50 mg/kg over 4 h, then 100 mg/kg until liver enzymes decreased to AST 884, ALT 2854, T bilirubin 3.7, PT 21.4, INR 2.2 and lactate 1.3. This ingestion produced significant maternal hepatotoxicity but minimal neonatal hepatotoxicity despite similar exposure and treatment supporting the hypothesis that newborns are relatively protected from APAP liver damage because of diminished cytochrome formation of NAPQI. The serious problems of the neonate may reflect significant prematurity and the relation of the APAP to those findings are unknown.

KEYWORDS Neonatal; acetaminophen; hepatotoxicity

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285. Severe hemolytic anemia due to ingesting naphthalene-containing moth repellent balls

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Background: The vast majority of pediatric mothball ingestions result in minimal toxicity. In 2016 the National Poison Data System reported only three major outcomes from naphthalene. We report a case of severe hemolytic anemia after ingestion of moth repellent balls containing naphthalene.
Case report: A 14-month-old male with history of sickle cell trait on no daily medications, presented to the emergency department with lethargy. His mother reported finding him eating naphthalene-containing mothballs 2 d prior. He initially vomited twice, then developed irritability, lethargy and fever over the following 24 to 48 h. Fragments of moth balls were noted by the mother in his diaper. On arrival, vital signs included: temperature of 38.9; HR 178 bpm; BP 102/82 mmHg; respiratory rate 40; SpO_2 95%. Physical exam revealed mild distress, crying, tachypnea and scleral icterus. Heart and lung exam was normal. Initial laboratory studies included hemoglobin 3.6 g/dl (10.9 g/dl 20 d earlier), indirect bilirubin 1.8 mg/dl, LDH 3331 u/l (0–85), haptoglogin 43 mg/dl (35–200) and methemoglobin of 6%. The patient was treated with a single transfusion of packed red blood cells and supportive care. Methylene blue was not used. Additional workup while hospitalized included peripheral blood smear and G6PD. He recovered fully and was discharged after a 2-d hospitalization.
Case Discussion: Hemolysis and methemoglobinemia have been reported from exposures to naphthalene but is rare. Toxicity can be more severe in those with G6PD deficiency, infants, sickle cell disease or sickle cell trait. Methylene blue was not used due to the combination of low methemoglobin level and concern for further hemolysis.
Conclusion: This was a case of severe hemolytic anemia due to ingestion of naphthalene moth balls, likely magnified due to his concomitant sickle cell trait.

KEYWORDS Mothball; naphthalene; hemolysis

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286. Pediatric guanfacine exposures reported to the National Poison Data System, 2000–2016

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Background: Guanfacine is a centrally acting a2 -adrenergic receptor antagonist similar to clonidine used in the treatment of attention-deficit/hyperactivity disorder (ADHD). Adverse effects of guanfacine are secondary to the drug's sympatholytic effects and include somnolence, bradycardia, and hypotension. Toxic manifestations seen in unintentional guanfacine exposures and overdose are largely an extension of these adverse effects, including significant central nervous system depression, and delayed and prolonged hypotension. The purpose of this study was to characterize the frequency, clinical manifestations, treatments, durations of effects, and medical outcomes of pediatric guanfacine exposures reported to the National Poison Data System (NPDS) from 2000 to 2016.
Methods: This study was a retrospective review of data extracted from poison control center call records for pediatric ($\leq$19 years of age), single-substance guanfacine ingestions reported to NPDS between 2000 and 2016.
Results: A total of 10,927 cases were identified for analysis. The average age was 7.1 ± 4.6 years (range: 2 months–19 years). Pediatric single-substance guanfacine exposures reported to NPDS increased more than six-fold during the study period, with 207 cases reported in 2000 compared to 1388 cases reported in 2016. The most commonly documented clinical effects were drowsiness ($n = 4262$, 39%), bradycardia ($n = 1696$, 15.5%), and hypotension ($n = 1127$, 10.3%). Coma was observed in only 24 patients (0.2%).

The most common therapeutic intervention was intravenous fluid administration ($n = 1815$, 16.6%). Naloxone was utilized in 271 patients (2.5%), atropine in 94 patients (0.86%), and vasopressors in 37 patients (0.34%). The duration of effect for most cases was >8 h but ≤24 h ($n = 2395$, 44.2%). The average documented quantity of guanfacine ingested was 0.16 ± 0.24 mg/kg (range: 0.004–7.8 mg/kg). Average quantity ingested increased with worsening medical outcome. The difference between mg/kg ingested and medical outcome was statistically significant.
Conclusions: Pediatric guanfacine exposures reported to U.S. poison centers have increased significantly in the last fifteen years. As previously reported, the most common clinical findings secondary to guanfacine exposure were bradycardia, hypotension, and CNS depression (i.e. drowsiness). Intravenous fluids were the mostly commonly utilized therapeutic intervention. No clinical effects were observed in half of patients. In those that did experience an effect, most had symptom resolution within 24 h. There was a statistically significant difference between the amount of guanfacine ingested in mg/kg between the groups experiencing mild, moderate, or major medical outcomes. However, the range of doses ingested in each group was wide and overlapping. For example, the maximum ingested dose reported in the "no effect" group was 2.72 mg/kg, while the minimum dose eliciting a "major effect" was 0.05 mg/kg. Based on this data, we agree with current recommendations that any pediatric patient exposed to guanfacine should be observed in a health care facility for at least 24 h.

KEYWORDS Guanfacine; pediatrics; epidemiology

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287. Cardiotoxicity resulting from yew plant ingestion

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Introduction: The American yew, Taxus canadensis, is a slow-growing, long-lived plant used ubiquitously for ornamental landscaping. It is a conifer native to North America and can be found predominantly north of the Ohio River. The toxic components of the plant, taxine alkaloids, are found in most parts of the plant, all but sparing the red flesh seed-covering aril. These alkaloids primarily interfere with myocardial sodium and calcium channels by increasing calcium concentrations and result in hypotension, decreased myocardial contractility, and life-threatening dysrhythmias.
Case report: A 48-year-old female presented to the emergency department (ED) after ingesting fragments of a yew plant in a suicide attempt. Upon arrival to the ED, blood pressure was 75/57 mmHg, temperature 95.5 °F, and heart rate 30 bpm. Her vital signs improved with intravenous (IV) fluids and 0.5 mg IV atropine, but she subsequently developed ventricular tachycardia. She was given a 150 mg bolus of IV amiodarone and converted to normal sinus rhythm. After 2 h, the patient exhibited ventricular fibrillation. She underwent successful electrical cardioversion and was administered IV calcium gluconate and magnesium sulfate. She was placed on norepinephrine, amiodarone, and bicarbonate infusions, with admission to the intensive care unit. Initial laboratory analysis was only significant for a serum lactate of 4.7 mmol/l (reference 0.5–1.0 mmol/l). After 3 d of hospitalization, the above medications were discontinued and repeat electrocardiogram normalized. She was discharged in stable condition to psychiatric care.
Discussion: Regional poison centers in the United States receive numerous calls regarding yew plant ingestions every year, with the majority of exposures occurring as exploratory ingestions in children. The precise amount of yew plant exposure required to cause toxicity in adults is unknown, but previous reports have estimated the LD50 to be 50–100 leaves. Our patient experienced significant toxicity after ingesting roughly 15 seeds and an undetermined amount of leaf and branch material. There is no specific antidote for exposure to yew taxine alkaloids and treatment is primarily supportive.
Conclusion: We present a rare case of Taxus canadensis toxicity in a suicide attempt. With supportive care, the patient recovered without further sequelae.

KEYWORDS *Taxus Canadensis*; American yew; cardiotoxicity

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288. Survival after severe methemoglobinemia secondary to sodium nitrate ingestion

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Background: Sodium nitrate is commonly used as a food additive, preservative, curing agent, and color fixative. Sodium nitrate poisoning has previously been reported in the setting of well water contamination with fertilizer or nitrogenous waste runoff. Most clinically significant exposures are accidental, as a result of improper labeling or unintentional misuse.
Objectives: We present a case of severe methemoglobinemia and hypotension after purposeful ingestion of sodium nitrate in a suicide attempt.
Case report: A 23-year-old female presented to the emergency department for an intentional ingestion of sodium nitrate. Vital signs on arrival were significant for a blood pressure of 89/42 mmHg and an oxygen saturation of 74% on 100% oxygen by bag-valve mask on pulse oximetry. Due to loss of consciousness and clinical decline, the patient was endotracheally intubated in the emergency department for airway protection. Co-oximetry demonstrated a methemoglobin level of 92.7%, to our knowledge, higher than any level previously reported in the peer-reviewed medical literature. The patient was treated with two doses of 1 mg/kg methylene blue and experienced dramatic clinical improvement and subsequent successful extubation.
Discussion: In healthy humans, erythrocytes are continually exposed to oxidative stress from normal metabolism resulting in spontaneous formation of methemoglobin. Reduction of methemoglobin to hemoglobin occurs primarily via the protective enzymes cytochrome-b5 reductase and NADPH methemoglobin reductase. Sodium nitrate acts as an oxidizing agent causing methemoglobinemia. Treatment includes methylene blue, which acts as a cofactor for NADPH methemoglobin reductase and increases reduction of methemoglobin.
Conclusion: We describe a case of severe methemoglobinemia and hypotension associated with intentional sodium nitrate ingestion. Management of this patient included methylene blue administration, endotracheal intubation, mechanical ventilation and intravenous fluids. Though rare, it is important to be aware of the possible clinical effects of methemoglobinemia and hypotension associated with sodium nitrate ingestion.

KEYWORDS Methemoglobinemia; sodium nitrate; methylene blue

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