

Abstracts from the 2016 American College of Medical Toxicology (ACMT) Annual Scientific Meeting

Abstract These are the abstracts of the 2016 American College of Medical Toxicology (ACMT) Annual Scientific Meeting. Included here are 121 abstracts presented in March 2016, including research studies from around the globe and the ToxIC collaboration, clinically significant case reports describing new toxicologic phenomena, and encore presentations from other scientific meetings.

Keywords Abstracts • Annual Scientific Meeting • Toxicology Investigators Consortium • Medical Toxicology Foundation • Pediatric Environmental Health Specialty Units

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Introduction

The ACMT received 159 eligible research abstracts for consideration for presentation at the 2016 Annual Scientific Meeting (ASM), including 92 research studies and 67 case reports. Each abstract was reviewed in a blinded fashion by at least four medical toxicologists. Each abstract was independently scored based on the clinical question, data source, analytic method, results/conclusion, and clarity of presentation. A total of 121 abstracts were accepted, for an overall acceptance rate of 76 %. The acceptance rate was 89 % for research studies, including nine “encore” research studies that were presented at other scientific meetings and deemed by the reviewers to be of high interest to the ACMT ASM participants. The acceptance rate was 56 % for case reports.

This work would not be possible without the hard work and diligence of our abstract reviewers: Vik Bebartha, Katie Boyle, Diane Callelo, Stephanie Carreiro, Jonathan Cole, Kirk Cumpston, Kristin Engebretsen, Yaron Finkelstein, David Jang, Louise Kao, Ken Katz, Russ Kerns, Eric Lavonas, Michael Levine, Gerry Maloney, Andrew Monte, Mark Mycyk, Anne Riederer, Dan Rusyniak, Sam Stellpflug, Richard Wang, Brandon Willis, and Luke Yip. Even more important is the contribution of the ACMT staff. Lizzy Nguyen led the process, with significant assistance from Tara Frutkin, Tricia Steffey, and Paul Wax.

Finally, we are grateful for the immense contributions of the late Jim Wiggins, who developed and refined the process for scientific abstract review since the inception of original research presentations at the ACMT Annual Scientific Meeting in 2013. We mourn the passing of an incredible colleague and a valued friend.

Congratulations to all the researchers whose work will be presented in Huntington Beach. The 2016 Annual Scientific Meeting promises to be the best yet. We look forward to seeing you there.

Eric Lavonas, MD, FACMT, Abstract Review Chair

Russ Kerns, MD, FACMT, Chair, Research Committee

Original Research: Platform Sessions

1. Randomized Controlled Study Comparing High Dose Insulin (HDI) to Vasopressors or Combination Therapy in Refractory Toxin-Induced Cardiogenic Shock (TICS)

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Background: Cerebral perfusion (PBrO₂) during toxic-induced cardiogenic shock (TICS) has not been formally studied. In an animal model of TICS, high dose insulin (HDI) was superior to vasopressors from a cardiovascular standpoint. However, the effects of HDI, vasopressors, or combination therapy on PBrO₂ in TICS are unknown.

Hypothesis: In a porcine model of refractory TICS, addition of norepinephrine (NE) after maximizing HDI therapy increases PBrO₂ when compared to HDI-alone or to vasopressor (NE + Epinephrine (Epi)) therapy alone.

Methods: Using an established porcine model of propranolol toxicity, 15 pigs were randomized to three groups (HDI, HDI+NE, or NE+Epi). At primary toxicity, defined as a 25 % reduction in heart rate (HR) × mean arterial pressure (MAP), HDI and HDI+NE groups were started on HDI (10 U/kg/h) and NE+Epi group started on NE (titrated to 0.5 mcg/kg/min). At secondary toxicity (PoT#2), defined as a sustained MAP <50 mmHg, the HDI group received normal saline (NS), the HDI+NE group received NE, and the NE+Epi group received Epi (titrated to 0.5 mcg/kg/min). Changes in PBrO₂ after PoT#2 were compared using a linear mixed model with repeated measures within pigs. Time from PoT#2 to death or censoring after 4 h was analyzed using proportional hazards regressions.

Results: The mean decrease in PBrO₂ was minimal in pigs with HDI+NE (0.4 mmHg/h) but substantial in pigs with HDI-alone (10.4 mmHg/h). Poor survival in the NE+Epi group prevented PBrO₂ comparisons. The mean (SD) time to death, in hours, was 1.9 (0.4) in the HDI-alone group, 2.9 (1.4) in the HDI+NE group, and 0.1 (0.1) in the NE+Epi group. Moderate evidence supported supplementing HDI with NE (HR = 0.31; 95 % CI 0.06 to 1.65; *p* = 0.15).

Discussion: PBrO₂ was better preserved in the HDI+NE group than in HDI-alone. A substantial and significant mortality benefit was demonstrated with HDI-alone compared to NE+Epi.

Conclusions: In a model of refractory TICS, HDI+NE treatment was superior to HDI-alone and vasopressors alone, at preserving PBrO₂ over time. If MAP is sustained at <50 mmHg after maximizing HDI, adjunctive treatment with NE should be considered to preserve PBrO₂. Our data suggests vasopressors alone should not be used due to significantly increased mortality.



MTF

Medical Toxicology Foundation

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2. Validation of a Prediction Rule for Adverse Cardiovascular Events from Drug Overdose

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Background: Adverse cardiovascular events (ACVE) complicate up to 16.9 % of hospitalizations for acute drug overdose. We previously derived a risk prediction rule for ACVE in acute drug overdose patients with 97.1 % negative predictive value.

Hypothesis: Our aim was to internally validate the ACVE rule test characteristics.

Methods: This prospective cohort study was conducted over 17 months (2012–2014) at two urban university hospitals. Patients were adults with suspected acute drug overdose enrolled from the emergency department. The composite study outcome, ACVE, was defined as any of the following: myocardial injury (elevated cardiac troponin I), shock (requiring vasopressors), ventricular dysrhythmia (VT/VF/TdP), or cardiac arrest (pulselessness requiring CPR). The risk prediction rule included any of these three factors: (1) prior cardiac disease (CAD or CHF); (2) QTc \geq 500 ms; (3) initial serum bicarbonate \leq 20 mmol/L. Sample size was predetermined in order to calculate the rule test characteristics with 95 % confidence interval (CI) widths $<$ 5 %, we calculated the need to analyze 900 patients.

Results: There were 1457 suspected acute drug overdose patients screened, of whom 552 were excluded (185 non-drug overdose, 145 pediatric, 111 missing data, 110 alternate diagnosis, 1 chronic), leaving 905 for analysis (mean age, 41 years; female, 44 %; suicidal, 40 %). ACVE occurred in 65 (7.2 %, CI 5.6–9.1) patients (myocardial injury, 44; shock, 31; dysrhythmia, 16; cardiac arrests, 17) and there were 16 (1.8 %, CI 0.9–2.6) deaths. The multivariable model adjusting for the previously derived risk factors, controlling for age, confirmed the following independent predictors of ACVE: QTc \geq 500 ms (OR 5.5, CI 2.8–10.9), bicarbonate \leq 20 mmol/L (OR 2.7, CI 1.5–4.9), and prior cardiac disease (OR 39.5, CI 17.9–87). The validated prediction rule had 75.4 % (CI 63.1–85.2) sensitivity, 82.3 % specificity (CI 79.9–85.1), and 97.8 % negative predictive value (CI 96.4–98.7). The presence of two or more risk factors had 51.5 % positive predictive value (CI 34.5–68.6).

Discussion: The rule performed with slightly improved sensitivity and negative predictive value in the validation cohort. External validation in distinct patient populations and clinical settings remains warranted.

Conclusion: We have internally validated the previously derived risk prediction rule for ACVE in patients with acute drug overdose.

3. Prospective Cohort Study of Intravenous Lipid Emulsion for Resuscitating Critically Ill Poisoned Patients

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Background: Intravenous lipid emulsion (ILE) therapy is increasingly used in the management of life-threatening drug overdoses. However, current literature is primarily limited to animal studies and human case reports/series, which are subject to publication bias. The clinical effectiveness of ILE has not been systematically evaluated.

In May 2012, the Toxicology Investigators Consortium (ToxIC) developed a prospective sub-registry to better evaluate the use of ILE in drug overdose. **Objectives:** This study aims to describe the use and outcomes of ILE during the resuscitation of acutely poisoned patients.

Methods: A prospective cohort study of individuals treated with ILE in the ToxIC lipid sub-registry between May 2012 and October 2015 was conducted.

Results: Sixty-eight cases (54 % female; median [IQR] age 47 [29–56] years) were reported. The majority involved suicide attempts (83 %). Thirty-eight unique xenobiotics were identified, with calcium channel blockers being most frequently implicated (20 %). Common clinical findings included CNS depression (65 %), heart rate (HR) $<$ 50 beats per minute (bpm) (36 %), (HR) $>$ 140 bpm (22 %), and ventricular dysrhythmias (37 %). Fifty-two subjects (76 %) survived to hospital discharge. Cardiac arrest during acute management occurred in 28 (41 %) patients, with the arrest occurring before (n = 15) or after (n = 10) ILE administration (timing unknown in 3 cases). In the 10 cases in which the arrest occurred after ILE administration, 30 % survived to hospital discharge. In the 15 cases in which ILE was given after arrest, 47 % survived to hospital discharge (p = 0.6). The percent survival by log of the partition coefficient (log P), stratified by quartiles ($<$ 2.29; $<$ 3.00; $<$ 3.79; $<$ 5.43), was: 72.2, 68.8, 81.3, and 86.7 %, respectively (r = 0.89; p = 0.11).

Following ILE administration, 10 % of patients had an increase in their oxygen requirement, 17 % developed acute lung injury/ARDS during hospitalization, 4 % developed pancreatitis, and 9 % demonstrated laboratory result interference.

Conclusion: ILE use is primarily reserved for critically ill patients. Poisoned patients who received ILE in this series demonstrated high survival, despite critical illness. Because multiple interventions often occur simultaneously, it is challenging to determine the exact contribution of ILE on survival of individual patients. Nonetheless, the mortality in this study population was lower than might otherwise be expected.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

4. A Novel Adsorbent System Rapidly Clears Amlodipine from Human Blood

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Background: Calcium channel blockers are not effectively removed by current extracorporeal removal techniques, such as hemodialysis or charcoal hemoperfusion. CytoSorb is a perfusion cartridge containing a novel sorbent polymer, approved and marketed in Europe for the removal of excess cytokines in sepsis.

Research Question: Can a cartridge containing CytoSorb polymeric beads efficiently clear amlodipine from human blood?

Methods: Twenty milligrams amlodipine was added to 4 L of citrate-anticoagulated whole human blood and stirred to equilibrate. This blood

was then recirculated through a Cole-Parmer Masterflex L/S Digital Drive blood circuit at a rate of 300 mL/min. In the experimental arm, a saline-primed 300-mL CytoSorb cartridge was installed in-line with the circuit. Whole blood samples were obtained prior to amlodipine instillation, following equilibration, and after 0, 15, 30, 60, 120, and 180 min of blood recirculation. Whole blood amlodipine concentrations were determined using previously validated ultra performance liquid chromatography methods. The lower level of quantification (LLQ) was 0.25 mg/L whole blood. Two experimental and two control runs were performed.

Results: All quality control checks were within 15 % of their respective nominal values. At the start of recirculation, whole blood amlodipine concentrations were 5.44 (± 0.63) mg/L in the experimental and 4.70 (± 0.16) mg/L in the control arms. In the experimental arm, amlodipine concentrations were 3.20 (± 0.42) mg/L after 15 min of recirculation, 1.93 (± 0.15) mg/L at 30 min, 1.02 (± 0.36) mg/L at 60 min, 0.62 (± 0.15) mg/L at 120 min, and 0.35 (± 0.12) mg/L after 180 min. Amlodipine removal was therefore 41.3 % after 15 min of perfusion, 64.6 % after 30 min, 81.3 % after 60 min, 88.7 % after 120 min, and 93.5 % after 180 min of recirculation. Amlodipine concentrations in the control arms were 107.2 % of baseline after 180 min.

Discussion: Amlodipine is not considered traditionally dialyzable due to high protein binding and large volume of distribution. CytoSorb adsorption appears to overcome protein binding issues and rapidly reduces whole blood amlodipine concentrations to near zero. This may promote diffusion of amlodipine from tissue and ultimately whole-body clearance.

Conclusion: Perfusion over polymer beads efficiently removes amlodipine from whole human blood.

5. A Novel Adsorbent System Rapidly Clears Verapamil from Human Blood

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Background: Calcium channel blockers are not effectively removed by current extracorporeal removal techniques, such as hemodialysis or charcoal hemoperfusion. CytoSorb is a perfusion cartridge containing a novel sorbent polymer, approved and marketed in Europe for the removal of excess cytokines in sepsis.

Research Question: Can a cartridge containing CytoSorb polymeric beads efficiently clear verapamil from human blood?

Methods: Ten milligrams verapamil was added to 4 L of citrate-anticoagulated whole human blood and stirred to equilibrate. This blood was then recirculated through a Cole-Parmer Masterflex L/S Digital Drive blood circuit at a rate of 300 mL/min. In the experimental arm, a saline-primed 300-mL CytoSorb cartridge was installed in-line with the circuit. Whole blood samples were obtained prior to verapamil instillation, following equilibration, and after 0, 15, 30, 60, 120, and 180 min of blood recirculation. Whole blood verapamil concentrations were determined using previously validated ultra performance liquid chromatography methods. The lower level of quantification (LLQ) was 0.25 mg/L whole blood. Two experimental and two control runs were performed.

Results: All quality control checks were within 15 % of their respective nominal values. At the start of recirculation, whole blood verapamil concentrations were 2.50 (± 0.09) mg/L in the experimental and 2.23 (± 0.31) mg/L in the control arms. In the experimental arm, verapamil concentrations were 0.87 (± 0.001) mg/L at 15 min, 0.31 (± 0.04) mg/L at 30 min, and below LLQ thereafter. Verapamil removal was therefore 65.1 % after 15 min of perfusion, 87.4 % after 30 min, and 90 % or greater at 60, 120, and 180 min. Verapamil concentrations in the control arm decreased 10.5 % from baseline at 180 min.

Discussion: Verapamil is not considered traditionally dialyzable due to high protein binding and large volume of distribution. CytoSorb adsorption appears to overcome protein binding issues and rapidly reduces

whole blood verapamil concentrations to near zero. This may promote diffusion of verapamil from tissue and ultimately whole-body clearance.

Conclusion: Perfusion over polymer beads efficiently removes verapamil from whole human blood.

6. Neurotoxicity, Mitochondrial and mtDNA Damage of Ketamine in Young Children Undergoing Procedural Sedation in the Emergency Department

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Background: Globally, ketamine is routinely administered to millions of children during procedural sedation in emergency departments (ED). However, its safety in young children has been questioned. In animal models, ketamine kills neurons via neuro-apoptosis. These studies have not been translated to humans.

Objectives: This study aims to explore potential adverse effects of ketamine on human brain cells and cellular mitochondrial structure, function and DNA (mtDNA) in young children undergoing ED procedural sedation.

Methods: We conducted a prospective, translational clinical trial with internal controls. We enrolled children aged 3–48 months who were administered intravenous ketamine for ED procedural sedation (1–3.5 mg/kg), between August 2013 and November 2015. Blood samples were drawn from each prior to and 2–24 h post ketamine. We compared post- to pre-ketamine levels of serum biomarkers (neuron-specific enolase [NSE], glial fibrillary acidic protein [GFAP], S100B), which correlate with death of three unique CNS cell types. To test for mitochondrial damage, we isolated lymphocytes from pre- and post-ketamine blood samples and analysed for changes: cells were stained with mitochondrial membrane potential-specific dye and imaged to reveal morphologic changes. Mitochondrial content and mtDNA damage were probed using quantitative PCR.

Results: We recruited 56 children (males = 35; median age = 20 month, range = 10–45 months); median time from ketamine administration to blood sampling was 150 (range 90–693) min. For biomarkers, total ketamine dose was associated with significant increase in serum NSE ($p = 0.042$) and with borderline significant increase in s100b ($p = 0.050$) and GFAP ($p = 0.051$) in children 2–4 years compared with those <2 years. For mitochondria, after exposure, peripheral cells exhibited 24 % reduction in mitochondrial biomass ($p < 0.004$) and 16 % increase in mitochondrial polarization, indicative of mitochondrial stress and increased mitophagy. We observed a mean 0.4 oxidative DNA lesions in mtDNA per 10 kb, corresponding to moderate oxidative stress.

Conclusions: Ketamine administered to young children for procedural sedation induces increase in serum biomarkers indicative of neuronal cell death and lysis. It also resulted in oxidative stress leading to measurable mitochondrial biomass changes and significant mitochondrial DNA damage.

* In memory of Dr. Michael W. Shannon, who passed away before study conduction

7. Efficacy of Hydroxocobalamin as Treatment for Nifedipine-Induced Shock

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Background: Calcium channel antagonist-induced shock remains a significant treatment challenge. Nifedipine, a dihydropyridine calcium channel antagonist, is thought to induce vasodilatation by increasing nitric oxide (NO) production. Hydroxocobalamin (HX), a hypothesized NO scavenger, may reverse hypotension associated with nifedipine toxicity.

Hypothesis: Hydroxocobalamin will improve survival and hemodynamics in a swine model of nifedipine toxicity.

Methods: This IACUC-approved prospective animal study used Yorkshire swine sedated with alpha-chloralose, mechanically ventilated, and instrumented for drug delivery and hemodynamic measures. After stabilization and basal measures, nifedipine (0.0266 mg/kg/min) was infused until toxicity, defined as a reduction in mean arterial pressure (MAP) of 20 %, was reached. Animals received a bolus of 20 mL/kg 0.9 % saline once toxicity occurred immediately followed by 60 mL of either saline as a sham treatment ($n=9$) or HX (150 mg/kg; $n=9$). The nifedipine infusion continued for 4 h after initiation or until death. Hemodynamics was monitored throughout the study. Surviving animals were euthanized. Survival data was analyzed using a log rank test and linear mixed models were used to compare the change in MAP from the nadir across time between groups.

Results: Nifedipine toxicity was characterized by vasodilatory hypotension and tachycardia with terminal bradycardia. Median time to death after reaching toxicity was 209 min (IQR, 177/240) in the HX group and 212 min (IQR, 201/240) for animals receiving the sham treatment. There was no significant change (NS) in mortality between groups. However, there was a significant improvement in the change in MAP from nadir over time ($p=0.0021$).

Discussion: While MAP improved significantly, we observed no decrease in mortality for swine treated with HX. Potential limitations of this experiment include the following: excessive severity of toxicity, insufficient dose of HX, the potential need for repeated dosing or continuous infusion of HX, untreated direct cardiac stress from prolonged compensatory tachycardia, and that NO production may play a minor role in nifedipine-induced hypotension. Further studies are needed to evaluate alternative dosing strategies of HX in treating calcium channel antagonist-induced shock and compare it to existing treatments.

Conclusion: Hydroxocobalamin demonstrated no improvement in survival of swine with nifedipine-induced toxicity, but did improve MAP.



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This research was supported by the MTF 2015 Innovative Research and Teaching Award

8. TNF- α Response After North American Crotaline Envenomation

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Background: Tissue necrosis factor alpha (TNF- α) is a key mediator in the immune cascade and is implicated in the inflammatory response following old world viper envenomation in animal models. Although limited, prior studies using murine models and old world vipers demonstrated decreased tissue necrosis when TNF- α antibody was used to neutralize the active TNF- α .

Hypothesis: Given similarities in morphology and local tissue injury patterns between old and new world vipers, we believe that TNF- α plays an important role in North American Crotaline envenomation. Our study aim was to assay serum for TNF- α during acute and convalescent phases and correlate with clinical severity.

Methods: The study design was prospective and non-interventional. Adults who presented within 6 h after a confirmed envenomation by a North American viper were eligible for this study. Severity of the envenomation was assessed via modified grading system used at our institution. Blood samples were obtained upon arrival, and at 6 h, 24 h, and 7 days. Serum was isolated via centrifuge, stored for batch analysis at -80°C , and

then analyzed in triplication via ELISA. TNF- α levels were compared using ANOVA with significant at $p < .05$.

Results: We enrolled nine patients and three control subjects. Five patients were women and the mean age was 41 years old (range 20–66). Six suffered moderate envenomation, two were mild, and one was a dry bite. One received antivenin therapy. All bites involved copperhead snakes. Mean patient TNF- α levels (pg/mL) were 1.01 ± 0.91 (arrival), 1.06 ± 0.73 (6 h), 0.78 ± 0.36 (24 h), and 0.69 ± 0.73 (7 days). The average concentration for controls was 0.97 ± 0.26 . We found no difference between control subjects and patients or between acute and convalescent stages.

Discussion: Our study found that serum TNF- α levels are not elevated after New World viper envenomation. However, there are limitations in this study that prevent generalization of the results including small sample size, compliance with follow-up, mild envenomation severity, and one crotaline species. Furthermore, serum TNF- α may not reflect tissue activity.

Conclusion: Additional studies that include a broader spectrum and larger number of patients are needed to further delineate the relationship of TNF- α and crotaline snake envenomation.

9. Safety and Efficacy of Physostigmine: a 10-Year Retrospective Review

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Background: Physostigmine is an effective antidote to reverse anti-muscarinic delirium. The safety of physostigmine came into question after case reports of complications in the setting of tricyclic antidepressant poisoning. We designed a retrospective review of patients reported to the California Poison Control System (CPCS) who received physostigmine to determine its safety and efficacy.

Hypothesis: Physostigmine is a safe and effective antidote for the management of anti-muscarinic delirium.

Methods: Retrospective chart review of patients reported to CPCS who received physostigmine to reverse anticholinergic delirium from 2002 to 2012 was conducted. The CPCS database was queried for all cases where ‘physostigmine’ was entered in the treatment field or reported in the case notes. The notes were carefully reviewed to confirm that physostigmine was given; to determine the response to physostigmine; to assess adverse reactions; and remove duplicate cases.

Results: Of a total of 1422 potential patients, 1231 were excluded: 794 patients did not receive physostigmine, 292 patients probably did not receive physostigmine (the case notes were unclear), and 145 were duplicate cases. Anticholinergic plants were the most common ingestions (67 [35 %]), followed by diphenhydramine (56 [29 %]). Of the 191 study patients, 130 (68 %) had improvement in or return to normal mental status after physostigmine, and 21 (11 %) had normalization of vital signs. Most patients (185 [97 %]) had no adverse reactions following physostigmine. Of the six patients with adverse reactions following physostigmine administration, four (2 %) vomited, one (0.5 %) experienced QTc prolongation, and one (0.5 %) had a seizure (in the setting of a quetiapine overdose). A single fatality was reported in a patient who was agitated and tachycardic after ingestion of 950 mg of diphenhydramine. There was no response to 0.5 mg physostigmine. More than 6 h later, the patient developed a wide complex tachycardia and subsequent cardiac arrest.

Discussion: This retrospective review found few adverse events associated with physostigmine administration. There was only one reported seizure in the setting of a multi-drug ingestion. The one fatality had a cardiac arrest more than 6 h after physostigmine administration.

Conclusion: In this retrospective case series, physostigmine appeared to be a safe and effective antidote to treat anti-muscarinic delirium.

10. Overdose Risk in Young Children of Women Prescribed Opioids

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Background: The USA is in the midst of a prescription opioid epidemic, resulting in more than 16,000 deaths annually. Whether children of parents prescribed opioids are at increased risk of overdose has not been systematically studied.

Objective: This study aims to explore the risk of overdose in young children of mothers who were prescribed opioids.

Methods: We conducted a nested case–control study of children younger than 10 years whose mothers' prescription was insured under the Ontario Drug Benefit program. Cases were children who presented to an emergency department, were hospitalized or died of opioid overdose between 2002 and 2014. Each case was matched with up to four controls on age and sex. We linked children with their mothers using birth records. The primary analysis included cases and controls whose mothers filled a prescription for an opioid or a non-steroidal anti-inflammatory drug (NSAID) in the preceding year. We examined the risk of opioid overdose in children of women who received an opioid, with maternal receipt of a prescription NSAID as the reference.

Results: We identified 560 children treated in hospital and 6 who died of opioid toxicity. Of these, 83 were children of women prescribed an opioid ($n = 73$) or NSAID ($n = 10$). These cases were matched with 331 controls. Maternal opioid prescription was associated with a threefold increase in the risk of pediatric opioid overdose (odds ratio 2.97; 95 % confidence interval 1.95 to 4.52). Among cases, the most commonly implicated opioids were codeine, oxycodone, and methadone.

Conclusion: Young children of women who are prescribed opioids are at increased risk of opioid poisoning.

11. Comparative Analysis of Trends in Opioid Queries on the Erowid Website 2009–2015

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Background: Many individuals who misuse opioids, or are considering nonmedical use, turn to online resources to gather information on opioid effects, availability, formulations, administration, and safety. Erowid.org receives ~93,000 unique visitors/day and is considered among the most widely used recreational drug education and harm reduction information websites on the Internet.

Hypothesis: Daily traffic for individual opioid pages on the Erowid website may represent trends in public interest in particular opioids.

Methods: Descriptive study of average daily visits to the prescription opioid index pages for oxycodone, hydrocodone, fentanyl, hydromorphone, morphine, oxymorphone, and tramadol normalized to that of the heroin pages on the Erowid website during the months January, April, July, and October for the period 2009 to 2015.

Results: During the study period, a decrease in the number of page visits versus heroin (1.00) occurred for hydrocodone (0.87 to 0.59, –32 %), oxycodone (1.38 to 0.99, –28 %), and morphine (0.26 to 0.25, –6 %). Increases in page visits compared to heroin occurred for fentanyl (0.18 to 0.47, +157 %), tramadol (0.43 to 0.88, +106 %), hydromorphone (0.19 to 0.24, +29 %), and oxymorphone (0.11 to 0.13, +18 %).

Discussion: Efforts to combat the rise in prescription opioid abuse are multifaceted and include prescribing guidelines, increased monitoring, and formulation changes to tamper-resistant products. The challenges of

increased expense and decreased availability of prescription opioids has led many opioid-dependent individuals to seek alternative agents including illicit opioids such as heroin. On the Erowid website, visits to hydrocodone and oxycodone pages have decreased compared to heroin. Additionally, tramadol site visits versus heroin increased substantially during the study period and in 2015 exceeded visits to the hydrocodone page (0.88 vs. 0.59), suggesting that tramadol is experiencing increased interest. Fentanyl had the largest percent increase when referenced to heroin (+157 %) site visits, which may reflect interest generated by recent outbreaks of fentanyl-tainted heroin or interest in fentanyl directly.

Conclusion: Trends in comparative site visit to opioid pages on the Erowid website may reflect national trends in public queries for individual opioids.



This research was supported by the MTF 2015 Prescription Drug Abuse Prevention Award

12. Relative Frequency of Unique Opioid Page Visits Versus Heroin on Erowid.org

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Background: Opioids account for epidemic levels of morbidity and mortality in the USA and around the world. Many individuals at risk for opioid-related adverse consequences turn to web-based resources to seek information about use of these drugs. Erowid.org receives ~93,000 visitors/day and is considered among the most widely used recreational drug harm reduction information websites. Opioids are often used for their psychoactive effects, but the relative likability of individual opioids is not well understood.

Hypothesis: Traffic to the various opioid pages on the Erowid website may reflect comparative public interest in individual opioids.

Methods: Descriptive study of average daily visits to the Erowid website for opioid pages normalized to that for heroin, averaged from July 2014–July 2015, using the seasonally representative months July, October, January, and April.

Results: Indexed to heroin (1.00) average unique page visit frequency from most to least were oxycodone (1.02), tramadol (0.81), hydrocodone (0.59), codeine (0.53), poppies (0.44), fentanyl (0.38), opium (0.34), buprenorphine (0.29), hydromorphone (0.23), methadone (0.23), morphine (0.23), oxymorphone (0.13), dihydrocodeine (0.08), meperidine (0.05), and naloxone (0.05).

Discussion: Visitors to the index opioid pages of Erowid.org seek information about identification, expected effects, formulations, administration, legal status, history, and safety of these drugs. News media attention; changes in link placement, frequency, and size; browser caches; and mobile access (not captured) affect frequency of visits to opioid pages. Despite those factors, when compared to heroin, opioid page visits may reflect the level of public interest in specific opioids. The finding that only visits for oxycodone exceed those for heroin is consistent with the popularity of this prescription opioid analgesic. Of note, page views for poppies and opium were surprisingly highly represented. Tramadol, which became a schedule IV drug in July 2014, had more page traffic on Erowid than hydrocodone, the most frequently prescribed opioid nationally. Naloxone page visits were low despite the increasingly important role of this antidote in harm reduction.

Conclusion: Oxycodone and tramadol represent the greatest number of Erowid.org opioid page visits compared to heroin.



Medical Toxicology Foundation

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13. 1,1-Difluoroethane (DFE): Prevalence, Toxicity, and Analysis as Reflected by Driving While Intoxicated (DWI) and Postmortem Cases

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Background: 1,1-Difluoroethane (DFE, HFC-152a), a common aerosol propellant, foam expansion agent, and refrigerant, has become a widely abused substance due to its easy access and low cost. While there are scattered reports of its abuse, there is no single review of a large database of findings with attempts to distinguish concentrations found in living individuals versus those that die from its use.

Hypothesis: We hypothesized that there would be a clear distinction between blood concentrations of DFE in driving while intoxicated (DWI) cases versus postmortem cases.

Methods: Analysis of DFE-positive blood from 192 drivers stopped for DWI and blood from 478 postmortem cases was analyzed over an approximate 5-year period using a headspace GC method for typical alcohols, but which also indicated the presence of DFE. Once indicated, blood was further analyzed for identification and quantitation by headspace GC-MS (LOQ = 0.14 mcg/mL). Results were then compared statistically to identify any differences between the concentrations detected and attempts were made to determine a detection window for DFE in collected blood.

Results: DFE concentrations in DWI cases ranged from 0.16 to 140 mcg/mL (mean, 14 ± 19 mcg/mL; median, 5 mcg/mL), while corresponding postmortem concentrations were 0.16–480 mcg/mL (mean, 99 ± 99 mcg/mL; median, 66 mcg/mL). The difference between the population means was significant ($p < 0.001$) using the Student's *t* test; however, there was overlap between the overall concentrations in the two data sets, thus precluding the ability to make firm statements about a particular concentration. Based on ancillary available data in some cases, it appears that a reasonable detection window for DFE in blood is approximately 3 h.

Discussion: DFE is a frequently encountered volatile inhalant capable of causing toxicity ranging from impairment of cognitive functions, to cardiac disorders to death. While blood concentrations of DFE trended higher in postmortem cases, some overlap existed with corresponding concentrations in DWI cases. Loss of DFE in breath in living individuals or those with prolonged survival prior to death may have contributed to the gap in concentrations between the two groups.

Conclusion: DFE is a rapidly acting inhalant with unpredictable case-specific toxicity that has gained significantly in popularity and should be considered in unexplained toxicologic emergencies.

14. Adulterated Xanax: a Case Series from San Francisco

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Background: Illicit drugs may be adulterated with contaminants, or substituted with alternative medications, which can result in unexpected reactions. A series of patients in San Francisco, including two fatalities, were treated for complications after ingesting counterfeit “Xanax” tabs purchased illegally off the street. Analysis of the pills found large quantities of fentanyl and etizolam.

Hypothesis. “Xanax” tablets sold on the street were substituted with fentanyl and etizolam resulting in fatalities and significant medical complications.

Methods: During the months of October and November 2015, five patients were treated at San Francisco General Hospital (SFGH) after ingesting “Xanax” purchased from an unknown source.

Results: All patients experienced prolonged and significant sedation after having ingested 2 mg “Xanax” pills purchased from the street. Two patients were treated for compressive neuropathies, one patient developed biventricular failure and cardiogenic pulmonary edema as well as obtundation requiring intubation, and two patients were treated for persistent somnolence. All patients had blood and urine samples analyzed in the clinical chemistry lab at SFGH. All but one of the patients had evidence of fentanyl and etizolam, while one patient had evidence of etizolam alone. Two fatalities were also identified by the San Francisco Medical Examiner's Office (SF-ME), with evidence of fentanyl on post-mortem analysis. Counterfeit tablets were available for analysis in three instances. The tablets appeared nearly identical to authentic 2 mg Xanax tablets, but were found to contain fentanyl and etizolam. One tablet contained 3.4 mg of fentanyl and 11 mcg of etizolam.

Discussion: California Poison Control System (CPCS) and the SF-ME identified five patients and two fatalities exposed to adulterated counterfeit “Xanax” product identified to contain potentially lethal concentrations of fentanyl and etizolam. Within 1 week of the presentation and identification of the first patients, CPCS and the San Francisco Department of Public Health created a health advisory and press release to alert both health care providers and consumers of this potentially life-threatening adulterated product.

Conclusion: Clusters of patients with unexpected effects after ingestion of illicit or illegally obtained substances should alert health care providers of a potential epidemic of adulterated products.

Research Poster Presentations

15. Benzodiazepine Badness? Alprazolam Versus Lorazepam

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Background: Epidemiological studies report increasing Emergency Department visits as well as deaths associated with benzodiazepine use and abuse. Like opioids, benzodiazepines are a proven public health threat with escalating prescriptions written for agents such as alprazolam.

Hypothesis: Our hypothesis is that over the last decade, US poison centers are experiencing a greater number of exposures and increased morbidity and mortality secondary to alprazolam compared to lorazepam.

Methods: This is a retrospective study utilizing National Poison Data System (NPDS) data. NPDS data were queried from January 1, 2004 through December 31, 2014 for all intentional cases of alprazolam and lorazepam in patients older than 6 years of age. Total number of cases, respiratory depression, respiratory arrest, and death from the years 2004 and 2005 (group 1) were compared to those from 2013 to 2014 (group 2). Descriptive statistics were used to compare the two time groups/time periods.

Results: Total number of cases for group 1 and group 2 for alprazolam and lorazepam were 85,781 vs. 106,616 and 40,748 vs. 56,824, respectively. An 87 % rise occurred in respiratory depression in alprazolam cases compared to a 99 % rise in lorazepam cases. Alprazolam-associated respiratory arrest increased 44 % comparing group 1 and group 2, while lorazepam resulted in a 15 % rise. A 162 % increase in deaths occurred in alprazolam cases when comparing group 1 and group 2, while a 79 % increase occurred when comparing lorazepam between group 1 and group 2.

Discussion: Alprazolam cases reported to US poison centers more than doubled lorazepam cases for both time periods. Morbidity associated with both alprazolam and lorazepam have increased significantly over time. Deaths associated with alprazolam and lorazepam have also increased over the last decade; however, those from alprazolam more than double the rise compared to those from lorazepam.

Conclusion: Over the last decade, US poison centers have experienced an increased number, an increased degree of morbidity, and an increased number of deaths from alprazolam compared to lorazepam.

16. Expanding the Medical Toxicologist's Role in Pediatric Environmental Health Specialty Units

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Background: The Agency for Toxic Substances and Disease Registry (ATSDR) and the Federal EPA fund a national pediatric environmental health (PEH) program to provide education, as well as consultative and referral services to health care providers and the public about PEH threats to children. This program supports a Pediatric Environmental Health Specialty Unit (PEHSU) in each of the 10 federal regions. The program is staffed by those with an interest in PEH. Prior to 2015, while most of the sites had a pediatrician as site director, only 3 of 10 had a medical toxicologist (MT) as director. Moreover, there was a general lack of awareness of this program in much of the MT community. In 2014, a new FOA was released to solicit national organizations to manage the PEHSU Program for the next 5-year cycle.

Hypothesis: Active MT engagement in PEH programs can increase the opportunity for MTs in public health.

Methods: The American College of Medical Toxicology (ACMT) responded to the 2014 FOA proposing the establishment of a hub-and-spoke delivery model to provide PEH consultative services. The model had two requirements: (1) each PEHSU was required to have four physicians as core consultants, one of which needed to be a board certified MT, and (2) each PEHSU needed to develop a network of regional consultants from adjoining states in addition to core consultants to ensure the regional reach of each PEHSU.

Results: Two cooperative agreements were awarded: one to ACMT to manage the PEHSUs in Regions 6–10, the other to the American Academy of Pediatrics (AAP) to manage the PEHSUs in Regions 1–5. These awards resulted in ACMT funding a PEHSU in Regions 6–10 each of which now has a MT in a principal (Regions 6, 7, and 9) or core consultative (Regions 8 and 10) position. As part of the required expansion of the PEHSU geographical reach, 14 additional MTs were recruited to serve as regional consultants in Regions 6–10.

Conclusion: MTs can play a major leadership role in PEH and expand the presence of MTs in PEH program delivery.



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17. Complexed Copper Algacide Toxicity: Case Report and Statewide Poison Center Exposures Review

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This is an encore research presentation. Publication information for this abstract is:

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18. Phantom Menace: Yellow Oleander Dietary Aids (YODA) Exposures Reported to a Statewide Poison Control System

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19. Acetaminophen Poisoning: Effect of a Toxicology Consultation Service on Length of Stay on a Single Academic Medical Center

This is an encore presentation of research that was presented at the 8th Asian Conference for Emergency Medicine (Taipei, Taiwan, November 2015). The abstract has not been previously published outside the meeting materials.

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Background: Acetaminophen is the most common cause of intentional poisoning in the USA, with variability in treatment patterns.

Research Question: We examined data from a single medical center to assess the impact of a bedside toxicology consult service on length of stay for poisoned patients.

Methodology: Patients over 14 years of age with acetaminophen poisoning presenting to a large, urban tertiary-care medical center with acute acetaminophen ingestion were screened. Patients were selected if acetaminophen levels mandated antidotal treatment. We compared the length of hospitalization in patients divided into two groups based on the year of presentation (124 patients in 2008–2010 vs 119 patients in 2011–2013), to determine the impact of a toxicology consult service, which began in 2011, on length of stay.

Results: Patients had shorter treatment times after the introduction of a toxicology service in 2011. In 2008–2010, the average length of stay was 83.69 (±15.26) h, in comparison to 72.82 (±11.18) h in 2011–2013. Assuming that cost of daily hospitalization in California was 3000 USD per day and 125 USD per hour (based on data available from American Hospital Association), the toxicology consultation service resulted in a cost savings of approximately 1375 USD per patient case, or \$163,625 USD.

Conclusions: Although limited by a single center's experience, this study documents how developing a bedside toxicology consult service can immediately benefit a medical center by enhancing disposition decisions.

20. A Season of Snakebite Envenomation: Presentation Patterns, Timing of Care, Antivenom Use, and Case Fatality Rate in South-Central Nepal

This is an encore presentation of research that was presented at the 18th World Congress of the International Society on Toxinology (Oxford, UK, September 2015) and the 14th International Scientific Conference of the Asia Pacific Association of Medical Toxicology (Perth, Australia, December 2015). The abstract has not been previously published outside the meeting materials.

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Background: Designated by the World Health Organization (WHO) as a Neglected Tropical Disease, snakebite envenomation affects thousands of people annually in rural Nepal, with a significant burden of morbidity and mortality.

Research Question: We conducted a prospective, observational study of hospitalized, envenomed snakebite cases in South-Central Nepal over a 1-year period. We sought to identify clinical management problems and suggest potential interventions to improve treatment of snakebites.

Methods: We identified snakebite patients in a single teaching hospital in South-Central Nepal and collected demographic and clinical information about prehospital care, hospital course, and development of complications.

Results: Among 39 envenomed patients admitted to Bharatpur Hospital enrolled in the study, 34 (92 %) exhibited features of clinically significant neurotoxicity and were treated with antivenom. Antivenom use ranged from 4 to 98 (10 mL) vials of Polyspecific Indian Antivenom per patient. Each victim ($n = 34$) received antivenom an average of 4.3 (median) \pm 0.73 (standard error of mean) h after receiving the snakebite. The overall case fatality rate was 21 %. Neurotoxicity developed up to 25.8 h after suspected elapid snakebites. This was not observed for viperid snake bites. No enrolled patients received any of the current WHO recommended first aid treatments for snake bite.

Conclusions: South-Central Nepal is a region characterized by poor pre-hospital care of snakebites, limited supply of antivenom, and a high case fatality ratio.

The prevalence of nocturnal elapid snake bites, the practice of inappropriate first aid measures, and highly variable administration of antivenom were identified as major challenges to appropriate care in this study.

21. Pediatric Mushroom Exposures in California: a Decade of Poison Center Calls

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Background: Pediatric mushroom exposures resulting in ED visits are common in California. There is a need for better clinical information and triage recommendations for this diverse set of toxins.

Research Question: This study aims to identify clinical patterns and outcomes relating to pediatric mushroom cases based on calls to the California Poison Control System between 2004 and 2014.

Methods: Following IRB approval, the electronic medical records of the CPCS were queried for exposures relating to mushrooms exposures in children under age 17. Cases were reviewed for demographic, clinical, and outcome information.

Results: The query resulted in 1418 exposures, of which 1108 exposures (78 %) occurred at home. Overall, there was a decline in number of exposures over the study period, with annual peaks in the fall months (October–December). The average age of the patients was ~6 years (range <1 to 18 years) and 837 (59 %) were male. There was a bimodal

distribution by age, with peaks noted at ages 2 and 17 years; all patients aged 5 and younger had unintentional (exploratory) ingestions, whereas older children and teens endorsed self-harm and misuse/abuse as reasons for mushroom exposure. The most common effects were gastrointestinal (17 %), delirium (15 %), and tachycardia/hypertension (4.5 %). Severity was listed as no effect in 942 (70 %) cases, minor effect in 211 (16 %) cases, and moderate effect in 180 (13 %) single-substance cases. Five cases registered major effects, including one liver transplant in a 17-year old; there were no deaths. Younger children (<12 years) were more likely to remain asymptomatic: only 1.29 % of children <7 years required care at a health care facility. Notably, there were a higher number of exposures in institutionalized patients (2.4 %) and developmentally delayed children (1.15 %).

Conclusion: This large case series of pediatric mushroom exposures demonstrates a general decline in reported mushroom cases over the past 10 years in California. Although limited by small sample size, incomplete assessments, voluntary reporting, and lack of analytical confirmation, this statewide study indicates that teens, autistic patients, and the institutionalized population may be at higher risk of mushroom ingestions, with more severe effects generally affecting older children who consume them for abuse purposes.

22. A Falsely Elevated Ethylene Glycol Level Using Laboratory Enzymatic Assay

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Background: The diagnosis of ethylene glycol intoxication is challenging in settings where an accurate history cannot be obtained and is dependent on traditional laboratory quantification methods.

Research question: Is the enzymatic screening method for measuring ethylene glycol in serum reliable in critically ill patients?

Methods: This is a case report. A 54-year-old man presented to the emergency room after having sustained multiple bony injuries from a 30 ft fall. His initial blood alcohol level was elevated. Six hours later, he developed multi-organ dysfunction, including hypotension, acute respiratory distress syndrome, renal insufficiency, elevated transaminases, and a significant metabolic acidosis with a pH of 6.98 and anion gap of 37. Lactic acid was 23.4 mmol/L and lactate dehydrogenase was 3551 U/L. An enzymatic spectrophotometric method was used to quantify ethylene glycol through production of NADH monitored at 340 nm.

Results: The serum ethylene glycol level was 37.4 mg/dL measured 8 h after clinical decompensation. The patient was treated for ethylene glycol poisoning with fomepizole, hemodialysis for 3 h, and then continuous veno-venous hemodialysis. Repeat serum ethylene glycol levels were undetectable and the patient had transient resolution of his acidosis and renal insufficiency. Twenty-four hours later, his clinical picture once again deteriorated. He developed fever, worsening respiratory status, sepsis syndrome with persistent lactic acidosis, severe pancytopenia, and compartment syndrome of his fractured extremity requiring fasciotomy. Despite aggressive medical therapy, the patient died on hospital day 7. Post-mortem laboratory analysis of initial serum samples using a gas chromatography injection method found no ethylene glycol. In the presence of high serum lactate dehydrogenase, lactic acid also produces NADH, which produced a false positive ethylene glycol result.

Discussion: The findings indicate that the ethylene glycol level was falsely elevated in the setting of elevated serum L-lactate dehydrogenase and lactic acid.

Conclusion: Clinicians should be aware of the limitations of traditional hospital enzymatic assay in the setting of an unclear history of ethylene glycol ingestion, as interference from markedly elevated levels of L-lactate dehydrogenase and lactic acid can lead to misdiagnosis and inappropriate treatment.

23. The Use of Intravenous Lipid Emulsion Therapy in Acute Methamphetamine Toxicity

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Background: Lipid emulsion therapy has been shown to be effective in cases of lipophilic drug overdose. It is not previously known if it may be effective in cases of severe methamphetamine toxicity.

Hypothesis: Intravenous lipid emulsion therapy can be used as an effective treatment for severe methamphetamine toxicity.

Methods: This is a single patient case report. A 55-year-old male presented to the Emergency Department after swallowing an egg-sized amount of methamphetamine. He became progressively more tremulous after arrival with a notable rise in his heart rate, respiratory rate, and temperature consistent with sympathomimetic intoxication. His autonomic instability was refractory to aggressive intravenous fluid resuscitation, cooling measures, and progressively larger doses of benzodiazepines. Intravenous lipid emulsion therapy was initiated after discussion with the ED pharmacist and medical toxicologist.

Results: The patient was given a 100-mL bolus of Intralipid 20 %. Within 20 min of administration, his pulse, respiratory rate, and temperature started to normalize and the remainder of his Intralipid dosing was held. Intubation and critical care admission was deferred given his clinical improvement. His urine drug screen confirmed the presence of amphetamines and marijuana while his complete blood count, chemistries, creatine kinase, salicylate, and acetaminophen levels were unremarkable. His chest X-ray and head CT were normal. He was subsequently admitted to the telemetry floor and discharged home after an uneventful 5-day hospital stay.

Discussion: Lipid emulsion therapy has been shown to be effective for a wide range of lipophilic drug overdoses but no prior studies have substantiated its use in methamphetamine toxicity. The use of lipid emulsion therapy in our patient produced an immediate improvement in his clinical presentation and avoidance of endotracheal intubation and costly intensive care unit admission. Our findings suggest that lipid emulsion therapy should be considered as an adjunct treatment for all cases of acute methamphetamine intoxication.

Conclusion: Intravenous lipid emulsion therapy is an effective adjunct treatment for acute methamphetamine intoxication.

24. Reversible Amphetamine-Induced Cardiomyopathy in a 15-Year-Old Female

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Background: Cardiac complications of stimulant abuse include valvular disease, coronary vasospasm, and myocardial ischemia, but there are less data on stimulant-induced cardiomyopathy, particularly in the pediatric population.

Hypothesis: Amphetamine/dextroamphetamine preparations can induce cardiomyopathy in pediatric patients.

Methods: This is a case report of reversible amphetamine-induced inverted Takotsubo cardiomyopathy with a corresponding literature review of PubMed for search terms “amphetamine” and “cardiomyopathy”.

Results: A 15-year-old female presented with tachycardia (128 beats per minute) and chest pain after intentionally ingesting six 20 mg extended release amphetamine/dextroamphetamine, fifteen 25 mg sertraline, and an unknown amount of loratadine. Her exam was remarkable for an S3 gallop. Urine drug screen by immunoassay was positive for amphetamines, with a confirmatory level of 1958 ng/mL. Troponin peaked at 0.33 ng/mL and B-type natriuretic peptide 480 pg/mL. EKG showed sinus tachycardia, a prolonged QTc (maximum 503 msec), and no significant ST segment changes. Echocardiography demonstrated severe left ventricular systolic dysfunction with an ejection fraction (EF) of 19 %. Cardiac MRI excluded myocarditis. Troponin normalized within 24 h of

presentation. EF improved to 45 % on hospital day 3, with complete resolution on a follow-up echocardiogram 2 months later (61 %).

Discussion: Stress-induced (Takotsubo) cardiomyopathy is an acquired, reversible decrease in EF, without significant coronary artery disease. The “typical” presentation involves left ventricular apical wall abnormalities with concomitant basilar hypercontractility. The result is a ballooning of the left ventricular apex. Recreational and therapeutic drug use have been recognized as possible triggers, including a case of less severe dextroamphetamine-induced cardiomyopathy in a 19-year-old patient (EF 25–30 %), and cocaine-induced cardiomyopathy in a 54-year-old woman.

Conclusion: Severe reversible stress-induced cardiomyopathy is a potential toxic effect of amphetamine/dextroamphetamine overdose in the pediatric population.

25. Not Your Father’s N-methyl-D-aspartate Receptor Antagonists: Analytically Confirmed Toxicity from Concurrent Novel N-methyl-D-aspartate Receptor Antagonists Use.

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Background: Methoxetamine (MXE) and 3-methoxy-phencyclidine (3-MeO-PCP) are novel N-methyl-D-aspartate receptor (NMDAR) antagonists.

Hypothesis: Concurrent use of MXE and 3-MeO-PCP may cause prolonged symptoms.

Methods: This is a single patient chart review. A 27-year-old male was brought in by family for strange behavior 10 h after insufflating an internet-obtained powder. Initial vital signs were temperature 37.0 °C, pulse 114 bpm, blood pressure 185/116 mmHg, respiratory rate 19 bpm, and 98 % room air O₂ saturation. His physical exam was notable for a dissociated affect with delayed speech, ataxia, and intermittent vertical nystagmus.

Family supplied the substance he reportedly took along with seven other internet-obtained substances the patient may have been using. Lab evaluation revealed a normal blood counts and metabolic panel. A qualitative UDS was positive for phencyclidine (PCP) and cannabinoids. The patient was admitted for further observation. Eight hours from admission, his mental status and blood pressure normalized without intervention.

The substances and serial blood samples (0, 2, and 3 h from arrival) were analyzed by liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) against a library of 600 substances, including 303 novel psychoactive substances.

Results: MXE and 3-MeO-PCP were detected in all samples (279, 205, and 180 ng/mL for MXE; 167, 131, and 90 ng/mL for 3-MeO-PCP at 0, 2, and 3 h, respectively). No PCP or cannabinoids were detected. The substance he reportedly took contained MXE (concentration, 824 mg/g). A second substance also contained MXE (702 mg/g). One substance contained 3-MeO-PCP (38 mg/g). No substance contained both MXE and 3-MeO-PCP. The other substances contained 1-propionyl LSD, 5-methoxy-MiPT, 4-fluoramphetamine, ethylphenidate, and 5-MAPB. None of these chemicals were detected in his serum.

Discussion: MXE and 3-MeO-PCP are novel arylcyclohexylamines. They have been found to be potent NMDAR antagonists and may have other effects on monoamine transporters. Use of MXE has previously been shown to cause altered mental status, ataxia, and hypertension. There is a paucity of literature regarding toxicity from 3-MeO-PCP. There are no prior reports of concurrent use.

Conclusion: MXE and 3-MeO-PCP are novel NMDAR antagonist which may be misused together and cause prolonged symptoms.

26. Improvement of Neurologic Function Following Intravenous Lipid Emulsion Administration in Lamotrigine Overdose

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Background: Lamotrigine toxicity typically manifests with cardiovascular and neurologic toxicity. Intravenous lipid emulsion (IVLE) therapy is reported to improve cardiac conduction following lamotrigine overdose; however, the improvements of CNS toxicity are unreported.

Hypothesis: IVLE administration improves the neurologic symptoms associated with lamotrigine toxicity.

Methods: This is a three-patient case report via retrospective chart review.

Results: A 13-year-old girl presented with tremors, rigidity, hyperreflexia, and clonus following an intentional overdose of lamotrigine and fluoxetine, with elevated lamotrigine levels. Her symptoms transiently improved with benzodiazepines. However, IVLE was administered for recurrence of symptoms with acidosis and hyperthermia, with rapid resolution of her toxicity and neuromuscular excitation.

A 28-year-old bipolar woman presented with coma and paroxysms of agitation, hyperreflexia, rigidity, and clonus following an intentional overdose of lamotrigine, benzotropine, quetiapine, and naproxen, with elevated lamotrigine levels. She was intubated, received propofol and benzodiazepines, but only had mild improvement in her symptoms, with continued paroxysms and rigidity. IVLE was administered with rapid resolution of her neuromuscular excitation and agitation; she remained calm, only requiring low doses of propofol.

A 21-year-old woman presented soon after an intentional ingestion of lamotrigine and an unknown antidepressant. She was initially well however rapidly declined, requiring intubation, benzodiazepines, cyproheptadine, and phenobarbital for coma, severe neuromuscular hyperactivity, and tachycardia. With IVLE administration, her neuromuscular excitation dissipated. She remained significantly improved throughout her ICU stay.

Discussion: All three patients demonstrated significant improvement in neurologic function following a single dose of IVLE. However, the mechanism of action is not fully understood (drug sequestration by lipid vs enhanced delivery of lipid soluble antidotes to the CNS), and further study is required to elucidate the specific pathways by which IVLE exerts its effects. Although lamotrigine was the primary drug ingested and elevated levels were found in all three patients, concomitant ingestion and other drug effects cannot be completely excluded. Controlled studies are needed to determine if this effect is predictable, has a specific dose–response curve, and if certain symptoms offer specific indications to initiate therapy.

Conclusion: IVLE is a useful treatment option in patients presenting with neurologic symptoms following lamotrigine overdose.

27. Successful Treatment of Cannabinoid Hyperemesis Syndrome with Capsaicin

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Background: Cannabinoid hyperemesis syndrome (CHS) is characterized by refractory cyclical vomiting and abdominal pain in individuals chronically using cannabis. Symptom relief with hot bathing and cessation of cannabis use are major diagnostic criteria. Capsaicin cream, like heat, activates the TRPV1 receptor and has been suggested as a treatment option for CHS.

Hypothesis: Capsaicin cream is effective in treatment of CHS.

Methods: This is a case series of three ED patients treated with capsaicin cream for CHS.

Results: Case 1: A 25-year-old woman with a history of daily cannabis use and previous CHS presented with 15 h of nausea and vomiting initially relieved by hot showers. Multiple antiemetics failed to relieve refractory vomiting over 4 h in the ED, and labs were non-diagnostic.

Capsaicin 0.075 % cream was then applied to the abdomen and back with complete symptom resolution within 20 min. Case 2: A 23-year-old man with a history of daily cannabis use presented with 30 episodes of vomiting over 2 days that had become “coffee-ground” emesis. Abdominal CT and labs demonstrated no cause for the patient’s symptoms. Capsaicin 0.075 % cream was applied to abdomen and torso with significant symptom improvement on re-evaluation 90 min later. The patient was placed in observation for presumed Mallory-Weiss tear and discharged 26 h after presentation. Case 3: A 42-year-old woman with history of daily cannabis use presented with 20 episodes of vomiting over 4 h. She reported three prior similar episodes relieved only by hot baths. Previous work up over 5 years including abdominal MRI, ultrasound, CT, and HIDA scan was non-diagnostic. Abdominal X-ray, ultrasound, and labs were normal. Capsaicin 0.075 % cream was applied to the abdomen with complete symptom resolution noted at re-evaluation 2 h later.

Discussion: The pathophysiology of CHS is incompletely understood. Relief with hot water may suggest a role for TRPV1, a G protein coupled receptor activated by the endocannabinoid system and heat. TRPV1 is the only known receptor for capsaicin. To date, no studies of capsaicin treatment for CHS have been published.

Conclusion: In this case series, capsaicin 0.075 % cream was effective in the treatment of CHS.

28. Periorbital Edema Mimicking an Allergic Reaction After Black Widow Envenomation

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Background: Black widow (*Latrodectus* species) envenomation (BWE) can result in systemic effects known as latrodectism. Although facial and periorbital edema are manifestations of latrodectism, this phenomenon may not be recognized by healthcare providers and is not mentioned in many modern references. We present a patient with facial and periorbital edema from latrodectism that was mistaken for an allergic reaction, prompting potentially deleterious management decisions.

Methods: This is a case report of a 9-year-old boy who presented to an ED after sustaining a BWE to the shoulder. He developed severe muscular pain involving the trunk and extremities, diffuse diaphoresis, tachycardia, hypertension, nausea, and tremor consistent with a grade 3 envenomation. He was given opioids and benzodiazepines for pain with incomplete resolution of symptoms. Ten hours into treatment, he developed facial and periorbital edema, and a diffuse erythematous blanching rash to the lower extremities. There was no wheezing, oropharyngeal edema, throat tightness, or GI symptoms. Famotidine and Solu-Medrol were administered. The pediatric team recommended racemic epinephrine and discontinuation of opioids and benzodiazepines, citing concern for anaphylaxis. Thirty-six hours after envenomation, the patient was transferred to a toxicology service who averted administration of epinephrine. Physical exam was significant for HR 125, BP 140/82, diffuse diaphoresis, tremor, mild erythema at the bite site, significant periorbital and facial edema, and a blanching erythematous lower extremity rash. Antivenom was not available. Midazolam and fentanyl were titrated with gradual resolution of symptoms 48 h post-envenomation. No evidence of anaphylaxis occurred.

Discussion: This case of BWE highlights the importance of distinguishing classic findings of latrodectism, including periorbital and facial edema, from anaphylaxis. A misdiagnosis of anaphylaxis can lead to failure to administer appropriate analgesia, as well as inappropriate administration of deleterious medications. Administration of epinephrine is particularly concerning, given catecholamine excess is principal to the pathophysiology of latrodectism. Facial and periorbital edema, erythematous rash, and diaphoresis after BWE should raise concern for latrodectism, rather than anaphylaxis.

Conclusion: Periorbital and facial edema are clinical manifestations of latrodectism and should not be mistaken for anaphylaxis.

29. Bedside Ultrasound to Evaluate Effectiveness of Hyperbaric Oxygen Therapy After H₂O₂ Ingestion

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Background: Ingestion of concentrated H₂O₂ can result in significant morbidity and mortality due to embolic or caustic injury. Hyperbaric oxygen therapy (HBOT) is used to treat or prevent embolic complications of H₂O₂ ingestions. CT imaging is frequently obtained to detect presence of portal venous gas and to show resolution after HBOT. We present a case utilizing bedside ultrasound (US) to show resolution of gas collections after HBOT.

Hypothesis: In H₂O₂ exposures, bedside US can demonstrate resolution of portal venous gas after HBOT.

Methods: This is a case report of a 45-year-old man with chest and abdominal pain, vomiting, and right sided weakness immediately following ingestion of 100 mL 35 % H₂O₂. Upon arrival to the ED, chest and neurologic symptoms had resolved, but significant abdominal pain and refractory vomiting persisted.

CT imaging of the brain, chest, and abdomen were remarkable for severe esophagitis and gastritis, portal venous gas, and pneumatosis of the gastric wall with concern for impending perforation.

Due to radiologic findings, the decision was made to treat with HBOT. Thirty minutes prior to initiating HBOT, bedside US was obtained, demonstrating portal venous gas.

During HBOT at 3 atm, the patient experienced resolution of pain. Repeat US within 30 min of HBOT completion showed resolution of portal venous gas. Endoscopy showed grade IIA injury to the gastric fundus. He did not suffer from gastric perforation.

Discussion: Indications for HBOT after H₂O₂ ingestion are not standardized, and some recommend prophylactic HBOT for the presence of portal venous gas. Repeat CT imaging post HBOT is often obtained to document resolution of gas, exposing patients to additional radiation. Alternatively, bedside US is rapid, readily available, and without radiation risk. Previous publications reporting bedside US in the diagnosis and management of H₂O₂ are limited to an animal case report and an unpublished abstract. No previous cases describe US utilization to document resolution of portal venous gas after HBOT. Studies correlating bedside US and CT imaging are needed.

Conclusions: Bedside US showed resolution of portal venous gas after HBOT for H₂O₂ ingestion.

30. Comparison of Efficacy of Intermittent Hemodialysis Versus Continuous Venovenous Hemodialysis in a Case of Metformin-Associated Lactic Acidosis

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Background: Metformin-associated lactic acidosis (MALA) is a rare complication of metformin use. Estimates of mortality approach 50 %. Both intermittent hemodialysis (IHD) and continuous veno-venous hemodialysis (CVVHD) have been proposed as acceptable means of removal. Generally, higher flow rates and clearance rates are achievable with IHD than CVVHD.

Hypothesis: Intermittent hemodialysis is more effective as a means of extracorporeal elimination therapy than continuous veno-venous hemodialysis in MALA.

Methods: This is a single patient case report. An 87-year-old man with diabetes mellitus, coronary disease, stroke, hypertension, and dementia on metformin presented to an ED with 3 days of illness including nausea, vomiting, and confusion. He presented in rapid atrial fibrillation at 145 beats per minute, with an initial blood pressure of 116/82 mmHg. He was dehydrated with presumed acute on chronic renal injury with serum

creatinine 6.2 mg/dL and lactate-associated metabolic acidosis with venous pH of 7.06. Initially, lactate was 13.1 mmol/L and rose to 22.0 mmol/L over 4 h despite aggressive crystalloid fluid resuscitation. His initial metformin level was 57 mcg/mL (reference 1–2 mcg/mL) via high performance liquid chromatography/tandem mass spectrometry (LC-MS/MS).

Results: He initially underwent 8 h of IHD with dramatic improvement in his serum lactate concentration (22.0 to 9.0 mmol/L). This was followed by 18 h of CVVHD with less efficient lactate clearance (14 to 12 mmol/L). IHD was reinitiated with repeated improvement in lactate concentrations (15.0 to 6.9 mmol/L). However, the patient became hypoxic and required intubation. Care was withdrawn by family.

Discussion: This case suggests a greater efficacy of IHD over CVVHD for metformin clearance in metformin-associated lactic acidosis. Although we did not obtain serial, nor pre- and post-cartridge metformin levels, the improvement in lactate concentration suggests metformin removal. Intermittent hemodialysis achieves greater flow rates and likely more effectively removes metformin from circulation.

Conclusion: While CVVHD may offer decreased resource utilization and an improved hemodynamic profile compared to IHD, employment of both modalities in the treatment of this patient would suggest that IHD is a more effective means of metformin removal in the treatment of MALA.

31. Suspected Tetrodotoxin Ingestion in a Family Causing Neurologic Symptoms and Generating an Interstate Public Health Investigation

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Background: Tetrodotoxin is a potent neurotoxin found in the tissues of certain species of pufferfish. It causes symptoms including nausea, emesis, paresthesias, respiratory muscle paralysis, cardiac conduction abnormalities, and death through sodium channel blockade.

Hypothesis: Five patients from one family likely suffered tetrodotoxin toxicity following ingestion of varying quantities of pufferfish. Poison center and toxicologist recognition of a potential public health hazard can contribute to an effective intervention.

Methods: This is a case report of five related patients. The patriarch, a healthy 45-year-old male Chinese restaurateur, prepared a meal consisting of an unknown species of dried pufferfish that was consumed by his wife and three children, ages 21, 13, and 11. The man consumed the largest portion. Thirty minutes later, all five diners developed perioral paresthesias, and both the man and his wife developed nausea and emesis. All family members were evaluated in a community emergency department. The children's symptoms resolved without intervention and they were discharged. The man progressed to respiratory failure requiring intubation. The woman had vertigo and nausea but did not require ventilation. The regional poison center was consulted and the pair was transferred for tertiary care.

Results: On hospital day 2, the man was extubated. Both patients continued to complain of severe vertigo that improved with oral meclizine and intravenous prochlorperazine. No fish remained unconsumed for analysis. The toxicologist group and poison center collaborated with the Pennsylvania Department of Health, the New York Department of Agriculture, and the FDA to investigate and identify the retailer illegally supplying the puffer fish.

Discussion: Myriad neurologic symptoms resulting from pufferfish ingestion have been well documented. These cases illustrate a dose–response relationship among individuals who consumed different amounts of pufferfish. It also demonstrates a robust, coordinated effort by public health officials in multiple jurisdictions to attempt to identify the source of a food-based toxin.

Conclusion: In these cases, ingestion of fish thought to be contaminated with tetrodotoxin led to severe neurologic symptoms, requiring ventilator support in one individual. Toxicologists and poison centers can play a

pivotal role in the identification and investigation of potential public health threats across state lines.

32. Salicylate Poisoning: Risk Factors for Severe Outcome

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Background: Salicylate (ASA) poisoning remains a significant public health threat with upwards of 20,000 exposures annually in the USA and morbidity/mortality rates of up to 25 %. Identifying predictors of severe outcome allows for targeted treatment to lower these rates.

Research Question: What factors are early predictors of severe in-hospital outcomes in ED patients presenting with ASA poisoning?

Methods: This was a secondary data analysis of ASA overdoses from a prospective cohort study of suspected acute drug overdoses at two urban university teaching hospitals from 2009 to 2013. Patients were enrolled consecutively and were considered eligible for inclusion based on clinical suspicion of ASA ingestion. Children (<18) and alternate diagnoses were excluded. Demographics, clinical parameters, serum ASA concentrations, treatment modalities, and death/admission rate were collected from the medical record. Severe outcome was defined as a composite occurrence of any of the following: acidemia (pH <7.3 or bicarbonate <16 mEq/L), hemodialysis, or death.

Results: Forty-eight patients met inclusion criteria, with 43.8 % male, median age 32, mean initial ASA concentration 28.1, and 10 (21 %) classified as severe outcome. There were two deaths, neither of whom received hemodialysis. Patients were treated with sodium bicarbonate in one third of cases, while 54.2 % received activated charcoal and 64.6 % were admitted. Univariate analysis indicated that age ($p=0.04$, t test), respiratory rate (RR) ($p=0.04$, t test), creatinine ($p=0.05$, t test), lactate ($p=0.002$, t test), coma ($p=0.05$, chi square), and presence of co-ingestions ($p=0.04$, chi square) were significantly associated with severe outcome, while ASA alone had no association. However, when adjusted for serum ASA concentration, only age (OR 1.02 per additional year, CI 1.0–1.1), RR (1.09 per additional breath/min, CI 1.03–1.15), creatinine (2.8 per additional mg/dL CI 1.1–7.1), and co-ingestions (OR 6.4, CI 2.3–17.8) were independent predictors of severe outcome.

Discussion: We have derived independent predictors of severe outcome from acute ASA poisoning, which can aid in identifying patients who require more aggressive treatment, and does not include serum ASA concentration. Despite the severity of these cases, only one third received sodium bicarbonate, suggesting potential barriers to administration which require further study.

Conclusions: Age, RR, creatinine, and co-ingestions are predictive of severe outcome in ED patients with acute ASA poisoning.

33. A Retrospective Review of Local Anesthetic Toxicity from a Single US Poison Center

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Background: Lidocaine and bupivacaine are commonly used local anesthetics for inpatient and outpatient wound repair, nerve blocks, and minor operative procedures. Local anesthetic toxicity may manifest with serious, life-threatening symptoms. We analyzed all cases of lidocaine and bupivacaine exposures requiring hospital evaluation reported to a single US poison center.

Hypothesis: Local anesthetics are often administered in outpatient settings. Iatrogenic medication errors are an important etiology for local anesthetic toxicity.

Methods: We retrospectively reviewed lidocaine and bupivacaine exposures reported to our poison center (PC) between January 1, 1992 to October 21, 2015. We selected all patients who were referred for emergent medical evaluation and those already in an inpatient setting. Abstracted data included age, dose, medication, reported effects, exposure setting, route, and circumstances.

Results: Eighty-eight single-agent exposures of lidocaine or bupivacaine-containing products were reported during the study period. Thirty-two (36.4 %) were home calls, with 25 (28.4 %) and 14 (15.9 %) cases from outpatient clinics and hospitals, respectively. Twelve (13.5 %) of calls reported iatrogenic medication errors.

The following serious effects were reported: cardiac arrest ($n=4$, 4.5 %), respiratory failure ($n=5$, 5.7 %), respiratory distress ($n=3$, 3.4 %), seizure ($n=13$, 14.8 %), altered mental status ($n=13$, 14.8 %), paresthesias ($n=6$, 6.8 %), dizziness ($n=6$, 6.8 %), bradycardia ($n=2$, 2.3 %), and methemoglobinemia ($n=2$, 2.3 %). One fatality was reported.

Of 41 patients with reported serious effects, 26 (63.4 %) occurred in the outpatient setting. Routes of exposure varied: 16 (39 %) were intradermal; 6 (14.7 %) were intravenous; and 9 (22 %) were ingestion or oral rinses. Other routes of exposure include ocular, topical, vesicular, intranasal, and intra-articular. Seven (7.8 %) required mechanical ventilation.

Twenty-one of 32 (66 %) home calls involved unintentional ocular exposures, most frequently resulting in minimal local symptoms.

Discussion: Local anesthetic toxicity is a potentially life-threatening entity. The majority of serious cases reported to our PC occurred in an outpatient setting. There were many cases of toxicity occurring as a result of iatrogenic medication errors.

Conclusion: Lidocaine and bupivacaine are frequently used in outpatient settings. Providers should exercise caution in administration to prevent iatrogenic errors. Patients using this medication at home should be counseled on risks of toxicity.

34. Utility of Serum Rivaroxaban Levels Following Supra-therapeutic Dosing for Anticoagulation

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Background: Rivaroxaban is a new oral anticoagulant that works by inhibiting factor-Xa. Occasionally, unintentional supra-therapeutic dosing may occur. There is limited data/experience for when physicians can safely re-initiate rivaroxaban therapy in these situations.

Hypothesis: Serum rivaroxaban levels may be useful for determining when to safely re-initiate rivaroxaban therapy for anti-coagulation following unintentional supra-therapeutic dosing.

Methods: This is a single case report of an 80-year-old female started on rivaroxaban for treatment of pulmonary embolism. We reviewed her chart and collected information about her actual dosing regimen, adverse health effects, clinical course, and laboratory data including a rivaroxaban level.

Results: The patient was discharged with prescriptions for rivaroxaban 15 mg twice daily (to finish the 21-day initial course) and for 20 mg daily for 69 days, to start after completion of the twice daily regimen. The patient misunderstood instructions and took both prescriptions simultaneously—a total of 50 mg daily for 2 weeks. She denied signs or symptoms of bleeding, and all routine laboratory values were within normal limits (SCr = 0.5 mg/dL, Hgb = 10.5 g/dL, Hct = 33.2 %). She was instructed to hold her rivaroxaban and to return home from clinic. After consultation with the pharmacy service about re-starting the rivaroxaban, she was contacted and instructed to return in 2 days to have blood drawn for a serum rivaroxaban level. Relevant labs after 2 days included rivaroxaban level = 107 ng/mL (range 32–215 ng/mL), PT = 14.2 s, INR = 1.2, and anti-Xa = 0.55 IU/mL. Rivaroxaban was re-initiated at that time based on her therapeutic level.

Discussion: Coagulation markers such as PT, INR, and anti-Xa levels do not correlate well with rivaroxaban toxicity. The elimination half-life of rivaroxaban in the elderly with therapeutic dosing is 11 to 19 h. Given that the elimination half-life of supra-therapeutic dosing in the elderly is unknown, we obtained a serum rivaroxaban level to confirm if it was within the therapeutic range therefore allowing for safe re-initiation of rivaroxaban therapy.

Conclusion: The use of rivaroxaban serum levels may be helpful for guiding the re-initiation of therapy following supra-therapeutic dosing.

35. The Successful Treatment of 5-FU Overdose in a Patient with Malignancy and HIV/AIDS with Uridine Triacetate

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Background: According to the National Institutes of Health (NIH), more than 1300 deaths annually are attributed to 5-fluorouracil (5-FU) toxicity. Uridine triacetate is under investigation as an antidote for 5-FU toxicity. In an ongoing clinical trial, approximately 97 % of these patients recovered after 5-FU toxicity after receiving treatment, versus a survival of 10 % historically.

Hypothesis: Uridine triacetate is an effective antidote in 5-FU toxicity and may also be effective in patients who also have underlying immunocompromised states, like AIDS.

Methods: A 52-year-old male with history of HIV/AIDS (CD4 70), CNS toxoplasmosis, and anal cancer presented to the emergency department after receiving an entire course of 5-FU in 24 h. A root-cause analyses demonstrated that he was given a pump that administered 7640 mg (100 mg/kg dose) of the drug over 24 h instead of the intended 96 h (minimum toxic dose is 25 mg/kg). Uridine triacetate, Filgrastim, and other prophylactic measures were started to protect against hematological, gastrointestinal, neurologic, and cardiac toxicity.

Results: After starting treatment with uridine triacetate, the patient's complete blood cell count and ANC did not significantly change from his baseline values. His plasma uridine level drawn 2 h after initiating treatment was 157 μmol (therapeutic range is $>80 \mu\text{mol}$). His plasma uridine level drawn 2 h after his last dose of treatment was 172 μmol . The patient had an uncomplicated 6-day hospital course. During the 1-month follow-up period, the patient had no major events and his laboratory studies did not significantly change.

Discussion: Uridine triacetate has shown promising results in patients enrolled in a clinical trial who had developed 5-FU toxicity in the setting of cancer treatment; however, this is the first published case report of successful treatment of 5-FU overdose with uridine triacetate in a patient who also had the underlying immunocompromised state of HIV/AIDS.

Conclusion: Uridine triacetate should be considered in all patients at risk of 5-FU toxicity given its demonstrated efficacy, relatively safe side effect profile, and as demonstrated in this case is likely to be successful in a patient who is already severely immunocompromised.

36. Characterization of Adverse Health Effects in Children from Exposures to Alcohol-Based Hand Sanitizers Reported to Poison Centers

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Background: According to National Poison Data System (NPDS) data, call volume to poison centers (PC) regarding exposures to alcohol-based hand sanitizers, which may contain up 60–95 % alcohol, has increased.

Objective: This study aims to characterize the adverse health effects of calls to PCs reporting exposures to alcohol-based hand sanitizers by

comparison with non-alcohol hand sanitizer exposures in children under 12 years.

Methods: We determined the total number of annual exposures to alcohol and non-alcohol-based hand sanitizers in children (<12 years) reported to NPDS from January 1, 2011 to December 31, 2014. Calls reporting additional exposures to other products were excluded. Descriptive statistics for age, route, intentionality, adverse health effects, and medical outcome associated with alcohol sanitizers were calculated and compared with non-alcohol sanitizers. Categorical data comparisons were performed using chi-square tests or, when cell sizes were <5 , Fisher's exact tests using Microsoft SASTM version 9.3.1. Significance was defined as a $p < 0.05$.

Results: The total volumes of alcohol-based hand sanitizer exposures since 2011 was 65,293 while the non-alcohol hand sanitizers exposures was 4869. The majority were from alcohol (92 %) rather than non-alcohol sanitizers (8 %). The major route was ingestion in both alcohol (95 %) and non-alcohol (94 %) sanitizers. Older (6–12 years) children were more likely to intentionally expose themselves to alcohol sanitizers (20 %) as compared to non-alcohol sanitizers (8.9 %) ($p < 0.0001$). Older children were also more likely to intentionally expose themselves to alcohol sanitizers as compared to younger children (0.04 %) ($p < 0.0001$). Alcohol sanitizer exposures were more likely to report an adverse effect (14 %) compared to non-alcohol exposures (11 %) ($p < 0.0001$). Serious rare adverse effects like hypoglycemia, respiratory depression, hypotension, coma, and metabolic acidosis occurred more frequently in alcohol sanitizers but were not individually statistically significant. Alcohol sanitizer exposures were more likely to have more severe medical outcomes (18 %) compared to non-alcohol sanitizers (0.1 %) ($p = 0.0004$). There were no reported deaths.

Discussion: Children were more likely to be exposed to alcohol-based hand sanitizers. Exposure to alcohol sanitizers was associated with more adverse effects and severe medical outcomes than non-alcohol sanitizers.

Conclusion: Parental education about the hazards associated with alcohol sanitizer exposures may be helpful in minimizing adverse outcomes.

37. Development of a Medical Toxicology Curriculum in Spanish for Resident Physicians and Medical Students in the Dominican Republic

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Background: There is currently no formal training for Dominican medical trainees in toxicology. There is a scarcity of data on poisoning and no national surveillance systems including poison centers.

Objectives: This study aims to implement a curriculum based on the toxicology category of the American Board of Emergency Medicine (ABEM) with emphasis on exposures prevalent in the Dominican Republic (DR) with content informed by a population survey.

Methods: A survey was designed to identify common exposures, perceptions, and assess the fund of knowledge of community members and medical trainees in Santiago, DR. Informal interviews and a literature search were also used to guide curriculum development. An 84-item survey was distributed. Respondents were either from Pontificia Universidad Católica Madre y Maestra (PUCMMM) medical school or Juan XXIII or Cabral Hospitals, which are both public hospitals. Respondents were either (1) patients in ER or clinic waiting rooms, (2) basic responder course participants, (3) medical students, or (4) medicine or emergency medicine residents. A 72-page curriculum was taught and a 12-item pretest and posttest were given to the medical trainees who also attended toxicology-focused bedside rounds and lectures over a period of 1 month. The curriculum was made available online through the Global Educational Toxicology Uniting Project (GETUP).

Results: One hundred seventy-five surveys were completed by 134 community individuals, 22 resident physicians, and 19 medical students. Sixteen respondents (9 %) had history of exposures requiring medical

attention. Thirty-two (18 %) practice traditional remedies. Thirty-three (19 %) report heavy alcohol use. Six (3 %) use pain medications daily. Community members answered 44 %, medical students answered 61 %, and residents answered 73 % of the basic knowledge questions correctly. Nineteen emergency medicine and 15 medicine residents completed the course. The mean pretest and posttest scores were 61 and 83 %, respectively.

Discussion: Our survey demonstrates that the burden of disease from ingestions in this area is high. From the survey, approximately 40 % of respondents practice high risk behaviors including substance abuse, as well as the use of remedies or products that are either illegal, improperly labeled/handled or used.

Conclusion: The long-term goals of this project are to raise awareness and implement expanded toxicology training in DR.

38. Knowledge, Awareness and Practices of Workers Exposed to Pesticides in Qatar

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Background: Pesticide poisoning is a global public health problem. Annually, 3 million people are hospitalized due to pesticide poisoning with over 250,000 deaths all over the world¹. It is therefore vital to not only understand the existing knowledge, attitudes and practices about handling pesticides but also to explore the effectiveness of measures like education and personal protective equipment on the general well-being of the workers.

Hypothesis: We hypothesize that training the workers to handle pesticides is vital in maintaining high safety standards, thereby preventing associated toxicity while handling them, and that the use of personal protective equipment (PPE) improves the general health of pesticide handlers in the long run.

Methods: One hundred municipality employees in Qatar who work with pesticides were interviewed in person by trained bilingual staff using a structured questionnaire model. The questionnaire included demographic data, questions related to methods of pesticide storage, application and disposition, usage of PPEs, adherence to safety practices and views of the worker on the company safety protocols and their implementation. Data was then entered into Excel format and analysed using descriptive statistics and associations inferred by odds ratios.

Results: The mean age of the workers was 37.4 (SD 9.9). Amongst workers, nearly 2.9 % of them who did not use personal protective equipment visited hospital annually when compared to 1.4 % of workers who used personal protective equipment. Of the interviewed workers, 81.1 % did not know the contents or the name of the pesticides they were handling at work. Unsafe behaviours such as preparation of pesticides at the site of its usage rather than in a specified preparation room (29.6 %), noncompliance with wearing protective clothing (38.8 %), handling of drinking water (22 %) and food (10 %) on site where pesticides are used, and not washing clothes every day after work (45.9 %) were observed. Around a quarter of the interviewees did not receive any training on preparation and handling of pesticides. Workers who received training in pesticides usage were more likely to be aware of its effects on the environment (61.6 %) (OR 3.9), less likely to eat or drink while handling pesticides (83.6 %) (OR 4.3) and more likely to give household members appropriate instructions prior to application of pesticides (90.4 %) (OR 5.0).

Conclusion: Workers who received prior training handled pesticides with better safety standards, highlighting the importance of training in pesticide handling. Wearing protective clothing most likely has a positive impact on the general well-being of the workers.

39. Assessment of Patterns of Substance Abuse Among Adolescents and the Associated Severity of Outcome: a 5-Year Retrospective Cohort Study.

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Background: Adolescence has long been known as a developmental period during which risk-taking behaviors and substance use emerge. However, little has been published regarding how patterns of use change as adolescents age and how these changes correlate to severity of outcome.

Hypothesis: We hypothesize that the agent classes used illicitly by adolescents change by age and lead to different levels of toxicity among age groups.
Methods: This is a retrospective cohort study of data obtained from the Toxicology Investigator's Consortium (Toxic) database from 2010 to 2015. Patients aged 12–21 years with an identifiable toxicologic exposure to pharmaceutical or non-pharmaceutical agents with the intent to elicit a pleasurable sensation were studied. Cases were assigned based on widely accepted models of adolescent development to cohorts of “Early” (12–14), “Middle” (15–17), and “Late” (18–21). Data were analyzed using ANOVA and Chi-square testing.

Results: Four hundred forty-four cases were studied, including 38 early, 182 middle, and 224 late adolescence patients. These cohorts demonstrated distinct patterns of substance use and the middle cohort was more likely to require a higher level of care (admission to floor or ICU status) than the late cohort when exposed to the following substances: stimulants ($p = 0.002$, Chi-square), anticholinergic/antihistamines ($p = 0.039$, Chi-square), alcohols ($p = 0.019$, Chi-square), and opiates/opioids ($p = 0.044$, Chi-square). Additionally, sedative/hypnotic agents were more likely to be admitted ($p = 0.012$, Chi-square) while psychoactive agents were less likely ($p = 0.004$, Chi-square) than other agents.

Discussion: Level of toxicity is correlated to type of exposure, particularly during middle adolescence, a period where neurodevelopment changes in brain organization and function (especially in the dopamine and serotonin systems) are seen. These neurobiological changes may influence the type and amount of agent used, resulting in higher levels of toxicity. Limitations exist (e.g., exposures not presenting to the ED are not included in this data) and will serve as the basis for further investigation utilizing this and other data sets.

Conclusion: Distinct patterns of substance use exist between adolescent developmental stages and are associated with difference in severity of outcome.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

40. One Last Kick: a Case of Heroin-Induced Transverse Myelitis Without Neurologic Recovery

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Introduction: Transverse myelitis (TM), an inflammatory condition and demyelination of the spinal cord, has been rarely associated with heroin use.

Case: A 17-year-old female with past history of depression and opioid dependence on buprenorphine/naloxone was found unresponsive with shallow respirations. Four milligrams of naloxone was administered with subsequent improvement. She had no neurologic deficits on initial physical exam. She admitted to insufflation of an unknown amount of heroin. On hospital day (HD) 1, she began to complain of numbness to her legs. Within 6 h of her initial evaluation, she was found to have lower extremity paralysis with 0/5 muscle strength and no sensation of bilateral lower extremities. Immediate MRI demonstrated findings consistent with TM. Neurology was consulted and the patient was started on intravenous steroids. On HD 5, she received plasmapheresis and started on intravenous immunoglobulin, without any improvement. The patient's had an extensive workup, which did not point to an alternative etiology. On HD 20, the patient was transferred to inpatient rehabilitation. Approximately 5 months later, she remained paraplegic during an ED visit for chest pain.

Discussion: Acute inflammation of isolated segments of the spinal cord is known as transverse myelitis and is relatively uncommon.² There are various etiologies with few reports of heroin use being associated with this condition. To our knowledge, there has only been one previous documented case of TM presented in the literature after nasal insufflation of heroin in which the patient made a full recovery within 7 weeks.³ The etiology of TM is often unknown, but mechanical, toxic, and immunologic factors have all been considered.^{4,5} A complete neurological workup for other demyelinating disorders was negative, and the diagnosis of TM due to heroin use was made. The patient received extensive treatments with corticosteroids, plasmapheresis, immunoglobulin, and extensive physical therapy, but did not make significant neurological progress. To our knowledge, she is the first reported case of heroin nasal insufflation-induced TM to remain paraplegic for such an extended time.

Conclusion: Transverse myelitis should be kept in the differential of any patient who presents with neurologic symptoms after use of heroin via any route.

41. Valacyclovir-Induced Neurotoxicity Treated with Hemodialysis

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Background: Neurotoxicity has been reported following exposure to valacyclovir in patients with both chronic and acute kidney disease due to accumulation of the active metabolite, acyclovir.

Hypothesis: Valacyclovir use without renal dose adjustment is associated with neurotoxicity in patients with chronic kidney disease and can be treated with hemodialysis (HD).

Methods: This is a single patient case report of a 67-year-old woman with chronic kidney disease on peritoneal dialysis. She was diagnosed with herpes zoster infection and prescribed valacyclovir for abdominal pain and a rash. Valacyclovir was prescribed 1000 mg PO three times daily. Two days after beginning these medications, she presented to the emergency department with disorientation and delirium.

Results: The patient was admitted for further evaluation of her altered mental status. Valacyclovir was continued with renally adjusted dosage to 500 mg PO daily. The patient's neurologic status continued to deteriorate and she was transferred to the ICU on hospital day 2. HD was initiated to hasten removal of the drug. The patient completed two 4-h sessions of HD after which her mental status significantly improved. The patient was discharged to home on hospital day 5. On the day of admission, the patient's acyclovir level was 5.6 mcg/mL [2.0–4.0 mcg/mL]. After two sessions of HD, the level had decreased to 1.3 mcg/mL.

Discussion: We present a patient with valacyclovir-induced neurotoxicity secondary to failure to adjust dosing for her chronically impaired renal

function. HD rapidly cleared the active metabolite with associated improvement in the patient's mental status and return to baseline. Without HD, clearance of the drug can be up to 14 days in patients with renal failure given that valacyclovir and its metabolites are primarily renally excreted. Valacyclovir has both low protein binding and volume of distribution leading to rapid clearance with HD. At therapeutic levels, HD clears 33 % of acyclovir. Similar rates of clearance were seen in this patient with acute toxicity. **Conclusion:** Valacyclovir can cause neurotoxicity in patients with kidney disease that may be prevented by appropriate dose adjustment at the outset of treatment and corrected by withholding the medication and initiating HD.

42. Life-Threatening Arrhythmias Associated with Loperamide and Cimetidine Abuse

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Background: There is sparse but growing evidence that loperamide when taken in chronic, high dosages is associated with cardiac conduction disturbances and arrhythmias.

Hypothesis: High dose loperamide abuse is associated with significant cardiac conduction dysfunction and ventricular arrhythmias.

Methods: This is a case report. A 28-year-old female with remote history of opioid dependence was admitted for syncope. Initial vitals signs and physical exam were unremarkable. Electrocardiogram showed sinus bradycardia, rate 56 beats per minutes (bpm), with 1st degree heart block, right axis deviation, and QRS interval of 192 ms and QTc of 642 ms with deep t wave inversions in leads V2-V4. Initial laboratory tests were only remarkable for potassium of 3.2 mg/dL. Two witnessed syncopal events occurred with wide complex ventricular rhythms. Both resolved spontaneously without intervention. Later in the hospital course, she divulged a chronic, massive intake of loperamide and cimetidine to self-treat for "opiate withdrawal." For the past several months on a daily basis, she had ingested 400–600 mg of loperamide and 2000 mg of cimetidine. More so, she had still been continuously ingesting during her hospitalization. She soon after had bradycardia-induced torsades de pointes and was started on isoproterenol infusion. Serum was analyzed by high resolution time of flight mass spectrometry (HR-TOF-MS) to measure loperamide and cimetidine concentrations.

Results: Serum concentration of loperamide was 83.2 ng/mL (therapeutic range 0.24–3.1 ng/mL) and cimetidine was 6 mg/mL (therapeutic range 0.5–1.5 mg/mL). Isoproterenol successfully increased heart rate and no arrhythmias occurred during the 5-day duration of infusion. Her QRS and QTc shortened considerably over her 16-day hospital course with cessation of loperamide and cimetidine and she was discharged home.

Discussion: This case details the very serious and potentially life-threatening cardiac dysrhythmias that are associated with chronic and very high doses of loperamide. Cimetidine inhibits cytochrome p450 3A a known metabolizer of loperamide. We propose cimetidine was taken concurrently to deter metabolism and enhance drug effect.

Conclusion: Loperamide may not be as innocuous as once thought, when purposefully abused in chronic, high quantities and is associated with life-threatening ventricular arrhythmias.

43. Treatment of Congenital Methemoglobinemia During Pregnancy with Methylene Blue: a Case Report

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Background: Little data exist on the safety of intravenous methylene blue for treating methemoglobinemia during pregnancy. The administration of intra-amniotic methylene blue to test for rupture of membranes was previously associated with hemolytic anemia, intestinal atresia, and fetal death; it is now contraindicated for use in obstetric procedures.

Hypothesis: Intravenous (IV) methylene blue may be used to treat methemoglobinemia during pregnancy.

Methods: This is a single patient chart review. A 23-year-old pregnant female (29 weeks gestation) presented to the emergency department complaining of dyspnea, chest pain, and abdominal pain. She was tachycardic with perioral cyanosis. Pulse oximetry revealed an oxygen saturation of 80 %. Co-oximetry showed a methemoglobin level of 28.9 %. The patient had no recent exposure to any agent known to provoke methemoglobinemia. Medical toxicology and obstetrics were consulted. Sixty milligrams (1 mg/kg) IV methylene blue was administered due to the concerning nature of her symptoms.

Results: Repeat methemoglobin was less than 2 % after 1 h. Symptoms resolved and the patient was admitted for observation. The methemoglobin level rose to 10.7 % 2 days later. At the suggestion of hematology, an exchange transfusion of 400 ml was performed, and the methemoglobin level fell to 8.7 %. The patient was then discharged with weekly monitoring of methemoglobin levels. Genetic testing for a congenital cause of methemoglobinemia was ordered. Her methemoglobin level has ranged between 10 and 14 % at follow-up visits. Fetal monitoring and repeat non-stress tests have been reassuring. Genetic testing showed the patient has cytochrome b5 reductase deficiency, the most common cause of congenital methemoglobinemia.

Discussion: Most cases of methemoglobinemia are acquired and occur after exposure to an oxidizing agent. In patients with a genetic deficiency of cytochrome b5 reductase, however, methemoglobinemia has been reported to occur spontaneously after physiologic stress. IV methylene blue can effectively and rapidly reverse methemoglobinemia in both acquired and congenital cases. Exchange transfusion is also an effective treatment modality, but it requires more time and resources to implement.

Conclusion: Although little data exist on the safety of IV methylene blue during pregnancy, administration rapidly reverses methemoglobinemia and may be considered in symptomatic pregnant patients.

44. Inhalational Mercury Toxicity Among Artisanal Gold Miners Reported to the Oregon Poison Center, 2002–2015

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Background: Mercury exposure has been described among artisanal and small-scale gold mining communities in developing countries. These cases are predominantly related to commercial or industrial mining operations. To date, a paucity of cases has been described involving gold miners in the USA.

Research Question: To what extent do inhalational mercury exposure and toxicity occur among artisanal gold miners?

Methods: This is a systematic retrospective review of the Oregon Poison Center Toxicall database. All cases of “mercury” or “mercury inhalation” exposures were reviewed, and those involving mining were included in the analysis.

Results: Between 2002 and 2015, there were seven cases of mercury exposure from mining incidents reported to the Oregon Poison Center. Six cases explicitly involved the patient heating a mercury-gold amalgam; one exposure had limited information but the case description implied gold mining. Every incident was recreational (i.e., not related to a commercial or industrial mining operation) and involved trying to extract a precious metal for personal financial gain. All patients were male, ranging in age from 32 to 81 years. Six patients had symptoms consistent with mercury inhalation toxicity. Five patients had measured whole blood mercury concentrations: two were normal (5 and 7 mcg/L), one was mildly elevated (39 mcg/L), and two were markedly elevated (340 and 346 mcg/L).

L). Both patients with markedly elevated mercury concentrations received chelation therapy, and one required intubation for ARDS. Two patients were using methamphetamines at the time of their exposure.

Discussion: Inhalational mercury toxicity with elevated blood mercury concentrations may occur following independent recreational gold mining in the USA.

Conclusion: Toxicologists should be aware of the association of mercury toxicity and artisanal gold mining.

45. Poison Center Experience Managing Laundry Detergent Pod Ocular Exposures

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Background: Most research has focused on complications from laundry detergent pod (LDP) ingestions. There is limited data on ocular exposures.

Research Question: How are LDP ocular exposures managed by our regional poison center (PC)?

Methods: We retrospectively searched electronic PC records, from January 1 through December 31, 2014, using the generic code “Laundry Detergents: Liquids (Unit Dose).” Exposure characteristics were expressed as defined variables abstracted to a data collection form by a trained and monitored data abstractor. Confusing data points that were flagged by the abstractor were reviewed and resolved by the project coordinator. Cases not involving ocular exposures were excluded.

Results: We identified 91 cases of ocular LDP exposure. There was concomitant LDP ingestion in 21 cases and a concomitant LDP dermal exposure in 13 cases. Ages ranged from 1 to 25 years old (mean 4, median 3). Forty-six calls originated from home, 28 were referred to an emergency department (ED), 10 were discharged, and 27 were lost to follow-up. Forty-four patients presented to the ED prior to PC call (28 discharged, 3 admitted, 14 lost to follow-up, 1 lost after admission). All three admitted patients also ingested LDPs. Patients complained of ocular symptoms (irritation, redness, swelling) in 84/91 cases. Large corneal abrasions were documented in five patients. PC recommendations included the following: irrigation (46), fluorescein staining (23), and ophthalmology consultations (11).

Discussion: The vast majority of patients with LDP ocular exposures reported symptoms at the time of PC call, and approximately half received a recommendation to irrigate. Only a fraction of these cases were referred to an ED, five of which were found to have corneal abrasions. A limitation of PC data is the high number of cases with no follow-up. Further study is needed to accurately describe outcomes.

Conclusion: LDP exposures can cause significant ocular injury. PCs and practitioners should have a more consistent approach to the management of these cases. Irrigation should be recommended in all symptomatic patients and an eye examination should be performed if symptoms persist.

46. Laundry Detergent Pod Exposures in Patients Older than 6 Years

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Background: Most research on laundry detergent pod (LDP) exposures focuses on children ≤6 years. The data on exposures affecting older patients has not been well documented.

Research objective: This study aims to describe LDP exposures in patients >6 years at a regional poison center (PC).

Methods: This was a retrospective study using electronic PC records, which were searched using the generic code “Laundry Detergents: Liquids (Unit Dose)” from January 1 through December 31, 2014. Exposure characteristics were expressed as defined variables abstracted to a data collection form by a trained and monitored data abstractor. Confusing data points that were flagged by the abstractor were reviewed

and resolved by the project coordinator. Cases involving patients 6 years old and younger were then excluded.

Results: We identified 33 cases, ages 8–86 years old (mean 31.7, median 20.5). Routes of exposure included the following: ingestion (19), ocular (9), dermal (8), multi-route (3). Twenty-seven cases were coded as unintentional, six intentional. Regarding ingestions, two were suicide attempts, three were elderly or had dementia, two had mental retardation, one was drunk, and one was transporting a LDP in her mouth. Regarding ocular exposures, six occurred when a LDP burst open during normal use. Regarding dermal exposures, two were transporting LDPs in their bras. Twenty-three calls originated from home and eight were referred to an emergency department (ED). Eight presented to the ED prior to PC call, seven discharged, and one admitted to the ICU (a 21-year-old female, who attempted suicide via LDP ingestion). Two calls originated from outpatient clinics, one discharged. Follow-up was incomplete in 21/33 cases.

Discussion: Dermal and ocular exposures were referred in to the ED more frequently than ingestions. Ingestions in older patients resulted in no documented cases of toxicity. Dermal exposures resulted in chemical burns (1 s degree). Ocular exposures resulted in eye irritation (one corneal abrasion). A limitation of PC data is the high rate of cases with no follow-up.

Conclusion: LDP exposures occur in patients >6 years. Further study is needed to accurately describe outcomes in this age group.

47. Up in Smoke: Carbon Monoxide Poisoning from Hookah (Water Pipe) Smoking

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Background: In comparison to cigarette smoking, little is known about the adverse health consequences of water pipe smoking (WPS). Clinically significant acute carbon monoxide (CO) poisoning is an uncommonly reported adverse effect of WPS.

Hypothesis: WPS may be associated with serious adverse effects related to CO poisoning.

Methods: This is a case series of consecutive patients treated at a large metropolitan hyperbaric oxygen (HBO) treatment referral center associated with a level 1 trauma center and burn unit. The patients either presented primarily to the ED or were referred for evaluation, between March 2015 and September 2015. Each patient smoked a water pipe immediately before the onset of symptoms consistent with CO poisoning, had an elevated COHb documented, and had other environmental sources of CO excluded.

Results: Five patients (three males) between the ages of 14 and 50 years were evaluated for CO poisoning after WPS. Four patients were smoking a water pipe inside their homes, while one patient smoked outdoors. Only two patients smoked cigarettes at least occasionally. On presentation, three patients had also consumed alcohol; all denied any other drug use. Their initial COHb concentration and presenting symptoms were as follows: 11 % (seizure); 21 % (syncope); 22 % (syncope); 24 % (seizure); 25.4 % (syncope and seizure). All patients were hemodynamically stable and all underwent a single HBO treatment at 2.6 ATA. All were asymptomatic and clinically normal after HBO.

Discussion: Although this is a large series of carbon monoxide-poisoned patients associated with WPS, it remains unclear why only some users develop an elevated COHb. Additionally, without epidemiological data, the incidence of CO poisoning with WPS is unknown. Furthermore, the relationship between COHb concentrations in the setting of WPS and the development of symptoms is unclear. Surveillance and research are necessary to better define these relationships.

Conclusion: WPS may be an underappreciated source of significant CO poisoning.

48. Pediatric Dosing Calculator for the Reduction of Pediatric Medication Errors

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Background: Medication errors are a significant and potentially avoidable source of morbidity and mortality to patients. In pediatric patients, where weight-based calculations are necessary to determine the correct dosages, mathematical errors can cause serious adverse effects.

Hypothesis: We hypothesized that through the use of a Microsoft Excel-based medication calculator we would be able to reduce the number of pediatric medication errors, as determined by Patient Safety Reports (PSRs).
Methods: This is a cohort study using a Microsoft Excel-based Pediatric Dosing Calculator designed to aide in weight-based medication dosage calculations. This calculator was, by order of the Chief of Emergency Medicine, mandated to be used when ordering pediatric medications. PSRs related to pediatric medication errors were monitored for 12 months prior to the implementation of the calculator and for 7 months following the calculators use.

Results: In the preceding 12 months prior to the use of the pediatric dosing calculator, there were 9 PSRs recorded in 15,787 patient visits, approximately 1 error per 1973 patient visits. Since implementation, only 1 PSR was documented, shortly after commencement of the calculators use, equating to 1 error in 8729 (NS, *t* test) patient visits.

Discussion: This Pediatric Dosing Calculator decreased the rate of pediatric medication errors by a factor of 4.4, from 1 error in 1973 patient visits to 1 error in 8729 (NS) patient visits. This decrease does not meet the definition of statistical significance ($p < 0.05$); however, the trend is such that when a full year of implementation is completed, we anticipate a statistically significant decrease in errors. Limitations of our quality improvement initiative include the method used to identify pediatric errors is imperfect, relying on PSRs. Likely not all errors are being identified or recorded. As there are approximately 100 medical errors for every one PSR written, the PSR serves as a surrogate for the number of actual medication errors.

Conclusion: This project was successful in reducing the overall number and rate of pediatric medication errors and has the potential to prevent serious and potentially fatal pediatric dosing errors.

49. Snakebite Neurotoxicity: a Retrospective Review of Patients Reported to the ToxIC North American Snakebite Registry

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Background: Neurotoxicity is a well-described but uncommon effect of North American snake envenomation (NASE). Reports are generally limited to small case series and may represent more severe cases rather than the complete spectrum of neurotoxicity. Further investigation is warranted.

Research Question: What are the characteristics of neurotoxicity following NASE?

Methods: Data reported to the ToxIC North American Snakebite registry (NASBR) between January 1, 2013 and October 22, 2015 were reviewed. Inclusion criterion was any neurotoxic effect observed after snakebite. Patient demographics, snake species, and clinical findings were collected. Microsoft Excel and descriptive statistics were used.

Results: Four hundred thirty-three cases representing 10 US states were reviewed. Twenty-four cases with neurotoxicity were reported in Arizona, California, Colorado, and Texas. Mean age was 41 years (2–78). Nineteen (79 %) were male. Thirteen (54 %) were upper extremity and 11 (46 %) lower extremity bites. Snakes included the following: 20 (83 %) North

American rattlesnakes (2 Grand Canyon, 1 sidewinder, 1 southern pacific, 16 unknown species), 1 Texas coral snake, 1 cottonmouth, 1 copperhead, 1 non-native South American rattlesnake. Neurotoxic symptoms included the following: 11 (46 %) extremity paresthesias, 11 (46 %) fasciculations/myokymia, 7 (29 %) perioral paresthesias, 2 (8 %) objective weakness, 1 (4 %) seizure without history of seizure disorder. Texas coral snake and copperhead neurotoxicity involved extremity paresthesias and cottonmouth involved paresthesias and fasciculations/myokymia. No patients required intubation.

Discussion: Reports of neurotoxicity after NASE typically describe fasciculations or myokymia, and in many, respiratory failure. In this cohort, fasciculations were common but respiratory failure did not occur, suggesting it is a very rare event with NASE neurotoxicity. Seizure has been reported previously, though in association with respiratory arrest. NASE neurotoxicity has been most associated with coral snakes and Mojave, timber and southern pacific rattlesnakes. Copperheads and cottonmouths (both *Agkistrodon* spp.) have not previously been reported to produce neurotoxicity. This NASBR neurotoxic cohort included Grand Canyon and Sidewinder rattlesnake, and *Agkistrodon* envenomations. Limitations include retrospective nature of review as well no standardized method of snake species identification.

Conclusions: Fasciculations and paresthesias were the most commonly reported neurotoxic symptoms after NASE in this cohort. Neurotoxicity may be associated with *Agkistrodon* envenomation.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

50. Massive Bupropion Ingestion: Another Brain Death Mimic

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Background: Coma and absent brainstem reflexes are used to determine brain death. Case reports demonstrate intoxication with drugs like baclofen and phenobarbital can mimic brain death. One previous report describes dilated pupils and EEG burst suppression after bupropion overdose with elevated measured bupropion and hydroxybupropion levels. We present a patient with coma, absent corneal and pupillary reflexes following massive bupropion ingestion. Quantitative levels were obtained.

Hypothesis: Bupropion toxicity may mimic brain death with coma and absent brainstem reflexes.

Methods: This is a case report of a 32-year-old man found unresponsive after ingesting 180 tablets of 150 mg extended-release bupropion. Bystanders initiated CPR prior to EMS arrival. In the ED, PEA arrest was confirmed, ACLS protocol initiated, and intubation performed. ROSC was achieved and epinephrine and norepinephrine were initiated for refractory hypotension. Flumazenil and naloxone were administered and the patient developed tonic-clonic seizure activity that ceased after 4 mg IV lorazepam. Toxicology was contacted and exam on admission revealed coma, fixed/dilated pupils with no oculocephalic, corneal, or gag reflex. No sedatives or paralytics had been given for hours. EEG showed diffuse suppression and slowing of background activity. Therapeutic hypothermia was initiated. On hospital day (HD) 2, posturing and non-purposeful movements were noted and controlled with propofol infusion. Pupils were equal and reactive on HD 3. Neurologic exam gradually

improved. He was extubated on HD 5, and discharged without motor or cognitive deficits on HD 11. Bupropion and hydroxybupropion levels obtained on HD 1 were 5898.8 ng/mL (50–100) and 3521.8 ng/mL (600–2000), respectively. No other drugs known to mimic brain death were present on GC/MS urine drug testing.

Discussion: Bupropion toxicity causes seizures, status epilepticus, cardiotoxicity, and cardiopulmonary arrest, but there is only one published report of absent brainstem reflexes. This case is similar with coma and absent pupillary and corneal reflexes, yet with significantly greater quantitative bupropion and hydroxybupropion levels. Both experienced neurological recovery. Caution is required when determining brain death following massive bupropion overdose. Limitations to this case include PEA arrest as a confounder of his initial neurologic examination.

Conclusion: Bupropion toxicity may cause fixed/dilated pupils and mimic brain death.

51. Racial Disparities in the Treatment of Acute Overdose in the Emergency Department

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Background: Racial disparities continue to exist in many disciplines of medicine extending to care in the Emergency Department (ED). A disparity can be defined as a difference in the quality of health care due to environment, access to care, health status, or particular health outcomes.¹

Hypothesis: We hypothesized that Blacks would be less likely to receive treatment with activated charcoal or antidotes when presenting to the ED for acute drug overdose.

Methods: We completed a secondary analysis of a prospective cohort of 3242 cases of patients presenting to two urban tertiary care hospitals with suspected acute overdose between 2009 and 2014. Categorical variables were analyzed with a chi square test with two-sided *p* values and 5 % alpha. OR were calculated with 95 % CI. Assuming a baseline rate of 25 % and alpha = 0.05, we had >80 % power to detect an 18 % difference in the rate of antidote administration.

Results: We screened 3242 patients, of those, 2664 were included and 410 were excluded (alternate diagnosis (93), a lack of data (188), pediatric age (53), and other (76)). Mean age was 41.5 years, 55 % were men; Black 21.8 % (580), Whites 33.67 % (897), Asians 6.9 % (183), other 6.9 % (185), and Hispanics 30.4 % (811). Overall 219 cases were treated with activated charcoal, either single or multi dose, and 523 people were treated with an antidote (naloxone (257), N-acetylcysteine IV or PO (136), calcium (101), sodium bicarbonate (91), glucagon (39), octreotide (29), digoxin immune fab (10), high dose insulin therapy (6), physostigmine (6), fomepizole (5), dantrolene (2), flumazenil (2), or intralipids (1)). Results of the statistical analysis indicated that Blacks were less likely to receive activated charcoal, either single or multi dose [Black 16.4 %, non-Black 83.56 %, *p* 0.04, OR 0.687, CI 0.48–0.99] and were much less likely to receive any antidote at presentation [Black 14.1 %, non-Black 85.9 %, *p* 0.000002, OR 0.533, CI 0.41–0.69]

Discussion: Blacks are significantly less likely to receive either activated charcoal or any antidotes when presenting to the ED for acute drug overdose.

Conclusion: Further studies are needed to determine national prevalence and how race plays a role in management of acute overdose.

52. The Impact of Hemodialysis on Survival in Intubated Salicylate-Poisoned Patients

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Background: Severe salicylate toxicity is associated with high mortality if mechanical ventilation is required due to the reliance of hyperventilation to keep acid–base homeostasis. Timely hemodialysis may be a life-saving therapy in these cases. We evaluate the impact of hemodialysis on survival rates in severely poisoned intubated patients.

Hypothesis: Patients with severe salicylate toxicity requiring intubation have an increased mortality without prompt hemodialysis.

Methods: This is a retrospective observational study. All salicylate cases reported to the Illinois Poison Center were reviewed from 2007 to 2014. Intubated patients with a salicylate level greater than 45 mg/dL were included for analysis. Charts were reviewed for data including age, sex, initial and peak aspirin levels, arterial blood gas results, ventilator settings, and if the patient received activated charcoal, urinary alkalinization, and/or hemodialysis. Particular attention was paid to implementation of dialysis.

Results: Fifty-five cases were identified; overall survival rate (41/55) was 74.5 %. The average peak aspirin level in deaths ($n = 14$) was 92 mg/dL compared to 74.9 mg/dL in survivors ($n = 41$). In undialyzed patients, a peak aspirin level greater than 45 mg/dL was associated with 76.5 % (13/17) survival; there were no survivors with aspirin level greater than 80 mg/dL (three deaths). When patients received hemodialysis, a peak aspirin level greater than 45 mg/dL had a 87.5 % survival rate (28/32) and 78.6 % survival (11/14) when the level was greater than 90 mg/dL. Only 28.6 % of all deaths (4/14) received hemodialysis before time of peri-arrest; six patients had dialysis started immediately before cardiac arrest (session was not completed) or after patient had already arrested with return of spontaneous circulation and four patients never had dialysis attempted.

Discussion: Expelling carbon dioxide is an essential mechanism to alkalinize the blood and becomes even more apparent when sodium bicarbonate is required for urine alkalinization. Intubated aspirin patients may do more poorly as it is difficult to provide the high minute ventilations necessary to maintain hyperventilation; hemodialysis should be considered early to decrease the salicylate level and improve chances of survival.

Conclusion: Timely dialysis prior to intubation is associated with a mortality benefit in severely salicylate-poisoned patients.

53. Trends in Emergency Department Utilization for Poisoning-Related Visits, 2003–2011

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Background: In recent years, there has been an increase in poisoning-related emergency department (ED) visits. How ED resource utilization has changed for poisoning-related visits is less well described.

Hypothesis: We hypothesized there would be an increase in resource utilization for poisoning-related visits in EDs over time.

Methods: A retrospective review of data from the National Hospital Ambulatory Medical Care Survey, 2003–2011, was conducted. All ED visits with a reason for visit or ICD-9 code related to poisoning were included. We examined the number of ED visits and resources used including diagnostic studies and procedures performed, medications provided, admission rates, and length of stay. The proportion of visits involving resource use was tabulated and trends analyzed using survey-weighted logistic regression, grouping into 2-year periods to ensure adequate sample size.

Results: Of an estimated 843 million ED visits between 2003 and 2011, 8 million (0.9 %) were related to poisoning. Visits increased from 1.8 million (0.8 %) visits in 2003–2004 to 3.0 million (1.1 %) visits in 2010–2011, $p = 0.001$. Use of laboratory studies, EKGs, plain radiographs, medications ordered, and procedures remained stable across the study period.

CT use more than doubled, increasing from 5.2 to 13.7 % of visits, $p = 0.001$. ED length of stay increased 35.5 % from 254 to 344 min, $p = 0.001$. Admission rates increased 45.3 %, from 15.0 to 21.8 %, $p = 0.046$. Over the entire study period, 52.0 % of poisoned patients arrived via ambulance, and 3.0 % of patients had been discharged from the hospital within the previous 7 days.

Discussion: There was nearly a doubling in ED visits for drug poisonings comparing 2003–2004 to 2010–2011. These visits consumed considerable resources with high rates of laboratory, EKG, and radiography use. CT use increased more than 100 %, and length of stay increased by 35.5 %, therefore poisonings increasingly contribute to ED crowding, which is associated with poorer outcomes. We were unable to investigate individual charts to determine appropriateness of care or underlying reasons for and impact of these changes over time.

Conclusion: Poisoning-related ED visits nearly doubled over the 8-year study period; poisonings are resource-intensive visits that increasingly rely on CT and require increasingly longer lengths of ED stay.

54. Emergency Department Resource Utilization for Adverse Drug Reaction-Related Visits, 2001–2011

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Background: Adverse drug reactions (ADRs) are a common occurrence in healthcare. This study characterizes and describes resource utilization for ADR-related visits in US emergency departments (EDs).

Hypothesis: We hypothesized that ADRs would occur more commonly in high-risk populations and would require significant use of ED resources.

Methods: A retrospective review of data from the National Hospital Ambulatory Medical Care Survey, 2001–2011, was conducted. All ED visits with a reason for visit labeled “adverse drug reaction” were included. We examined the number of ED visits and associated patient characteristics, including age, sex, race, and payer. We investigated ED resources used, including diagnostic studies, procedures performed, medications provided, admission rates, and length of stay. The proportion of visits involving resource use was also tabulated and differences in frequency calculated using Chi square analysis.

Results: Of an estimated 1.3 billion ED visits between 2001 and 2011, 2.2 million (0.2 %) had a reason for visit of ADR. ADRs were more common among patients aged 18–64 years (68.5 %) compared to under 18 (12.3 %) and 65 and older (19.2 %). White patients involved 73.5 % of visits and 26.4 % were non-White. Private insurance was the most common payment source, with 47.0 % of visits compared with 20.2 % Medicare and 18.3 % Medicaid. Of patients, 35.8 % arrived via ambulance and 13.4 % had been seen in an ED in the prior 72 h. Of visits, 40.1 % included a procedure, the most common of which were laboratory studies. Of patients, 20.8 % got EKGs. 15.2 % of patients got X-rays, and 7.1 % got CTs. The mean number of diagnostic tests for ADR visits was 3.3 and an average of two medications were provided. Average ED length of stay was 190 min. Admission rates to a general floor were 8.0 % and 1.7 % were admitted to the ICU.

Discussion: Our data likely underestimated ADRs as many ADRs go unrecognized and unreported. We were unable to determine individual agents that caused the ADR.

Conclusion: ED visits for ADRs can occur across all demographics, and can be time and resource intensive. Additionally, a considerable number of patients had been seen in the ED in the preceding 72 h.

55. Use of Naloxone in Alpha-2 Agonist Overdoses

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Background: Naloxone reportedly reverses the toxic effects of clonidine with variable success rates. Little is known about its use in other alpha-2 agonist overdoses and about what factors correlate with successful reversal.

Research Question: Is naloxone effective for all centrally acting alpha-2 agonists?

Methods: This is a retrospective cohort study assessing patients reported to a regional poison center from 2002 to 2015. Patients with reported exposure to clonidine, guanfacine, tizanidine, or xylazine and treated at least once with naloxone were included for full review. Primary outcome was response to naloxone, either “full/partial” or “minimal/none.” Patients with no description of a response to naloxone were excluded from the primary analysis. Other data collected include reported coingestants, dose(s) of naloxone used, other reported therapies, reported clinical effects, and final outcome.

Results: Two hundred forty-eight patients were included: 209 clonidine, 7 guanfacine, 2 guanfacine with clonidine, 13 tizanidine, and 1 xylazine. Positive response to naloxone was noted in 43 % of both the overall cohort and the sub-group of patients with no coingestants (95 % CI 36–50 %). Of the 29 patients who coingested opiates, 66 % responded (95 % CI 48–83 %). Patients ingesting guanfacine in any combination without opiates had a 67 % response rate (95 % CI 36–98 %). Of the six tizanidine patients without opiates, only two responded to naloxone. In pediatric patients receiving at least 2 mg of naloxone initially, 62 % responded (95 % CI 41–83 %). Outcomes were predominately (62 %) reported as “moderate” (95 % CI 56–68 %); one patient died.

Discussion: This study supports the use of naloxone as an effective reversal agent for multiple alpha-2 agonist medications, despite conflicting evidence from previous reports. In pediatric patients receiving an initial dose of at least 2 mg, response rates approached those of patients with opiate coingestions, supporting the notion that larger than typical doses of naloxone may be needed. This study is limited by its retrospective design and the small sample sizes in many of its subgroups.

Conclusion: Naloxone reversed the effects of centrally acting alpha-2 agonists as a class 43 % of the time. Larger, non-weight-based doses were more effective in pediatric patients.

56. Rapid Development of Extreme Leukemoid Reaction Following Amlodipine Overdose

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Background: Leukemoid reactions (LR) are rare, poorly understood, systemic hematologic reactions in response to a specific insult—including certain drugs—associated with high mortality. Very few cases of drug-induced extreme LR in which WBC counts exceed 100,000/mcL have been reported.

Hypothesis: A rapidly progressive leukocytosis up to 137,400/mcL 14 hours after overdose is indicative of a LR secondary to amlodipine poisoning.

Methods: This is single patient case report. A 37-year-old man presented after intentional overdose on amlodipine. The patient stated he had overdosed on his blood pressure medication. Upon presentation 2 h after ingestion, he was found to have leukocytosis to 39,100/mcL. He became comatose and hypotensive and developed vasodilatory shock responsive to norepinephrine. Leukocytosis increased to 81,200/mcL at 8 h and to 137,400/mcL at 14 h post ingestion. He developed refractory ARDS leading to cardiopulmonary arrest and died 17 h after ingestion. The patient was prescribed amlodipine, the presence of which was confirmed by GC/MS.

Results: White blood cell differential revealed marked neutrophilia with increased immature granulocyte precursors, elevated myelocytes and metamyelocytes, but no blasts. Peripheral blood smears revealed normal

WBCs in two samples, with one showing vacuolization, indicating a nonmalignant reaction to a toxic state. The patient had no history of malignancy or hematologic disease, and prior complete blood counts had been within normal range. Given these findings, we believe that this represents LR stemming from amlodipine overdose. Aspiration, pneumonia, or shock itself would be unlikely to cause this degree of leukocytosis. This time course is inconsistent with development of sepsis and blood cultures were negative.

Discussion: Calcium channel blocker toxicity causes hypotension and vasoplegia contributing to systemic inflammatory response, which may have led to LR. Furthermore, ARDS in this case could have been caused by or complicated by leukostasis or cytokine-mediated injury from extreme leukocytosis. Literature review reveals no documented extreme leukemoid reaction from calcium channel blockers.

Conclusion: This report describes a unique case of extreme leukemoid reaction following fatal amlodipine overdose with clinical toxicity most consistent with calcium channel blocker poisoning, but death due to ARDS rather than hemodynamic collapse.

57. Successful Use of Extracorporeal Membrane Oxygenation (ECMO) for Treatment of Refractory Cardiac Arrest in a Pediatric Propranolol and Doxepin Overdose

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Background: Propranolol is a nonselective β -adrenergic antagonist and blocks fast sodium channels. Doxepin is tricyclic antidepressant (TCA) and can cause sodium channel blockade in overdose. Acute combined toxicity can result in hemodynamic compromise refractory to vasopressor administration. Extracorporeal life support with venous-arterial extracorporeal membrane oxygenation (VA ECMO) in poisoned patients has generally been described in patients prior to cardiac arrest.

Hypothesis: Extracorporeal membrane oxygenation (ECMO) is efficacious for the treatment of refractory cardiovascular collapse secondary to combined propranolol and doxepin toxicity even after cardiac arrest.

Methods: This is a single case retrospective chart review. A 16-year-old female presented for medical care after a reported seizure and witnessed asystolic cardiac arrest. She was resuscitated using epinephrine, sodium bicarbonate, magnesium sulfate, and calcium chloride with return of spontaneous circulation (ROSC). An electrocardiogram obtained following initial resuscitation showed sinus rhythm and QRS complex widening (152 ms). After a second cardiac arrest with ROSC, she was transferred to a pediatric tertiary care center and arrived intubated, ventilated, and hypotensive despite norepinephrine and epinephrine infusions. Upon arrival, she arrested a third time with PEA and an episode of a wide complex tachycardia. Following ROSC, VA ECMO was initiated in conjunction with continued vasopressor support and serum alkalization.

Results: Urine gas chromatography mass spectrometry (GCMS) demonstrated propranolol, doxepin, and naprosyn. Echocardiogram demonstrated severely depressed right and left ventricular function. Following initiation of ECMO, inotropic support was successfully weaned. Cardiovascular status progressively improved and ECMO was discontinued on hospital day 3. Repeat echocardiogram demonstrated a normal ejection fraction of 71 %. The patient had satisfactory neurologic recovery and inpatient psychiatric care was recommended after an uncomplicated hospital course.

Discussion: Combined propranolol and doxepin toxicity can result in refractory hemodynamic collapse and cardiac arrest. Extracorporeal life support can support vital organs until cardiotoxicity resolves. The majority of previous cases describe the use of ECMO prior to cardiac arrest. We report the successful use of VA ECMO after repeated cardiac arrest and failure of supportive care including maximal inotropic support.

Conclusion: Extracorporeal life support should be considered in select poisoned patients even after cardiac arrest.

58. Acetaminophen Toxicity Complicated by Hepatorenal Failure and Posterior Reversible Encephalopathy Syndrome: a Case Report

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Background: Posterior reversible encephalopathy syndrome (PRES) is a clinical entity characterized by altered mental status, headaches, visual changes, and characteristic radiologic findings. Although PRES is associated with hypertension and renal injury, it has been infrequently reported in the setting of drug overdose.

Methods/Case Report: This is a single patient case report. A 31-year-old man presented complaining of several days of abdominal pain for which he reported taking 500 mg acetaminophen every 4–5 h. He also reported vomiting multiple times over the preceding 3 days and denied using NSAIDs. His initial vital signs were as follows: T 36.5 °C, HR 102 bpm, and BP 144/72 mmHg. On exam, the patient demonstrated icteric sclera and diffuse abdominal tenderness. His initial bloodwork revealed an ALT/AST of 6100/7000 IU/L, total bilirubin 9.6 mg/dL, INR 2.2, lipase 279 IU/L, APAP 30.2 mcg/mL, BUN 44 mg/dL, and Cr 7.95 mg/dL. A right upper quadrant ultrasound was normal, and an abdominal CT scan was significant for duodenal thickening and stranding around the pancreas. The patient received N-acetylcysteine from hospital day (HD) #0–8. Liver function gradually improved and creatinine peaked at 10.96 mg/dL on HD #3, but showed improvement with supportive care thereafter. On HD #6, the patient awoke with complaints of headache and new vision impairment, a blood pressure of 220/120 mmHg, and a Cr of 6.24 mg/dL. His ophthalmologic exam was normal. After treatment with antihypertensives, the patient's blood pressure and visual impairment improved. The rest of his hospital course was uneventful.

Results: An extensive workup for other causes of hepatorenal failure was negative, and consensus among providers was that this patient's initial presentation was secondary to acetaminophen toxicity. A brain MRI performed on HD #6 showed widespread bilateral T2 hyperintensities, consistent with PRES with atypical features.

Discussion: The etiologies of PRES are many, and the syndrome has well-established associations with hypertension and renal injury. We suspect that acetaminophen-induced hepatorenal failure contributed to our patient developing PRES.

Conclusion: PRES may occur as a sequelae of acetaminophen toxicity.

59. Metoprolol-Related Adverse Drug Events: a 5-Year Experience

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Background: Adverse drug events (ADEs) are an important and preventable cause of inpatient morbidity and mortality. Metoprolol is a commonly prescribed medication with multiple formulations, increasing the potential for drug errors. Further complicating safe use of metoprolol are recent shortages (e.g., diltiazem and certain metoprolol formulations), which are often used for similar indications. We identified themes in severity, metoprolol formulation involved, and nature of error in metoprolol-related ADEs.

Research Question: Characterization of metoprolol-related ADEs at our institution.

Methods: Five years of standardized ADE reports were obtained from our medical center's internal database. Incidents were classified by hospital location, event type, date, medication(s) involved, severity, and event description. Data were organized quantitatively in each category to identify overall trends in ADE occurrence. Two independent reviewers examined all data, and results were compared for agreement.

Results: Fifty-five cases were reported between October 2010 and October 2015 involving metoprolol tartrate (78 %) and metoprolol

succinate (22 %). ADEs occurred during errors in transcribing or documenting (45 %), dispensing (35 %), and administration (20 %). The most common types of errors were drug/dose omission (28 %), extra dose (22 %), and incorrect timing (18 %). Only one case involved an interchange of metoprolol tartrate for succinate, which did not result in patient harm. Events associated with patient harm ($n=4$), classified by a National Coordinating Council for Medication Error Reporting and Prevention index severity score E-I, were all associated with drug omission except for one case, which had a 10-fold drug underdose. Three of these patients developed tachydysrhythmias, while one experienced dyspnea and hypertension.

Discussion: The most common and harmful metoprolol-related ADEs involved drug/dose omissions. A unified electronic medical record and computerized medication reconciliation and ordering system could potentially help prevent a number of these errors. National and hospital-wide AV nodal blocking agent shortages likely also contribute to confusion pertaining to the ordering, dispensing, and administration of these medications as physicians may not be able to prescribe the medication most familiar to them.

Conclusion: A single-institution review of metoprolol-related adverse drug events demonstrated omission as the most common reason for voluntary reports.

60. Undifferentiated Toxin-Induced Cardiogenic Shock Treated with High Dose Insulin

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Background: Insulin is a recognized inotrope used to treat drug-induced cardiogenic shock, primarily for direct cardiotoxins like calcium channel antagonists. Few reports describe using high dose insulin (HDI) to resuscitate cardiogenic shock from noncardiovascular agents.

Hypothesis: Insulin is a useful inotrope for opiate-induced cardiogenic shock.

Case Report: This single chart review describes HDI use for severe myocardial depression following an opiate overdose. A 17-year-old, 84-kg male with a history of substance abuse was found unresponsive in his driveway with bradypnea (4 breaths/min). Mental status and respiratory rate improved following naloxone; however, he remained hypoxic (O₂ saturation 88 %) and hypercarbic (pCO₂ 73 mmHg) requiring intubation. Seven hours after arrival, he suffered bradycardic and then tachydysrhythmic cardiac arrests. He was successfully resuscitated with compressions, vasopressors, sodium bicarbonate, magnesium, and intravenous 20 % lipid emulsion. Post-resuscitation, he required increasing vasopressor doses and ventilator support with an oscillator and nitric oxide. Echocardiogram showed biventricular systolic dysfunction with a 21 % ejection fraction while on norepinephrine, vasopressin, and dopamine. Addition of epinephrine and milrinone did not improve cardiac output or perfusion. Twenty hours after admission, HDI was started with a 2 unit/kg bolus (170 units regular insulin) and 2 unit/kg/h infusion. Within 30 min of starting HDI, blood pressure improved and vasopressors were decreased. The maximum HDI infusion was 3 units/kg/h without hypoglycemia or hypokalemia. Repeat echocardiogram on HDI showed normal ventricular function. Over the next 24 h, all vasopressors and then insulin were stopped. He was discharged on day 6 with a full recovery. Comprehensive urine drug screen, obtained after arrest, demonstrated the presence of morphine (2604 ng/mg creatinine), which was not administered in hospital.

Case Discussion: This patient developed severe cardiopulmonary compromise following recreational opiate overdose. Cardiogenic shock was refractory to standard therapy. Extracorporeal membrane oxygenation was considered but not undertaken due to improvement with HDI. Although the definitive cause of cardiac dysfunction was

not determined, cardiac function improved and hemodynamics stabilized quickly after initiation of HDI.

Conclusion: This case adds to a small body of literature demonstrating HDI is a useful inotrope for cardiogenic shock from drugs without direct cardiac activity.

61. Acute Overdose of Sotalol and Rivaroxaban with Prolonged Ventricular Dysrhythmias

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Background: Sotalol is a β -blocker that also antagonizes potassium channels. Rivaroxaban is a competitive factor Xa inhibitor anticoagulant. Overdose experience is limited in either of these agents.

Hypotheses: 1. Sotalol may not behave like a prototypical β -blocker following overdose. 2. Rivaroxaban overdose may pose bleeding risks during invasive resuscitation procedures.

Case Report: This single chart review describes a 43-year-old female with history of atrial fibrillation, pulmonary embolism, polysubstance abuse, and prior overdoses who ingested sotalol and rivaroxaban. Eight hours post-ingestion, she presented with bradycardia (50 bpm) and fluid responsive hypotension. Initial ECG demonstrated sinus rhythm and QTc of 613 ms. Cardiac ultrasound revealed normal contractility. The first hours of care were complicated by recurrent monomorphic ventricular tachycardia (VT) that responded to intravenous magnesium. Hemodialysis was planned for sotalol removal; 4-factor prothrombin complex concentrate, fresh frozen plasma, and phytonadione (INR 4.1) were administered prior to catheter placement. Four hours into HD, she developed sustained torsades de pointes (TdP) requiring CPR but not cardioversion. A magnesium bolus restored sinus rhythm. Epinephrine, isoproterenol, and dopamine infusions failed to provide pharmacological overdrive pacing. She received 12 h of HD. The patient's course was complicated by recurrent, episodic VT and TdP until initiation of a lidocaine infusion on day 4. On day 5, heart rate and QTc normalized (485 ms) and pharmacological support was discontinued. No bleeding complications developed and patient recovered fully. The serum sotalol level after 2 h of hemodialysis was >8000 ng/mL (ref range 500–4000). Rivaroxaban levels during hemodialysis were as follows: 870 ng/mL (0 h), 1000 ng/mL (2 h), 890 ng/mL (8 h), 1100 ng/mL (12 h) (ref range, 355–474).

Case Discussion: This patient experienced severe sotalol cardiotoxicity manifesting as bradycardia and recurrent ventricular dysrhythmias. The duration of cardiotoxicity was markedly longer than prior reports. Dysrhythmias responded to magnesium and lidocaine, but not chronotropic agents. No bleeding occurred despite elevated rivaroxaban levels. Rivaroxaban levels did not decrease during hemodialysis.

Conclusion: This case experience supports that sotalol toxicity is primarily dysrhythmic and may be prolonged. Rivaroxaban did not preclude the use of invasive procedures and did not appear to be removed by HD.

62. Atypical Baclofen Toxicity Presenting First with Seizure Followed by Coma

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Background: Baclofen, a GABA-B agonist, is used in the treatment of muscle spasticity. Significant baclofen toxicity often presents with delirium then somnolence and has been implicated in findings consistent with brain death.

Hypothesis: Baclofen toxicity can present first with tonic-clonic seizures followed by non-convulsant status epilepticus causing persistent coma.

Case Report: This single chart review describes the clinical course of baclofen overdose in a 12-year-old, 76-kg female with a history of migraines, optic neuritis, and psuedotumor cerebri taking gabapentin, naratriptan, and magnesium. She reported suicidal ideation by texting a friend but denied ingestion when confronted. She was at her baseline when she acutely developed vomiting followed by generalized, seizure-like activity. She was unresponsive in the emergency department and intubated (vital signs: BP 113/69 mmHg; HR 67 bpm; RR 14 breaths; PO₂ 100 %; T 97 °F). Following intubation, she had a tonic-clonic seizure treated with lorazepam and levetiracetam. She was transferred to a tertiary pediatric hospital for workup of seizures and continued unresponsiveness. EEG was “markedly abnormal” and suggestive of seizure activity. This improved but remained abnormal for 48 h despite treatment with benzodiazepines, pyridoxine, fosphenytoin, and levetiracetam. She was extubated on day 2 but remained encephalopathic. On day 5, she returned to her baseline neurological status. An extensive workup was negative for anatomic and infectious etiologies. Immunoassay urine drug screen was negative. Drug levels of medications in the home were obtained: lamotrigine, lacosamide, gabapentin, and zonisamide were undetectable. She was discharged on zonisamide with a diagnosis of new seizure disorder. A baclofen level (160 ng/mL, reference range 100–400) was obtained day 2 and returned after patient discharge. After confirming baclofen ingestion, long-term seizure prophylaxis was discontinued.

Case Discussion: This case demonstrates an unusual presentation of baclofen toxicity, devoid of many of the common initial neurologic findings (somnolence, delirium). The seizure activity was resistant to treatment. The baclofen did not belong to the patient; this was the sibling's medication and an accurate pill count was initially reported.

Conclusion: Baclofen toxicity may present with seizures and an unexpected complication may include prolonged unresponsiveness from non-convulsant status epilepticus which may be difficult to treat.

63. Bupropion Toxicity Associated with QT Prolongation: a Case Series

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Background: Bupropion, an aminoketone antidepressant, is used for the treatment of depression. Bupropion overdose is known to cause seizures, QRS prolongation, and ventricular dysrhythmias.

Hypothesis: Bupropion toxicity can cause QT/QTc prolongation independent of QRS effects.

Methods: This is an IRB approved, retrospective chart review of four patients who developed QTc prolongation after bupropion overdoses.

Results: Patients 1 and 2 are 9-year-old females who took their grandmother's bupropion XL 150 mg. Patient 1 developed seizures, EMS was called, and during transport she developed sustained ventricular tachycardia requiring cardioversion. She had multiple seizures in the emergency department (ED) and during subsequent transport to a tertiary pediatric hospital. She remained agitated with sinus tachycardia (129–158 bpm) and QTc prolongation (QRS 82 ms; QT/QTc 354/536 ms). While visiting her cousin in the ED, patient 2 developed hallucinations, agitation, nausea, and vomiting. She was also transferred to the tertiary pediatric hospital. She had sinus tachycardia (138–145 bpm) and QTc prolongation (QRS 84 ms, QT/QTc 338/523 ms). Patient 3 is a 17-year-old female with history of autoimmune hepatitis, ADHD, depression, and drug use who overdosed on bupropion and fluoxetine through insufflation and ingestion. She

presented with altered mental status, sinus tachycardia (121–135 bpm), and QTc prolongation (QRS 86 ms, QT/QTc 440/624 ms). Patient 4 is a 14-year-old female with history of depression taking quetiapine and sertraline who overdosed on bupropion. She developed seizure activity at home with multiple episodes in the ED, sinus tachycardia (102–119 bpm), and QT/QTc prolongation (88 ms, QT/QTc 348/495 ms). Urine drug levels confirmed the presence of bupropion (>1200 ng/mL), hydroxybupropion (10,000 ng/mL), quetiapine (>1000 ng/mL), sertraline (48 ng/mL), trazodone (2.6 mcg/mL), and meta-chlorophenylpiperazine (>500 ng/mL).

Discussion: These cases demonstrate QTc prolongation after bupropion overdose that may be related to cardiac potassium channel blockade in the overdose setting. Only patient 1 developed dysrhythmias; patients 2 through 4 did not. QTc prolongation resolved by day 2 in all four cases and all patients recovered fully. Age, gender, and route of administration may have an effect on the development of toxicity.

Conclusion: Bupropion toxicity can cause QTc prolongation independent of QRS prolongation.

64. Assessment of Bleeding Risk in Patients with Intentional Overdoses of Novel Anticoagulants and Antiplatelet Agents

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Background: In recent years, the use of antiplatelet (AP) and novel anticoagulants (NOACs) has increased. Overdose experience with these agents is limited.

Hypothesis: We hypothesize that overdose of these agents can result in significant bleeding. The primary objective of this study is to evaluate the prevalence of bleeding in this population.

Methods: A retrospective cohort study using poison control data from two states involving adults (age >14 years) with an acute or acute-on-chronic, intentional ingestion of one of the AP agents (clopidogrel, prasugrel, ticagrelor, ticlopidine) or NOACs (apixaban, dabigatran, rivaroxaban) between January 2005 and December 2014 was conducted. Bleeding was classified as trivial, minor, or major, based on previously published criteria. Deaths were evaluated as likely or unlikely to be related to the antiplatelet or NOACs by a panel of toxicologists not involved with the study.

Results: The median (IQR) age was 51 (42–60) years; 58 % were male. Thirty overdoses of NACs (apixaban = 1; endoxaban = 0; dabigatran = 4; rivaroxaban = 25) and 142 overdoses on APs (clopidogrel = 136; prasugrel = 3; ticagrelor = 1; ticlopidine = 2) were identified. One death was reported, but it was deemed unlikely related to clopidogrel.

Bleeding developed in 7/30 (23 %) of NOAC overdoses vs. 3/142 (2.1 %) of AP overdoses ($p < 0.001$). Among the NOAC overdose patients, bleeding was considered major ($n = 4$), minor ($n = 1$), and trivial ($n = 1$). In contrast, among the AP overdose patients, there was one each of major, minor, and trivial bleeding.

Four patients received vitamin K, two received pooled complex concentrates, two received DDAVP, and nine received FFP. Two patients who overdosed on both dabigatran and lithium underwent hemodialysis. Among the factor Xa inhibitors, the median (IQR) international normalized ratio (INR) was 3.1 (1.6–4.7)

The median (IQR) duration of poison center follow up is 1 (1–2) days.

Discussion: Our data demonstrate that intentional overdose with APs and NACs can result in bleeding and that it is significantly more common following overdose of the NACs compared to the APs.

Conclusion: Because of the increased use of APs and NACs, clinicians need to be aware that intentional self-poisoning with these agents can result in serious toxicity.

65. F(ab')₂ Antivenom Used to Treat Rattlesnake Envenomation in the Pediatric Population

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Background: A new F(ab')₂ antivenom directed at rattlesnakes is soon to be commercially available in the USA. This antivenom has been shown to be both effective and safe in its use, but it has not been well studied in the pediatric population. Furthermore, the F(ab')₂ antivenom has been suggested to decrease the rate of recurrent coagulopathy in rattlesnake envenomations compared to its Fab predecessor.

Hypothesis: We hypothesized that a F(ab')₂ antivenom would be both safe and effective in the treatment of rattlesnake envenomation.

Methods: We present a case series of pediatric patients under 16 years of age who suffered rattlesnake envenomation and were treated with the new F(ab')₂ antivenom. The primary endpoint was stabilization of the patient, defined as resolution of any fibrinogenemia, thrombocytopenia, and the cessation of the advancement of swelling. Safety was also assessed by monitoring for adverse events. A secondary endpoint was recurrent coagulopathy (defined as fibrinogen <150,000 mg/dl and platelets <150,000/mm³) between the end of stabilization and post-treatment day 8.

Results: Twenty-one pediatric patients received the F(ab')₂ antivenom. All patients receiving the F(ab')₂ antivenom achieved stabilization of their rattlesnake envenomation. There were no cases of recurrent coagulopathy recorded in the study between time of infusion and post-infusion day 8. None of the patients evaluated suffered serious adverse events.

Conclusion: In this series, the F(ab')₂ antivenom appeared to be both safe and effective in pediatric patients in the treatment of coagulopathy and local tissue toxicity from rattlesnake envenomation.

66. Left High and Dry of Δ⁹-Tetrahydrocannabinol: the Oral Ingestion of a THC Beverage.

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Background: Δ⁹-Tetrahydrocannabinol (THC) is the main psychoactive ingredient in marijuana. With the advent of legalization of marijuana in many states, new edible forms are coming to market including THC infused drinks. The metabolism of marijuana differs greatly with oral ingestion versus inhaled use.

Hypothesis: THC metabolism differs based on the route of ingestion.

Methods: This is a single patient case report.

Results: We report a male to female transgender individual who presented to the emergency department with a complaint of acute anxiety, visual hallucinations, and tremulousness after drinking nearly half of a 473-mL commercially available, marijuana lemonade called “Cannabis Quencher” 3 h prior. She was naïve to marijuana use. She initially presented with a heart rate of 112 beats per minute and blood pressure of 91/34 mmHg, and all other vital signs were normal. Metabolic panel and cell blood count were within normal limits. A urine drug screen was only positive for THC. A comprehensive urine drug panel was positive for THC and negative for 61 different tested substances. The remaining beverage was analyzed by mass spectrometry, and it was found to contain 0.1 mg/mL of THC for a total of 47.3 mg in the beverage. Interestingly, her serum had no detectable THC, only the metabolite THC-COOH with a concentration of 120 ng/mL. The beverage contained no measurable THC-COOH.

Discussion. The metabolism of orally ingested cannabinoids is not as well studied as smoked marijuana. There seems to be an extensive first pass mechanism when THC is ingested orally. When ingested, a greater proportion of THC undergoes hepatic hydroxylation and leads to the formation of 11-OH-THC, which is then oxidized to the inactive metabolite THC-COOH. In addition, some THC may be degraded by acidic gastric contents. Our patient was having significant psychoactive effects after consuming a THC-containing beverage, a rather unusual method of exposure, with no measurable THC in her serum. Further studies need to be done to determine the bioavailability and pharmacokinetics of orally administered cannabinoids.

Conclusions: Oral liquid ingestion seems to greatly decrease the bioavailability of THC and increase the presence of its metabolite THC-COOH.

67. Uncomfortably Numb: Pediatric Exposures to Topical Benzocaine Preparations Reported to a Statewide Poison Control System

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Background: Topical benzocaine is a local anesthetic commonly used to relieve pain caused by teething, burns, and insect bites. Exposure to over-the-counter benzocaine preparations may result in methemoglobinemia, hemolysis, and complications of hypoxia, especially in children.

Research Question: What is the incidence and clinical severity of pediatric exposures to topical benzocaine products?

Methods: This is a retrospective study utilizing electronic records of a statewide poison control system. After IRB approval, the database was queried for clinical details related to exposures to topical benzocaine products in children below age 18 from 2004 to 2014.

Results: There were 99 study cases after 58 were excluded due to co-ingestants or miscoding. The majority (98 %) of exposures occurred in children aged less than 5 years old. In this age group, 87 cases were accidental exposures with 5 cases of therapeutic errors, 4 cases of adverse reactions, and 1 unknown reason for exposure. Patients remained asymptomatic in 59 % of cases. Serious adverse effects were observed in 10 patients who were exposed to a range of benzocaine concentrations (7.5–20 %).

Methemoglobin levels, ranging from 20 to 59 %, were available in seven patients. Methylene blue was administered in seven cases, of which six exhibited major clinical effects. Three patients were admitted to a medical floor and four to a critical care unit; the remainder were either kept at home or discharged after a brief treatment/observation period in an emergency department. There were no intubations or fatalities.

Conclusions: This study confirms the potentially serious outcomes associated with widely available topical benzocaine products in children. The majority of exposures were accidental ingestions by young children, although both dosage errors and idiosyncratic reactions were also reported with these products. Most exposures resulted in minor to no effects. However, some patients required treatment with methylene blue and admission to a critical care unit. This study is limited by sample size, incomplete laboratory results, and selection bias inherent in voluntary reporting to a poison control system. Recommendations to mitigate the hazard from this agent include the following: increased public and healthcare provider education, better warning and instruction labels, and tighter regulation at the retail pharmacy level.

68. Potassium Overdose from Guava Consumption in a Patient with Renal Failure

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Background: Hyperkalemia remains a commonly seen clinical problem. With the burden of kidney disease ever growing, vigilance concerning the avoidance of this frequently fatal state must remain high, including close attention to potassium intake from dietary indiscretion. The literature contains only rare case reports of hyperkalemia as a result of various fruit juices, and none have ever mentioned the guava—which the FDA has found to contain more potassium than even the oft-cited banana.

Hypothesis: Indiscriminate guava intake can result in significant hyperkalemia in the setting of renal failure.

Methods: In this single-patient chart review, we describe a 52-year-old woman with a history of diabetes mellitus and end-stage renal disease on hemodialysis thrice weekly who presented with profound and diffuse weakness limiting ambulation, a significant change from her baseline. However, mental status was normal and her neurological exam was non-localizing; her vital signs were stable. Her electrocardiogram (ECG) demonstrated peaked T waves.

Results: Laboratory workup yielded a potassium of 8.1 mmol/L, despite compliance with scheduled hemodialysis and a creatinine at her baseline. Upon further history, she reported that she had been consuming approximately 20 guavas daily for the past month, as the tree in her backyard had been yielding fruit over the month leading up to her presentation. She did not note any other changes in her diet. Chart review revealed her pre-dialysis potassium concentrations had been 6.1–7.1 mmol/L during the past month, notably higher than her usual concentrations, which reliably ranged in the 4–5 mmol/L range. She was treated with emergent dialysis, her generalized weakness abated, and she was discharged without complication. Potassium concentrations after this event remained normal after guava intake was ceased.

Discussion: Frank muscle weakness and ECG changes are common manifestations of hyperkalemia, both of which were exhibited in our case of accidental potassium overdose. Patients can easily mistake “natural” lifestyle choices as completely benign; certain fruits, and in particular guavas, should be consumed with great caution in those with risk factors for hyperkalemia.

Conclusion: Guava fruit is a potassium-rich source of food that can cause clinically significant and life-threatening hyperkalemia.

69. Antibiotic Use with Native Venomous Snakebites: Recommended by Poison Centers?

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Background: North American snake envenomations may produce clinical effects similar to infections. However, infections are uncommon with such bites. Toxicologists do not routinely recommend antibiotics in the management of snake envenomations. At the 2015 ACMT Annual Scientific Meeting, an abstract from the North American Snakebite Registry reported that 10 % of the 276 patients had received antibiotics. It is unclear if poison centers are recommending the use of the antibiotics or if there is trending over time in their use.

Methods: This retrospective epidemiologic investigation included all native venomous snakebites reported to a state-wide poison center system during 2000–2014. Bites not followed to a final medical outcome were included. Whether antibiotics was recommended or used was identified for each case. The antibiotic rate (percent where antibiotics were recommended or used) was determined for various factors.

Results: Antibiotics were used in 886 (14.2 %) of 6243 total native venomous snakebites. Among those who received antibiotics, 89.5 % had received the antibiotics prior to the poison center being contacted. Poison centers recommended antibiotics in only 93 of all snakebites (10.5 %). The antibiotic rate by type of snake was copperhead (15.0 %), rattlesnake (15.1 %), cottonmouth (12.2 %), and coral snake (5.5 %). Antibiotics were used in 17.4 % of cases during 2000–2004, 14.6 % of cases during 2005–2009, and 11.7 % of cases during 2010–2014. The

antibiotic rate by medical outcome was no effect (0.8 %), minor effect (12.2 %), moderate effect (17.5 %), major effect (21.7 %), death (50.0 %), not followed-nontoxic (0.0 %), not followed-minimal effects (6.8 %), unable to follow-toxic (4.3 %), and unrelated (0.0 %).

Discussion: Most antibiotic use in snakebite patients is done by providers and not recommended by poison centers. This suggests that the targets of continued education on this topic are clinicians. Our data are limited in that it is from only one state's poison system.

Conclusion: Ninety percent of antibiotics in snakebite cases are given by providers prior to contacting a poison center; however, the use of antibiotics is decreasing over time.

70. Physostigmine Use Among Medical Providers Who Evaluate Patients with Suspected Overdose

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Background: Physostigmine can reverse anticholinergic delirium, potentially reducing complications and the need for invasive procedures. Despite adverse events reported 35 years ago in the setting of cyclic antidepressant toxicity, subsequent studies have supported the safety of physostigmine in the absence of specific contraindications such as QRS widening or bradycardia.

Research question: Are providers who care for suspected overdose patients familiar with the risks and benefits of physostigmine, and in what situations would they consider its use?

Methods: An electronic survey link was distributed to a convenience sample of ED and critical care providers in one poison center's (PC's) service area. The link was e-mailed to providers for whom the PC had contact information ($n = 157$). A letter was faxed to ED directors in the PC's service area ($n = 137$), asking them to share the survey link with their colleagues. Providers were queried about past physostigmine use and awareness of its indications, precautions, and potential benefits. They were asked about situations in which they might consider administering this antidote and factors that would influence their decision.

Results: A total of 38 responses were received. Most (65 %) were ED providers. Twenty-nine (76 %) had never used physostigmine, 5 had used it once, 2 twice, one more than twice, and one did not recall. Respondents indicated that they would consider using physostigmine in patients with agitated delirium (62 %) and CNS depression (46 %). Although a majority expressed concern for potential adverse effects, most indicated that they would be more likely to use physostigmine if they had the opportunity to discuss their patient with a toxicologist (89 %) or were given a written guideline by the poison center (68 %).

Discussion: Although most respondents indicated limited experience with physostigmine and concerns for potential serious adverse events, the majority were receptive to additional information and guidance on the use of this antidote. The primary limitation of this study was its small sample size.

Conclusion: Medical providers managing suspected overdose patients may be more likely to consider using physostigmine if discussion with a toxicologist and/or a written poison center guideline is available.

71. Poison Center Recommendations for Physostigmine Treatment in Anticholinergic Toxicity

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Background: Physostigmine can reverse anticholinergic delirium, potentially reducing complications and the need for invasive procedures.

Despite adverse events reported 35 years ago in the setting of cyclic antidepressant toxicity, subsequent studies have supported the safety of physostigmine in the absence of specific contraindications such as QRS widening or bradycardia.

Research question: Do poison centers have guidelines for physostigmine administration, in what situations are they recommending its use, and are those recommendations being followed?

Methods: A survey link was sent by e-mail to managing and medical directors of all 55 US poison centers (PCs). They were invited to share the link with associated toxicologists who advise providers on patient management. Respondents were asked to identify situations that would prompt them to consider physostigmine as an antidote, as well as clinical features that would discourage or prevent them from doing so, how often they have recommended it, how frequently their recommendations were followed, and whether their PC has guidelines addressing physostigmine use.

Results: There were 60 respondents, including 25 medical directors, 19 managing directors, and 16 affiliated toxicologists. Sixteen (27 %) said they recommended physostigmine more than 5 times/year, 22 (37 %) 2–5 times/year, 18 (30 %) ≤ 1 time/year, and 4 (7 %) never recommend it. Of the 56 that recommended physostigmine, 50 % thought most hospital providers followed their recommendations. Most respondents (67 %) said that their PCs do not have guidelines addressing physostigmine. They were most likely to recommend physostigmine for agitated delirium with a history of anticholinergic ingestion (81 %). The most common factor that would prevent physostigmine recommendation was QRS widening. Some respondents expressed hesitancy to recommend this antidote for other reasons including short duration of action, perceived minimal benefit, and lack of appropriate patients. Most (92 %) acknowledged that physostigmine treatment is appropriate in selected patients.

Discussion: The variability in PC recommendations suggests a need for additional study related to the impact of physostigmine on patient outcomes, perhaps focusing on length of stay and cost.

Conclusion: Although most PC directors acknowledge that physostigmine can play a positive role in anticholinergic toxicity, their practice varies considerably with regard to recommending its use as an antidote.

72. Home Observation of Tended-Yard Mushroom Ingestions in Idaho

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73. Trends of Acute Intoxication in the Republic of Korea (2011–2014)

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Background: Acute intoxication is one of the leading causes of death in the Republic of Korea. In addition, the trend of acute intoxication is changing rapidly recently. Therefore, we analyzed trend of acute intoxication of the injury surveillance data to reflecting in the emergency medical system and establishing the toxic substances research system based on emergency room.

Research question: The characteristics of acute intoxication in the Republic of Korea

Methods: We surveyed the data of Emergency Department based Injury In-depth Surveillance (2011–2014), Korea Centers for Disease Control and Prevention, retrospectively. We included the patients that mechanism of injury is coding by acute intoxication. We surveyed the patients of sex and age, and the result of emergency treatment such as discharge,

admission or transfer, and death. Also, we surveyed the patients with intentional intoxication or not, the types of toxic substances, and the pathway of intoxication.

Results: The total number of Emergency Department-based Injury In-depth Surveillance, between 2011 and 2014, was 974,571. The patients with acute intoxication were 22,493. Male and female were 10,190 (45.30 %) and 12,303 (54.70 %). Mean age was 41.34 ± 22.33 years old. The patients with intentional intoxication were 13,916 (61.87 %). In the result of emergency treatment, discharge, admission or transfer, and death were 13,124 (58.35 %), 8910 (39.61 %), and 459 (2.04 %), retrospectively. According to categorizing the type of toxic substances, therapeutic agent, pesticide, gas intoxication, artificial toxin, natural toxin, and others were 10,403 (46.33 %), 4201 (19.2 %), 3962 (17.87 %), 2425 (11.07 %), 853 (4.56 %), and 641 (3.40 %), retrospectively. In annual patterns of toxic substances, acute intoxication of therapeutic agent was increased little by little. Acute intoxication of pesticide was decreased, gas intoxication were more than twice.

Discussion: This study is limited by the results based on descriptive and retrospective analysis.

Conclusion: The intoxication by therapeutic agents and gas is seen a tendency to increase, whereas intoxication by pesticide showed the decreasing trend.

74. Characteristics of Scorpion Envenomation Reported to US PCCs for Infants ≤ 6 Months of Age

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Background: Bark scorpions (*Centruroides sculpturatus*) are found in the southwest US and are the only native scorpion species of clinical concern. Due to the scorpion's ability to climb walls and furniture, the limited mobility of young infants creates a unique vulnerability. Since there is no data on the risk factors for envenomation in this population, we sought to identify patterns that may be used in future prevention efforts.

Question: What are the patterns of scorpion envenomation in infants?

Methods: This was a retrospective review of scorpion envenomations in Arizona for infants ≤ 6 months of age reported to the National Poison Data System between 2004 and 2013. Confirmed non-exposures and patients with unrelated effects were excluded.

Results: A total of 149 Arizona scorpion stings were reported for this age group, and all but 3 occurred at home. Although cases occurred year-round, there were more reports in June–October, accounting for 65 % of exposures (see graph). Cases also occurred at all hours of the day and night but 13 of the calls came between 7 and 11 pm. Many infants ($n = 61$; 41 %) had moderate-severe clinical effects. A total of 93 (62 %) infants were either referred to or already at a healthcare facility at the time of the initial call. Of these, 54 patients (58 %) received antivenom (youngest was 11 days old) and 8 (8.6 %) were intubated. Twenty-five patients (26.9 %) were admitted with 6 (6.5 %) of these to intensive care.

Discussion: In this population, the greatest risk of a scorpion sting is at home, during the warmer months of June–October, and in the evening between 7 and 11 pm. It may be beneficial to remind parents in Arizona of the potential for scorpion stings beginning at birth. Limitations include reliance on voluntary reports to a PCC, errors in data entry, and the assumption that the time of the call is temporally related to the exposure time.

Conclusion: Scorpion stings are a risk to even the youngest infants in Arizona, with most occurring at home during warmer months and evening hours. Knowledge of times of greatest risk may guide preventive education.

75. Development of the Headspace-Solid Phase Microextraction Gas Chromatography Mass Spectrometry (HS-SPME-GC-MS) for Determination of 35 Pesticides in Plasma

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Background: Pesticide poisoning is the leading cause of death concerning toxicological exposure in developing countries. Effective determination of pesticides in biological samples especially in plasma despite low concentration of parent compounds may enhance favorable management outcome in such victims.

Hypothesis: Thirty-five pesticides from five major classes including organochlorine, organophosphorus, fungicide, pyrethroid, and organonitrogen pesticides in plasma can be detected simultaneously by using headspace-solid phase microextraction gas chromatography mass spectrometry (HS-SPME-GC-MS) technique.

Methods: This is an in vitro study to develop sensitive analytical procedures to quantitatively identify 35 pesticide standards added to plasma obtained from healthy supposed non exposed subjects by using solid-phase microextraction (SPME) method coupled with gas chromatography mass spectrometry (GC-MS). Our study included selection of an appropriate coating of required small diameter optical fiber, optimization of parameters and analysis of HS-SPME procedure; extraction and analysis of pesticides by GC-MS analysis; and validation of developed method according to the US Food and Drug Administration guideline and Eurachem (The Fitness of Purpose of Analytical Method) guide 1998. This study was funded by Routine to Research Grant from the authors' institute.

Results: The best setting of our developed HS-SPME-GS method included using Polydimethylsiloxane/Divinylbenzene/Carboxen-coated fiber, extraction temperature of 70 °C for 40 min, and the 30 % (weight/weight) NaCl added to the extraction solution. This method yielded a good linearity with the coefficient of determination (r^2) more than 0.995 at the concentration of 0.05–1 mcg/mL. The coefficient of variance (CV) was less than 15 %. The percent relative value (%RV) was between 85 and 120 %. The lower limit of detection was 0.02 mcg/mL. This method could not detect abamectin.

Discussion: Our developed method can detect wider spectrum of pesticides simultaneously by using HS-SPME-GS technique compared with previously published methods. It had good accuracy, high precision with low threshold limit of detection. This can be applied to serum samples from exposed patients.

Conclusion: We successfully developed a method to quantitatively determine 34 pesticides in five major classes including organochlorine, organophosphorus, fungicide, pyrethroid, and organonitrogen pesticides in plasma simultaneously by using the HS-SPME-GC-MS; however, abamectin was not detected by this technique.

76. Prescription Opioid Death Rates are Greater for Females than Males

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77. GABA GABA Hey (I Wanna Be Sedated): Phenybut Exposures Reported to a Statewide Poison Control System

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78. A Retrospective Review of a US Poison Center's Experience with Loperamide-Induced Cardiotoxicity

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Background: Loperamide is a widely available nonprescription anti-diarrheal intestinal opioid agonist, which decreases peristalsis and transit time. It has poor blood–brain-barrier penetration and is thought to have low abuse potential. However, loperamide is increasingly used extra-medically for recreational abuse and to ease opioid withdrawal symptoms. Life-threatening arrhythmias and conduction disturbances have been reported in patients abusing large doses of loperamide. Because of limited availability of epidemiologic data, we analyzed loperamide-induced cardiotoxicity reported to a single US poison center (PC).

Methods: We retrospectively reviewed collected data on loperamide exposures presenting with cardiotoxicity reported to a single PC between January 1, 1992 and August 31, 2015. Data extracted include age, gender, dose, exposure, cardiac effects, and outcome.

Results: Eight cases of loperamide-induced cardiotoxicity were reported to the PC, with the first case occurring in 2012. Three (38 %) patients presented to ED after cardiac arrest; three (38 %) patients presented with sedation and/or respiratory depression; and two (25 %) patients presented following syncope. Five (63 %) patients had a known history of opioid abuse or dependence. The mean age was 29 (range, 25–41) years, and the majority were male ($n = 6$, 75 %). The dose of loperamide ingested was estimated in seven cases (mean = 477 mg; range, 100–800 mg). Four cases involved chronic daily ingestions (range, 100–440 mg daily). The cardiac abnormalities reported include the following: bradycardia ($n = 8$, 100 %), ventricular tachycardia ($n = 5$, 63 %), ventricular fibrillation ($n = 2$, 25 %), torsades ($n = 3$, 38 %), QRS widening ($n = 7$, 88 %; range, 120–236 ms), and QTc prolongation ($n = 7$, 88 %; range, 520–587 ms). Seven (88 %) patients required ICU care. There was one fatality, presumably from loperamide-induced cardiotoxicity.

Discussion: Loperamide is increasingly abused for its opioid-like central effects. In large ingestions, loperamide is associated with cardiac conduction disturbances and life-threatening arrhythmias. The rhythm disturbances described in our dataset include bradycardia, ventricular tachyarrhythmias, QT prolongation, and QRS widening. The reported loperamide dosages in our patients that developed cardiotoxicity are consistent with prior reported cases.

Conclusion: Loperamide-induced cardiac toxicity should be considered in patients presenting with cardiac arrest or syncope with abnormal ECG findings, especially those patients with a history of opioid abuse or dependence.

79. Thai Eggplant Seed Ingestion Resulting in Anticholinergic Poisoning and ECG Abnormalities

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Background: Anticholinergic toxicity can occur from plant ingestions. This is the first case reported in the USA of toxicity from “Thai eggplant” (*Solanum melongena*) ingestion.

Hypothesis: Thai eggplant seeds contain glycoalkaloids in the Solanaceae family that may lead to anticholinergic toxicity.

Methods: Case presentation is set in an urban emergency department. A 73-year-old Thai female presented with confusion, inability to speak, and tongue discomfort after eating a meal. Vital signs are as follows: T 97.9; HR 114; BP 150/100; RR 20; O₂sat 100 %. Physical exam shows dilated pupils, dry mucus membranes, tachycardia, and incomprehensible phonation. Neurological exam shows inability to follow commands, up-going Babinski's, but moving all extremities equally and spontaneously.

Results: Electrocardiogram result includes sinus tachycardia with a terminal right axis deviation consistent with sodium channel blockade. Chest X-ray, head CT, and blood tests are unremarkable.

The family revealed that the meal included uncooked “Thai eggplant” obtained from a garden. A photograph of the ingested plant was confirmed by a botanist to be *S. melongena*. Although initially withheld due to the abnormal ECG, physostigmine was given on admission day 2 for persistent anticholinergic toxicity with her mental status vastly improving.

Discussion: Physostigmine was initially withheld due to the ECG abnormality. Select case reports of physostigmine use showed adverse cardiac effects, including asystole in patients with sodium channel blockade. The safety of using physostigmine in patients with abnormal ECGs requires further study.

Conclusion: Clinicians should identify and treat anticholinergic poisoning after *S. melongena* ingestion. It is important to educate the community regarding the potential for anticholinergic toxicity when ingesting this plant uncooked. Antidotal therapy with physostigmine should be considered, unless there is ECG evidence of concomitant sodium channel blockade.

80. Supratherapeutic Ingestions of Oral Dofetilide at Home: a Retrospective Case Series

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Background: Dofetilide is a class III antiarrhythmic used for treating atrial dysrhythmias. Though its adverse effects are well described in routine use, very little is known about dofetilide toxicity in supratherapeutic exposures at home.

Research Question: What clinical effects are seen with supratherapeutic dofetilide exposures occurring at home?

Methods: This is a retrospective case series of consecutive patients reported to our poison center (May 2002–September 2015) after supratherapeutic dofetilide exposure at home. Data collected included dose ingested, usual dose, coingestants, vital signs, electrocardiogram findings, treatments, and final disposition.

Results: Twenty-three cases were included. Median age was 70 years (range 50–91). Ten patients were observed at home, 13 at a healthcare facility, 6 admitted, and 7 discharged after a period of ED observation. Nineteen patients took one extra tab, two took someone else's medication, and one took four tabs instead of one. Seven patients had co-ingestants reported, including two QT-prolonging agents (bupropion and escitalopram). Heart rates were available for ten patients and ranged from 50 to 102 beats per minute. There were no reported hypotensive episodes. Median QTc on presentation for 11 patients was 460 ms (IQR 448–488). The longest QTc reported was 526 ms. Reported serum potassium, magnesium, calcium, and creatinine concentrations were within normal limits. Two patients received magnesium and three received potassium supplementation. None of the patients required cardioversion, defibrillation,

CPR, or overdrive pacing. There were no fatalities. The only patient to have significant clinical effects intentionally overdosed on 90 times his usual dose. He experienced multiple dysrhythmias, including an 8-beat run of nonsustained ventricular tachycardia, frequent multifocal PVCs, and ventricular bigeminy. This patient received supplemental magnesium sulfate and potassium chloride and fully recovered.

Discussion: In this series, unintentional small ingestions did not result in significant clinical effects and were often managed successfully at home, in contrast to warnings about even a single extra tablet resulting in life threatening dysrhythmias. This study is limited by its small sample size, retrospective design, and incomplete data.

Conclusion: Small dofetilide oral ingestions did not result in significant dysrhythmias or symptoms, though further study is warranted. The larger intentional ingestion resulted in ventricular dysrhythmias.

81. Predictors of Tissue Necrosis Following Upper Extremity Rattlesnake Envenomation

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Introduction: Rattlesnake envenomation (RSE) causes edema, hemotoxicity, and tissue necrosis. Necrosis may result in permanent disability. No human study has explored patient-related factors associated with tissue necrosis after *Crotalus* envenomation.

Methods: Prospective cohort study of patients admitted to the Medical Toxicology service with diagnosis of RSE between April 2011 and November 2014 was conducted. Inclusion criteria were age ≥ 18 years and upper extremity (UE) envenomation site. Study was IRB approved. Predefined data included demographics, comorbidities, medication and substance use, envenomation history, physical exam, laboratory findings, treatment, and follow-up. Primary outcome was tissue necrosis, including dermonecrosis, manifesting as bullae. Secondary outcome was amputation.

Results: Seventy-seven subjects, age 18 to 88 years, met inclusion criteria. Rattlesnake species was unknown in most cases. All received Fab antivenom. Sixty-two (82 %) had a digital envenomation. Thirty-one (40.3 %) had necrosis. Necrotic area ranged from 0.1 to 14 cm². Procedural interventions (superficial debridement, dermatomy, surgical exploration, and operative debridement of devitalized tissue) occurred in 25 (32.5 %). Five (6.5 %) underwent dermatomy and six (7.8 %) operative debridement. No amputations were performed. Patients with cyanosis on presentation had increased risk of developing necrosis (11/12; RR 2.98 95 % CI 1.99–4.46). Ecchymosis on presentation was also associated with increased risk of necrosis (24/32; RR 4.04 95 % CI 2.08–7.86). Patients with social or regular ethanol use were more likely to develop necrosis than those without (28/53; RR 4.23 95 % CI 1.42–12.6). Regular cocaine use was associated with increased risk of operative debridement (4/6; RR 9.13 95 % CI 2.33–35.8). A nonsignificant risk of operative debridement occurred with tobacco use ($p=0.08$). Time to antivenom did not correlate with risk of necrosis.

Discussion: Necrosis after UE RSE is common, is not prevented with antivenom, and may result in permanent disability. We identified potential predictors of necrosis upon presentation, including ethanol use and presence of cyanosis or ecchymosis. Prospective studies might investigate modifying treatment based on predictors to improve outcomes.

Conclusion: UE RSE patients who presented with cyanosis, ecchymosis, or history of ethanol use were at increased risk of developing necrosis. Cocaine use was associated with increased risk of operative debridement.

82. Antineoplastics as Agents of Suicide Reported to US Poison Centers from 2000 to 2014

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Background: Oral chemotherapy for cancer has become common. An estimated 25 % of the chemotherapy agents in development are oral agents. Patients with cancer are a high risk group for attempting suicide. The development of oral chemotherapy agents and their use in home settings greatly increases the potential exposures to the drugs, including as agents of suicide in a vulnerable population.

Research Question: Are chemotherapeutic agents being used for suicide?

Methods: The National Poison Data System was accessed for all chemotherapy exposures for the purpose of suicide attempt reported in the USA to US poison centers from 2000 to 2014. Analysis used SAS and Epi Info.

Results: There were 1460 intentional ingestions for the purpose of suicide using chemotherapeutic agents over the study period with death in 0.8 %. The annual incidence of use of chemotherapeutics for intentional ingestion increased over the study period; 50 cases were reported in 2000, increasing to 129 cases in 2014. Sixty-seven percent of exposures were female. The average patient age was 36 years, ranging 10–89. The most commonly reported agent was methotrexate, with 623 exposures, followed by azathioprine with 238, anastrozole with 104, and 6-mercaptopurine with 90 exposures. All but six were managed at a health-care facility. A major effect was seen in 126 cases, while 399 cases were reported to have moderate effects, and 695 had minor or no effects. Hospital admission was required in 821 cases, with 576 intensive care unit admissions. Twelve deaths were reported, eight of which were due to methotrexate and one each due to azathioprine, anastrozole, erlotinib, and imatinib.

Discussion: Rising use of chemotherapeutics in the outpatient and home settings parallels the increase in use of these agents for suicide. While many had only minor or no effects, some were severe enough to necessitate intensive care or cause death.

Conclusion: Oral chemotherapeutic agents are being used more often over time as suicidal agents.

83. Adverse Drug Events Related to Oral Anticoagulants: a Single-Center 5-Year Experience

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Background: Oral anticoagulants are increasingly prescribed for a variety of disease conditions. As patients are admitted to the hospital, adverse drug events (ADEs) related to transcription, prescribing, administration, and monitoring can lead to significant morbidity and mortality. In this study, we identify ADEs related to oral anticoagulants in our institution.

Research Question: Characterization and outcomes of oral anticoagulant ADEs at our institution.

Methods: Five years of standardized, voluntary ADE reports were extracted from our hospital system by querying ADEs related to oral anticoagulants. Adverse events were categorized as errors in monitoring, administration, dispensing, prescribing, or transcription. Two independent reviewers examined the data independently, and results were compared for agreement.

Results: Eighty-eight ADEs involving oral anticoagulants (warfarin, Xa inhibitors, direct thrombin inhibitors) were reported between October 2010 and October 2015. Warfarin was implicated in 77 (87.5 %) of cases. Twenty-one cases were errors in medication administration, 19 cases were errors with dispensing, 14 cases were related to transcription errors, and 13 cases occurred during medication monitoring. Only six ADEs were related to novel factor Xa inhibitors. These included incorrect dosing, incorrect medication reconciliation, and prescribing additional anticoagulants by the inpatient team.

Discussion: In our institution, errors in administration and order transcription make up the majority of ADEs relating to oral anticoagulants. Even with electronic ordering, patients still received oral anticoagulants at an incorrect dose or dosing frequency. Errors in medication reconciliation as patients are admitted to the hospital contribute to ADEs which can have significant morbidity and mortality. Patients who were on novel Xa inhibitors were prescribed additional anticoagulation by inpatient services. Our data provides the opportunity to improve medication reconciliations to prevent oral anticoagulant-related ADEs. Limitations include the voluntary basis of reporting and a user-initiated ADE system.

Conclusion: Adverse drug events involving oral anticoagulants continue to be an identifiable source of error in an inpatient setting.

84. Deliberate Self-Poisoning with a Lethal Dose of Pentobarbital: Survival with Supportive Care and Documented Serial Serum Concentrations.

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Objective: Pentobarbital (PB) is a recommended euthanasia drug in doses of 2 to 10 g. Rapid onset of coma and cardio-respiratory arrest occur within 15 to 30 min. We report a case of severe pentobarbital deliberate self-poisoning with full recovery and serial blood concentrations.

Case Report: A 45-year-old male, with a history of depression, purchased 10 g of pentobarbital (PB) powder over the Internet 2 years earlier. On the day of presentation, he told his mother 10 min after impulsively ingesting the powder mixed in water. She found him unresponsive and commenced CPR immediately. Within 30 min of the ingestion, EMS arrived and he was in PEA arrest. Advanced life-support and endotracheal intubation were instituted and cardiac output returned after 15 min.

In the emergency department: P122/min, BP 117/69 on epinephrine infusion (100 mcg/min). He was hypotonic, hypothermic (33.8 °C), with fixed dilated pupils, and no brain stem reflexes. ECG and CT brain were unremarkable. Venous blood gas showed pH 7.02, pCO₂ 60 mmHg, Bic 15 mmol/L, lactate 11.9 mmol/L. A single-dose of activated charcoal was administered and he was admitted to ICU. He developed diabetes insipidus on day 1 treated with DDAVP and required epinephrine infusion for 5 days to support BP. He remained comatose without any supplemental sedation, with absent brain stem reflexes until day 8. A four-vessel cerebral angiogram on day 3 was normal. He was extubated on day 10. Serum PB concentration 2.5 h post-ingestion was 112 mg/L (therapeutic 1.8–4.7 mg/L), peaking at 116 mg/L, 29 h. PB concentration fell slowly over the next 10 days: 110 mg/L at 42 h, 65 mg/L at 90 h, 20 mg/L at 140 h, 2 mg/L at 190 h. Elimination half-life varied: initially 76 h (42–90 h), then 29 h (90–140 h), and finally 15 h (140–190 h). The patient made a full recovery and confirmed taking pentobarbital 10 g.

Conclusion: Average PB concentration in fatalities is reported, as 30–40 mg/L. Previous reports of survival after massive PB overdose have not documented serial blood concentrations. This patient survived lethal serum concentrations with early CPR and ALS-resuscitation. Ongoing cardio-respiratory support in ICU is required for a prolonged period. Elimination half-life varied over time suggesting possible initial ongoing absorption or later auto-induction of metabolism during the course of the poisoning.

85. Angel Dust Trauma: Do Trauma Patients with PCP Positive Urine Drug Screens Have Increased Morbidity or Mortality?

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86. Prescription Opioid Use and Knowledge of Overdose Prevention Strategies Among ED Patients

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Background: The USA is experiencing a prescription opioid abuse epidemic. It is unclear what role knowledge about prescription opioids contributes to this epidemic.

Research Question: To survey patients presenting to an urban ED that have been prescribed an opioid medication in the past about risk and knowledge of prescription opioids.

Methods: Patients presenting to an ED that had previously been prescribed an opioid medication were surveyed about their prescription opioid use, including use patterns, sources, doctor-shopping, preferred opioids, reasons for using, history of substance abuse, history of mental illness, and overdose prevention strategies. All patients provided written informed consent and were reimbursed for participation.

Results: Seven patients were surveyed. Five out of seven patients visited the ED for a pain-related complaint. Three of seven patients reported daily use of opioid medications, two of seven reported using opioid medications 1–2 times/week, and two of seven patients reported using <1× per week. Six of seven patients reported their daily intake of opioid medications on an average day, with a range of 15 mg morphine equivalent (MME) to 415.5 MME, with a mean of 133.7 MME per day. Two of six patients reported greater than 200 MME/day. No patients reported receiving opioid medications from more than two prescribers in the past 6 months. No patients admitted obtaining opioid medications without a prescription. Six of seven patients reported that pain interferes with their daily activities often or very often. One patient reported a personal history of substance abuse treatment. Only one of seven was aware that NY State monitors prescriptions for opioids and other controlled substances. None of the patients surveyed were aware of out-of-hospital naloxone programs to treat opioid overdose.

Discussion: Daily opioid consumption of greater than 200 MME has been associated with a threefold mortality increase in patients with chronic nonmalignant pain. In NY, programs to train non-medical persons with community naloxone are common. However, none of the subjects surveyed in this study were aware of the existence of such programs, even though some of them may be at-risk based on their daily opioid intake.

Conclusion: These results highlight the importance of education regarding community naloxone training programs to treat prescription opioid overdose in at-risk patients.



Medical Toxicology Foundation

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87. Metformin Intentional Overdose and its Association with Metabolic Acidosis and Elevated Lactate—As Reported by Toxicologists

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Background: Metformin is the most commonly prescribed antidiabetic agent in the USA. Some have suggested that the potential for metabolic

acidosis and hyperlactatemia is spurious in patients taking this medication.

Hypothesis: We hypothesize that metabolic acidosis with hyperlactatemia occurs not infrequently in patients taking metformin.

Methods: We retrospectively analyzed Toxicology Investigators Consortium (Toxic) registry data from January 1, 2010 to September 30, 2015. We searched for all patients with metformin toxicity, with emphasis on metabolic acidosis (pH < 7.2) and lactate concentrations. We reviewed demographics, laboratory analyses, co-exposures, treatments, and survival.

Results: Seventy-seven cases with metformin listed as “primary agent, most consequential” were available for analysis. Intent was reported as intentional overdose ($n = 65$), unintentional ($n = 9$), adverse drug reaction ($n = 2$), and drug abuse ($n = 1$). Of 65 intentional ingestions, all of which were acute, the dose was reported in 12 (range, 4–100 g). Co-exposures were present in 47 (72.3 %). Twelve (18.5 %) cases reported no sequelae. Ten (15 %) experienced a blood glucose < 50 mg/dL. Twenty patients (31 %) had a pH < 7.2, with an additional six (9.2 %) with an anion gap (AG) > 20. Lactate was reported in 17 cases of metformin exposure (mean, 3 mmol/L; range 0.17–27.99 mmol/L). In patients coded with metabolic acidosis ($n = 7$), the mean serum lactate was 4.91 mmol/L (range, 0.44–27.99 mmol/L). Nine patients (13.8 %) had acute kidney injury (creatinine > 2.0 mg/dL). Four patients were decontaminated with activated charcoal; one received gastric lavage. Interventions included sodium bicarbonate (18.5 %), hemodialysis (12.3 %), and continuous renal replacement therapy (7.7 %). Hypoglycemic patients received glucose > 5 %. No fatalities were reported.

Discussion: In Toxic, the majority of metformin exposures were acute, intentional overdoses. Approximately 40 % of the patients with metformin overdoses in Toxic had metabolic acidosis (pH < 7.2 or AG > 20). Our analysis of lactate was limited as it was not specifically included in Toxic until 2015. Renal insufficiency occurred in 13.8 % of patients.

Conclusion: Metabolic acidosis was present in a significant number of patients with acute metformin exposures. Providers should be cognizant of this significant toxicity.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

88. The “K2” Epidemic: Preliminary Results of a Health Department’s Synthetic Cannabinoid Receptor Agonist (SCRA) Surveillance Project

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Background: SCRA’s are popular novel drugs of abuse. Despite their banning, use has skyrocketed in the USA. Current emergency department

(ED) presentations highlight the varied clinical effects associated with reported SCRA use.

Hypothesis: In this Department of Health investigation, we confirm SCRA use with biological testing and hypothesize that toxicity is predictable based on SCRA classification.

Methods: Since May 2015, ED patients reporting “K2” use with SCRA toxicity were identified. Those in possession of suspected SCRA product(s) had blood and urine specimens obtained and clinical features reported to the Poison Center (PC). Blood, urine, and product samples were linked with clinical effects but de-identified from the patient and kept in a separate, secure database. Specimens were stored and shipped at –20 °C to an independent laboratory for analysis. This public health surveillance investigation was approved by our local department of health.

Results: In this preliminary report, six product and seven biological results from 10 patients were available for analysis. SCRA’s found in products included the following: NM2201, MAB-Chiminaca, XLR11, AMB, AB-Chiminaca, and MDMB-Fubinaca, with some products containing multiple SCRA’s. SCRA’s found in biological specimens included the following: MAB-Chiminaca, MAB-Chiminaca metabolites, and AB-Chiminaca metabolites. Not all SCRA’s found in products could be identified in corresponding patient biological specimens. Some SCRA’s found in biological specimens were not found in corresponding products.

In patients with confirmed MAB-Chiminaca in biological specimens ($n = 4$), one had agitation and three presented with central nervous system (CNS) depression. CNS depression ($n = 1$), delirium ($n = 1$), and seizure ($n = 1$) were reported in patients with biological confirmation of AB-Chiminaca.

Discussion: Preliminary data from this Department of Health investigation identified multiple SCRA’s in products and biological specimens. Clinical effects varied from sedation to agitation in patients with the same SCRA’s. This variability may result from dose-dependent effects, individual host factors, or co-exposures. Not all suspected SCRA’s or their metabolites can easily be identified in biological specimens. It is unclear if the “K2” products obtained from the patients were the exact products used.

Conclusion: Individuals can develop varied toxicity after using the same SCRA. This surveillance project is still ongoing and additional results will be available in the future.

89. The Other Rodenticide: Bromethalin Exposures Reported to a Statewide Poison Control System

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90. Extracorporeal Membrane Oxygenation in an Opioid Overdose Patient with Hypothermia and ARDS.

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Background: Opioid abuse secondary to prescription medications and intravenous drug use has been a continued problem among the country’s youth. Prescribers now have an increased awareness of prescription opioid abuse, which has led to a decreased supply shifting addicted persons to intravenous drug use. Extra corporeal membrane oxygenation has been documented in case reports for toxicologic patients. It is most commonly

used in refractory cardiovascular collapse typically seen with beta and calcium channel blockers. We present a case where ECMO was utilized in a 27-year-old female heroin overdose with profound hypothermia and ARDS.

Case: Thirty-one-year-old female with a history of intravenous drug abuse presented to the emergency department after being found unresponsive in the snow. Her initial core temperature was 79.8° taken by esophageal probe. On EKG, her rhythm showed atrial fibrillation with signs of ischemia in the inferior leads. The hypothermia was refractory to active rewarming with bilateral chest tubes and foley irrigation. Her oxygen saturation was 88 % on 100 % FIO₂ and PEEP of 12. ABG demonstrated a pH of 6.9 with pCO₂ 91 and O₂ 47. The decision was made by cardiothoracic surgery that due to the refractory hypothermia and ARDS, the patient would benefit from venovenous ECMO. The patient spent 6 days on ECMO. She was extubated on hospital day 14. Her hospital course was complicated by *Klebsiella pneumoniae* and frostbite on bilateral feet. She was ultimately discharged on hospital day 40, neurologically intact and has since become a substance abuse counselor.

Discussion: ECMO has been growing in popularity as a bridge to recovery for a variety of clinical applications outside of ischemic heart disease. Toxicologic patients represent a unique subset of patients for which ECMO may be a lifesaving treatment. Opioid overdose patients are commonly, young healthy individuals who with appropriate intervention have the possibility for complete and meaningful recovery. As opioid abuse continues to be a problem among our nation's youth, these situations will likely become more frequent.

Conclusion: Venovenous ECMO may be a useful and life-saving modality for toxicologic patients especially those suffering from hypothermia and ARDS.

91. Status Epilepticus after Synthetic Cannabinoid Use Containing XLR-11

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Background: K2 is an umbrella term used to describe synthetic cannabinoid (SC) products. SCs have become increasingly popular as marijuana substitutes, and ED presentations following the use of these products has increased as well. We present a case of an adult male with status epilepticus following the use of a K2 product (K2P) found to contain XLR-11.

Case: A 23-year-old male had a self-limited convulsive episode after using a K2P while on a camping trip with friends. He was brought to the ED 24 h later because of sustained seizure activity that occurred immediately after using the same K2P. In the ED, he exhibited status epilepticus despite three doses of IV lorazepam. The patient was intubated and sedated with IV lorazepam and propofol infusions for seizure control. He experienced intermittent tonic clonic movements throughout the night despite heavy sedation. His seizure activity abated the next day, and he was discharged on hospital day #6. XLR-11 was identified in the patient's urine as well as the K2 product he smoked.

Discussion: K2Ps are marketed as “not meant for human consumption” and are sold legally with insufficient regulation. The exact SC found in K2 products is frequently unknown, dynamic, mixed, or all of the above. LC/MS-TOF has enabled clinicians to accurately characterize unknown products and correlate them with clinical presentations. Such analytical techniques have helped to create a library of symptoms and complications due to SC abuse. Nephrotoxicity, myocardial infarction, ischemic stroke, and even fatalities have been attributed to the use of products containing XLR-11. Seizures have been reported after SC use, but they do not specifically implicate XLR-11 as the offending compound. This is the first report of XLR-11-associated seizures, as well as status epilepticus.

Conclusion: XLR-11 has previously been associated with acute kidney injury, cerebral edema, stroke, and fatalities in humans. Status epilepticus may also occur after exposure to XLR-11.

92. Nucleoside Reverse Transcriptase Inhibitor Associated Lactic Acidosis and Delayed Intubation

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Background: Treatment of HIV consists of a regimen with multiple classes of medications. Nucleoside reverse transcriptase inhibitors (NRTI) are among the first line of treatment. Toxicity after an acute NRTI overdose causes acidemia and elevated lactate concentration due to decreased production of human DNA electron transport proteins and inhibition of oxidative phosphorylation. We present an unusual case of delayed acidemia and clinical deterioration despite initial severely elevated lactate and minimal symptoms.

Case Report: A 38-year-old female with HIV and dyslipidemia presented for 10 days of bilateral leg pain treated as cellulitis with clindamycin. She denied other complaints. Her home medications included stavudine, darunavir, ritonavir, raltegravir, atorvastatin, aspirin, iron, and vitamins. She presented oriented and appeared well nourished. Blood pressure was 128/75 mmHg, heart rate 105 bpm, and she was afebrile. On physical examination, her lower extremities were diffusely tender without edema, warmth, crepitus, or skin lesions. Her initial pH was 7.31 with pCO₂ of 32 mmHg, lactate was 7.4 mmol/L. Her electrolytes, renal function, and CBC were normal. Intravenous saline was administered and repeat lactate was 5.9 mmol/L. Vascular studies showed no evidence of lower extremity ischemia. The patient was started on thiamine, carnitine, multivitamins, and admitted to the ICU. On hospital day 6 she developed respiratory failure requiring mechanical ventilation coinciding with her pH nadir of 7.06 and lactate peak of 7.8 mmol/L. Vitamin therapy and supportive care were continued and she was extubated on hospital day 10. She was discharged on hospital day 16 without an NRTI.

Discussion: This is one of the only cases reported in which severe metabolic acidosis was delayed despite initial profoundly elevated lactate concentration with therapeutic NRTI use. Clinicians should not be reassured by minimal initial changes in blood pH or clinical symptoms. Patients can develop profound acidemia, may have a prolonged clinical course, and mortality is between 33 and 57 %. It has been demonstrated that L-carnitine, thiamine, vitamin C, and riboflavin may accelerate resolution of the acidosis.

Conclusions: Life-threatening acidemia can be delayed despite early elevated lactate concentration in therapeutic use of NRTI. Clinicians should be aware of this complication and adjunctive treatments.

93. Preliminary Findings of Carnitine and Acylcarnitine Metabolite Concentrations in Acute Valproic Acid Overdose

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Background: Valproic acid (VPA) is used for multiple conditions such as mood disorders, prophylaxis of migraines, and tobacco addiction. Accordingly, reports of VPA overdoses reported to poison centers has risen sharply. VPA can cause hepatotoxicity in the setting of beta-oxidation impairment and a functional carnitine deficiency. Serum ammonia and VPA concentrations do not correlate well with clinical toxicity.

Hypothesis: Serum carnitine levels can prognosticate toxicity in VPA overdose.

Methods: This is a prospective pilot study of serum carnitine levels in adult VPA overdose patients. Patients were identified through consultation calls to our poison center from three study hospitals starting in July 2015. Cases were defined as patients (age >18 years) with a history of VPA overdose and serum concentrations above 100 mg/L. In addition to clinical, demographic, and biochemical data, outcome variables included

plasma carnitine (free, esterified, total), and individual acylcarnitine concentrations. All carnitine analytes were quantified using electrospray tandem mass spectrometry from discarded frozen plasma (−20°C) in consented patients.

Results: As of September 2015, we have enrolled four cases of equal gender distribution, mean age of 38 (range, 23–55 years). The most common clinical finding was lethargy. Mean peak serum VPA concentration was 153 (range, 132–186 mcg/mL), and mean peak ammonia concentration was 95 (range, 73–151 mcg/mol/L). Transaminitis and significant metabolic acidosis did not occur. Most cases ($n=3$; 75 %) had free carnitine levels below the reference range (25–54 mcg/mol/L) and half ($n=2$; 50 %) had long chain (C12–C16) acylcarnitine concentrations above known internal laboratory standards.

Discussion: Low free carnitine levels in the majority of our patients most likely reflects chronic carnitine depletion. Elevated long-chain acylcarnitines in half of patients may reflect a more pronounced inhibitory effect on long-chain beta-oxidation in comparison with medium or short-chain fatty acids. As more patients are enrolled, should this finding of impaired long-chain beta-oxidation be consistent in unwell patients, it may be a new prognostic marker to use in the setting of VPA toxicity. Study numbers and data will be updated at time of presentation.

Conclusion: A subset of our cases had free carnitine deficiencies. Elevated long-chain acylcarnitines may represent impaired beta-oxidation specific to VPA exposure.

94. Impact of Coral Snake Antivenin Shortage on Bites Reported to Poison Centers

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Background: Coral snakes (Genus *Micrurus*) possess one of the most potent venoms of the snakes native to the USA. The only coral snake antivenin approved by the Food and Drug Administration (FDA) ceased being manufactured in 2003, and all existing supplies were set to expire in 2010, although the FDA has extended the expiration date. Concerns were raised that the coral snake antivenin shortage might increase the rate of serious medical outcomes from coral snake bite.

Research Question: This investigation examined temporal trends in the recommendation and use of coral snake antivenin and serious medical outcomes from coral snake bite reported by poison centers.

Methods: This retrospective epidemiologic study included all coral snake bites reported to a poison center system during 2000–2014. Bites not followed to a final medical outcome were included. The medical outcome and whether antivenin was recommended or used was identified for each case. The antivenin rate (percent where antivenin was recommended or used) was determined for each medical outcome. The antivenin rate and serious outcome rate (percent with moderate effect, major effect, unable to follow-potentially toxic) was determined for five time periods (2000–2002, 2003–2005, 2006–2008, 2009–2011, 2012–2014).

Results: The antivenin rate by medical outcome was no effect (28.1 %), minor effect (44.4 %), moderate effect (57.8 %), major effect (78.6 %), not followed-nontoxic (0.0 %), not followed-minimal effect (5.6 %), unable to follow-toxic (17.1 %), and unrelated effect (50.0 %). The number of total bites, antivenin rate, and serious outcome rate were evaluated by time period 2000–2002 ($n=49$, antivenin 65.3 %, serious 28.6 %), 2003–2005 ($n=56$, antivenin 64.3 %, serious 48.2 %), 2006–2008 ($n=116$, antivenin 47.4 %, serious 40.5 %), 2009–2011 ($n=94$, antivenin 37.2 %, serious 40.4 %), and 2012–2014 ($n=87$, antivenin 17.2 %, serious 43.7 %).

Discussion: Although the antivenin rate declined throughout the study period, the largest decline (−54 %) was observed between 2009 and 2011 and 2012–2014 (after antivenin supplies were originally due to

expire). However, the serious outcome rate increased by only 8 % between those two time periods.

Conclusion: While the antivenin recommendation and use rate with coral snake bites reported to this poison center system declined greatly after the antivenin supplies were due to expire, the serious outcome rate increased only slightly.

95. Chug, Chug, Toke, Toke, Chomp, Chomp, Chomp: Prevalence of Alcohol and Drug Use in a Snake-Bitten Population

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Background: Anecdotal reports suggest that some persons bitten by snakes may be under the influence of alcohol, illegal and/or prescription drugs, or other substances. However, few studies have assessed the prevalence of alcohol and/or drugs among persons who have been bitten by a snake.

Research Question: What is the prevalence of alcohol or drug use among all patients who are bitten by snakes in the USA?

Methods: The National Poison Data System (NPDS) was accessed for reports during calendar years 2000–2013 for all snakebites with co-ingestions of alcohol, illegal drugs, or prescription drugs. Analysis used SAS and Epi Info. The UT Southwestern IRB approved the study.

Results: Callers reported 643 snakebites during calendar years 2000–2013 with co-ingestions of alcohol and/or drugs, an annual mean of 46 (range 29–64 bites). This accounts for less than 1 % of all snakebites reported. Rattlesnake bites were the most commonly reported type of envenomations (270, 42 %). Alcohol was the substance most commonly co-ingested (553, 86 %). Cocaine and amphetamine were each reported as the co-ingested substance in less than 1 % of snakebites. Males were bitten in almost 90 % of the cases (576, 89.6 %) and the mean age of those bitten was 36.7 years. Bites were reported in 43 states, the District of Columbia and Puerto Rico with the highest numbers reported in Texas (86, 13.4 %), North Carolina (76, 11.8 %), and Arizona (61, 9.5 %). Seven persons who were bitten died and almost 40 % (248, 38.5 %) required admission to an intensive care unit (ICU).

Discussion: Snakebite victims with co-ingestions of alcohol and/or drugs are uncommon. This is less than expected given the common consideration that alcohol and drug use contribute to many snakebites. These data have the same limitations of any NPDS based study.

Conclusion: Co-ingestion of drugs and alcohol among snakebite victims is uncommon.

96. A 10-Year Retrospective Review of Hydrofluoric Acid and Fluorides Exposures

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Background: Dermal, inhalational, and enteral hydrofluoric acid (HFA) exposures are well known to cause both local and systemic hypocalcemia, leading to resultant pain and dysrhythmias, respectively. Various recommendations in the literature exist regarding the percent body surface area (%BSA) affected and concentration needed to produce systemic toxicity.

Research Question: The purpose of the study was to describe one Poison Center's (PC) experience with HFA and fluorides exposures, especially as it pertains to hypocalcemia and systemic toxicity.

Methods: This is a descriptive, retrospective cohort study of patients called into a single PC with hydrofluoric acid or ammonium bifluoride exposures from 2006 to 2015. Patients were excluded if they were asymptomatic or the exposure was unclear. Data was collected on product concentration, %BSA, calcium concentration, treatment rendered, body part affected, and disposition. Normal calcium

concentrations were defined as a serum calcium of 9–10.5 mg/dL or an ionized calcium of 1.1–1.4 mmol/L.

Results: Three hundred one patients with hydrofluoric acid exposures were found from 2006 to 2015. One hundred thirty eight patients met the inclusion/exclusion criteria. There were 123 (89 %) dermal, 12 (9 %) inhalational, and 3 (2 %) enteral exposures. The dermal exposures included 85 extremity, 33 head/neck, and 5 trunk exposures. Concentration ranged from 0.25 to 70 % (mean 26.2 %) and %BSA ranged from <1–10 % (mean 1.7 %). Of the dermal exposures, 66 (54 %) patients had a calcium measured. One (1.5 %) of these patients was hypocalcemic. This was a 70 % solution exposure to the face (2%BSA) and required IV calcium and ICU admission. Of the inhalational exposures, eight (75 %) had calcium measured. Of these, one (12.5 %) was hypocalcemic. He was exposed to vapor of a 40 % solution requiring nebulized and intravenous calcium. Of the ingestions, all three (100 %) were hypocalcemic and required PO and intravenous calcium. One had pulseless ventricular tachycardia.

Discussion: The study is limited by its retrospective nature, access to Poison Center charts only, and lack of measured calcium concentrations or ECGs on all patients.

Conclusion: This data set suggests that dermal exposures very rarely cause systemic toxicity, while all ingestions should be considered life threatening.

97. Cutting to the Chase: Observations on Debridement in Crotalid Envenomation. ACMT ToxIC North American Snakebite Registry

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Background: Skin necrosis and fluid-filled or hemorrhagic bullae may occur following crotalid-envenomation. Debridement has been described as treatment but there is limited published literature to support or refute this practice. Debridement may restore mobility where limited by bullae but may also expose unprotected tissue to pathogenic contamination and increase pain.

Hypothesis: We sought to compare clinical characteristics and outcomes in patients who underwent debridement versus those where debridement was not performed in crotalid-associated necrosis and/or bullae.

Methods: A retrospective case-series was constructed from the ACMT ToxIC North American Snakebite Registry for cases between January 2013 and November 2015. Patients in which skin necrosis and/or bullae were present were included for analysis. Cases of incision and drainage for infections were excluded from analysis. Age, gender, bite location, offending crotalid (rattlesnake, cottonmouth, or copperhead), antivenom administration, Snakebite Severity Score (SSS), administration of antibiotics, and length of hospitalization (LOS) were recorded. The SSS was calculated using an online score calculator. Comparisons between subjects with and without debridement were performed.

Results: Four-hundred-twenty cases of crotalid-exposures were identified during the time interval. Sixty-nine victims developed skin necrosis and/or bullae. Nineteen patients (28 %) underwent debridement. Debridement took place most commonly for male patients (100 % [95 % CI 82–100] vs 66 % [95 % CI 51–79], $P=0.03$ ChiSquare [CS]) and in upper extremity bites (95 % [95 % CI 74–100] vs 68 % [95 % CI 53–80], $P=0.02$, CS). There were no differences identified in age [35 (IQR 17.5–52.5) vs 20 (IQR 0–65), $P=NS$, Mann Whitney (MW)], SSS [2.5 (IQR 1.5–3.5) vs 3 (IQR 2–4), $P=NS$, MW], number of vials of antivenom administered [13 (IQR 11.5–15.5) vs 12 (IQR 7.5–16.5), $P=NS$, MW], or responsible crotalid (rattlesnake 89 % [95 % CI 67–99] vs 70 % [95 % CI 55–82], $P=NS$, CS; cottonmouth: 0 % [95 % CI 0.05–18] vs 2 % [95 % CI 0.05–11], $P=NS$, CS; copperhead: 11 % [95 % CI 1–33] vs 28 % [95 % CI 16–42], $P=NS$, CS). Performance of debridement was associated with statistically

significant higher rate of antibiotic administration for confirmed cellulitis (26 % [95 % CI 9–51] vs 4 % [95 % CI 0.5–15], $P=0.005$, CS) and longer hospital LOS (3d [IQR 2–4] vs 2d [IQR 0.5–2.5], $P=0.04$, MW).

Discussion: The present case series is limited by a small number of observations (especially amongst debridement group) and wide confidence intervals.

Conclusion: Patients who undergo debridement in the treatment of crotalid-associated skin necrosis and/or bullae may be at increased risk for cellulitis and increased hospital LOS. Future prospective studies are warranted to identify benefits or complications associated with debridement in the treatment of crotalid-associated bullae and/or skin necrosis.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

98. The Pharmacokinetics of IntraNasal DROperidol in Healthy Volunteers (INKDROP Study)

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Background: Droperidol can be used parenterally to treat nausea and vomiting, migraine, and acute behavioral disturbance. Its rapid onset of action after parenteral administration make it ideal for use in the Emergency Department. Intranasal (IN) use is not reported for droperidol. Intranasal drug administration reduces need for IV placement and risk of needle-stick. We hypothesized that intranasal droperidol is well absorbed intranasally.

Methods: Open-label crossover volunteer study comparing pharmacokinetics of single dose IV and IN droperidol. Volunteers received 0.02 mg/kg of droperidol (DORM, Phebra, Australia, 5 mg/ml) by each route with a 1-week washout period.

Intranasal droperidol diluted to a standardized volume (0.5 ml/nare), administered with LMA MAD Nasal device (Wolfe-Tory Medical, Utah, USA). Clinical observations, sedation, and serial ECGs were recorded throughout the study period. Blood samples were collected over 10 h and batch analyzed by high-pressure liquid chromatography tandem mass spectrometry. Pharmacokinetic variables including peak concentration (C_{max}), time to peak concentration (T_{max}), elimination half-life, area-under-the-curve (AUC) were calculated using non-compartmental analysis with EquivTestPK.

Results: Seven male volunteers, median age 23 years (range 20–43), median weight 73 kg (range 65–98), median height 180 cm (range 170–195) were included. Median C_{max} IV was 26.6 ng/ml vs IN 6.5 ng/ml ($p=0.0006$) at median T_{max} IV 0.25 h vs IN 0.5 h ($p=0.002$). Elimination half-life was IV 2.02 h and IN 2.37 h. Mean AUC for IV was 41.4 ng.h/ml vs IN 19.2 ng.h/ml ($p=0.002$) giving an intranasal bioavailability of 40 %. All subjects reported mild degrees of sedation/drowsiness with onset consistent with the T_{max} for both routes of administration. There were no adverse clinical effects or QT interval prolongation.

Conclusion: Droperidol intranasal bioavailability was 40 %. The dose used in this study was small and diluted. Larger doses, using undiluted 5 mg/ml (0.5 ml/nare) droperidol could be given intranasally for greater efficacy. Comparative bioavailability of intranasal haloperidol was 63 % in a similar study. Currently no psychotropics are administered intranasally in the clinical setting. Results suggest that intranasal droperidol could potentially be assessed in clinical trials treating nausea and vomiting, migraine, and also for behavioral sedation.

99. Polyneuropathy from Acute on Chronic Inhalation of Nitrous Oxide

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Background: Polyneuropathy and myelopathy are complications of chronic nitrous oxide (N₂O) abuse. We present a case of heavy acute N₂O exposure with polyneuropathy and vitamin B₁₂ deficiency, without megaloblastic anemia.

Methods: This is a single patient chart review. A 25-year-old man presented to the Emergency Department with bilateral upper and lower extremity paresthesias and decreased sensation for 1 week. His symptoms started in both hands and wrists. A day later, he noticed tingling in his feet and lower legs. Over the next 6 days, paresthesias progressed proximally to his knees and mid-forearms in stocking-glove distribution. On the night before the onset of symptoms, the patient shared 50 N₂O whipped cream canisters with friends. Prior to this heavy exposure, the patient had only abused N₂O intermittently. Neurologic examination revealed normal strength in all muscle groups with decreased sensation to light touch, vibration, pin-prick, temperature, and proprioception in his bilateral upper extremities to the level of his mid-forearm and lower extremities to the level of his knee.

Results: Laboratory results included hemoglobin, 14.6 g/dL; mean corpuscular volume (MCV), 102.7 fl; vitamin B₁₂, <146 pg/ml (reference range 211–911); homocysteine, 113.8 μmol/L (reference range 4.4–16.2); methylmalonic acid, 8.91 μmol/L (reference range 0.00–0.40); and folate, 9.4 ng/ml (reference range 7.0–31.4). Magnetic resonance imaging (MRI) of the cervical spinal cord revealed abnormal T2 signal consistent with demyelination along the dorsal columns. The patient was treated with intravenous vitamin B₁₂ (1000 mg daily) for 2 days, then intramuscular vitamin B₁₂ (1 mg daily for 5 days, then weekly for 4 weeks, then every month) as an outpatient. He had slow recovery of sensation but was asymptomatic 4 months after initial presentation.

Discussion: The neuropathic effects of N₂O are due to oxidation of the cobalt moiety of vitamin B₁₂ inhibiting the methylation processes important for membrane lipid formation used in neuronal myelin sheaths. The temporal relationship between heavy N₂O use and symptom onset suggests acute polyneuropathy, though the extent of N₂O abuse and subacute symptoms prior to presentation is unclear.

Conclusion: Acute heavy N₂O abuse can result in polyneuropathy and vitamin B₁₂ deficiency.

100. ACGME and Pediatric Cases: Do Enough Cases Show Up at the Hospital?

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Background: Proposed program requirements for Medical Toxicology to go into effect in 2016 state that each fellow must provide direct/bedside patient evaluation for “200 acutely poisoned patients, at least 10 % should be pediatric.” It is unclear if this is a data-driven requirement.

Hypothesis: Are there 10 cases per fellow, or 40 for a complement of 4 fellows per hospital in Illinois per year?

Methods: Illinois Poison Center (IPC) records were queried to determine the number of pediatric cases seen on average per hospital from 2011 to 2014. The number of pediatric cases that were treated and released and admits were determined. The rate of cases per hospital of these two categories was determined.

Results: From 2011 to 2014, 9887 cases were referred to a healthcare facility (HCF), 40,848 were treated at a hospital, and 139,003 were managed on site or not at a HCF. There were 5494, 5777, 5438, 5339 pediatric patients that were treated and released (TR), and 2676, 2803, 3600, and 3349 admissions in these years, respectively. The total of TR and admits per year divided by the 187 hospitals in Illinois was 44, 46, 48, and 58, respectively. These represent all potential consults that a fellow may see at the hospital. The number of admits per hospital for this time period is 14, 15, 19, and 18. Only 2.5 patients were admitted per hospital/year for patients 5 and younger.

Discussion: Seventy percent of pediatric poisonings are managed away from a HCF. In Illinois, only 17 pediatric cases are admitted per hospital annually over this period of study. Twenty-nine cases are TR on average per hospital. It is not known how many of the patients TR would have been treated at home if a poison center was called. The majority of pediatric patients with acute ingestions are managed by the IPC. There are very few opportunities for fellows to see high-yield pediatric poisonings at the bedside.

Conclusion: Few cases of acute pediatric poisonings are seen at the bedside per hospital. Future training rules should take these data into account.

101. Penetrance of an Educational Divisional Toxicology Conference Through Twitter

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Background: Twitter is utilized as a tool for real time education. Short messages of 140 characters (tweets) are composed and can be viewed by global users. Archived tweets with a hashtag (#) can be searched as a database of toxicology articles and clinical information. Individual views (impressions) and interactions (engagements) with tweets can guide the construction of a strong and relevant educational tool. In 2014, our division began tweeting at regular weekly education conference (#toxturs). In this study, we describe the penetrance and categories of tweets that generate high impressions.

Hypothesis: We hypothesize that Twitter can be used to generate impressions and engagements in a weekly toxicology educational conference.

Methods: Tweets from the @Umasstox feed labeled with our weekly conference hashtag, #toxturs, were aggregated and downloaded through Twitter Analytics and Symplur. Tweets were categorized by a toxicology fellow into seven categories: Educational Information, Link to Literature, Case Presentations, Differential Diagnosis, Treatment, and Clinical Image. Categorization was reviewed by a second fellow to ensure inter-rater reliability. Average impressions, engagements, and retweets were calculated for each category.

Results: Over a 6-month period, our weekly #toxturs conference attracted a total of 117 unique participants and generated 644,273 impressions. Our feed was responsible for 452,370 impressions. On a monthly basis, educational tweets generated an average of 175 impressions, tweets with a link to literature generated an average of 169 impressions, conference-related tweets generated 144 impressions, clinical images generated 193 impressions, treatment-related tweets generated 201 impressions, and tweets on differential diagnosis generated 150 impressions. Tweets with images or treatment guidelines were more commonly retweeted and engaging.

Discussion: Our study shows that Twitter is effective in disseminating a weekly toxicology educational conference. Tweets containing clinical images and plans for treatment of toxidromes generated the most impressions, retweets, and engagements. A balanced combination of tweet

categories can create an enriching toxicology educational experience through Twitter.

Conclusion: Twitter can be effectively used to disseminate information from a weekly toxicology conference.

102. To Be or Not to Be PCP: That Is the Question

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Background: The phencyclidine (PCP) urine drug immunoassays (UDS) screen is described to have multiple false positives. We sought to analyze PCP positive UDS samples from an academic medical center with liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) to further characterize true and false positive results.

Hypothesis: Analysis by LC-QTOF/MS will demonstrate the poor specificity of the PCP UDS.

Methods: This was a convenience sampling study. Urines which had tested positive for PCP by UDS were identified from January 2014 to July 2015 and sent for LC-QTOF/MS analysis using a library of 550 drugs including 285 novel psychoactive substances (NPS) and 10 designer PCP analogues. Results were grouped as PCP confirmed, known interfering substance (KIS) confirmed, or unknown interfering substance (UIS). Our institution's PCP UDS reporting limit is 25 ng/mL, the LC-QTOF/MS limit of quantification for PCP is 5 ng/mL. KIS were defined as dextromethorphan (DXM), diphenhydramine (DPH), doxylamine, tramadol, venlafaxine, meperidine, ketamine, lamotrigine, and thioridazine.

Results: Urine samples from 133 patients were analyzed. Eighty-nine (67 %) of samples were PCP confirmed, 13 (10 %) were KIS confirmed, and 31 (23 %) were considered UIS. In KIS confirmed cases, seven were DXM, three tramadol, one DPH, and two DXM and DPH combinations. Among UIS cases, 3-methoxy PCP was identified in one case. In the remaining UIS cases, cotinine was detected in 26 cases, caffeine/theophylline/theobromine in 19 cases, buspirone in 3 cases, alprazolam in 2 cases, citalopram in 2 cases, lorazepam in 1 case, norfluoxetine in 1 case, 5-MeO-DALT in 1 case, 4-methylmethcathinone in 1 case, paramethoxyamphetamine in 4 cases, phenylpropanolamine in 2 cases, methylenedioxyamphetamine in 1 case, and NRG-3 in 1 case.

Discussion: Multiple false positives with the PCP UDS have been described. This study suggests that there are many cases where the substance causing the false positive is not readily identifiable or expected. Further studies are warranted to better examine this finding. This study is limited by it being a convenience sampling.

Conclusion: Analysis by LC-QTOF/MS determined that PCP UDS has a high false positive rate, and in a majority of false positive cases, no known interfering substance could be identified.

103. Improving Sentinel Reporting in a Medical Toxicology Surveillance System by Strengthening Data Entry Requirements

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Background: Medical toxicology research and surveillance remains reliant on the content, quality, and completeness of the data reported by clinicians. Two sentinel areas of interest include emerging and novel toxic events (ENT), medication errors (ME), and adverse drug reactions (ADR). Concerns around potential under reporting to the American College of Medical Toxicology's

Toxicology Investigators Consortium ("Toxic") Registry led to 2015 Data Changes (effective January 1, 2015).

Research Question: Did adding mandatory reporting requirements for sentinel event questions increase their relative reporting in the Toxic Registry?

Methods: This descriptive analysis included all Toxic Registry cases reported by participating US sites 4 months prior to and after the initiation of new reporting requirements on January 1, 2015 (reference date). Relative frequencies and percent change were calculated and compared between two entry windows, period 1 (optional September 1 to December 31, 2014) and period 2 (mandatory January 1 to April 13, 2015), via significance testing of the difference between two proportions.

Results: Toxic sites entered 5459 cases into the registry over this 8-month period. Prior to adoption at the reference date, 2.4 % of Toxic cases were reported as ENT-related vs. 3.5 % afterwards (+44.8 % $P=0.018$). Two primary drug classes demonstrated significant increases as ENTs, Psychoactives (40.7 to 46.7 %, $P=0.013$), and Sympathomimetics (8.8 vs. 17.8 %, $P=0.006$). Synthetic cannabinoids were the major agent reported (31.9 vs. 35.5 %, $P=0.039$). Reporting of MEs and ADRs increased after the changes from 5.5 to 7.1 % (+28.9 %, $P=0.016$), driven by a 40 % increase in the relative frequency of ADR only cases (3.5 to 4.9 %, $P=0.010$).

Discussion: In addition to minimizing the risk of under reporting, the minimal changes in the required upper level mandatory questions enable improved tracking of data content for sentinel events. As with any voluntary surveillance system and particularly true with a clinical-based registry, Toxic needs to balance the core registry data requirements with the ease of entering the data. This descriptive analysis should be regularly updated to track the ultimate influence of these changes over time.

Conclusion: Data to date suggest that the additional mandatory reporting rules for Toxic sites improved identification for these select sentinel events.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

104. The Toxicology Investigator's Consortium Registry: Descriptive Analysis of the First 5 Years 2010–2014

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Background: The American College of Medical Toxicology created the Toxicology Investigators Consortium (Toxic) as a means to provide a tool for clinical toxicology and surveillance. Established in 2010, the Toxic Registry includes data related to demographics, encounter type, exposure, and clinical factors from patients seen in clinical consultation by medical toxicologists.

Research Question: What is the current qualitative and quantitative character of Toxic Registry that may influence the ability to consistently report on events over time?

Methods: This descriptive analysis included all Toxic Registry cases reported over the period January 1, 2010 through December 31, 2014. Summary descriptive statistics calculated included relative frequencies,

average annual percent change (AAPC), and chi-squared for trend for major categorical data fields.

Results: The ToxIC Registry has grown since 2010 in both the number of cases (+116 % absolute, +20.2 % AAPC) and member sites (+79 % absolute, +10.7 % AAPC). However, continuity in participation has varied. For example, among the 52 individual sites contributing cases, only 4 dropped out within 2 years (7.8 % CI 3.1–18.5 %), while 50 % indicated an increase in cases for the most recent 2-year period (2013–2014). Of cases, 87.6 % reported a toxic exposure (87.6 %), with the majority a single agent poisoning (61.1 %). The most common agent classes were analgesics, sedative-hypnotics, opioids, and antidepressants across all years. Linear tests for trend based on % total agents indicated significant downward trends for sedative-hypnotics ($P < 0.001$ chi-squared) and antidepressants ($P < 0.001$ chi-squared). In contrast, among single-agent poisonings only, significant positive trends appeared for analgesics (+12.6 % absolute, $P < 0.001$ chi-squared), opioids (+28.1 % absolute, $P < 0.001$ chi-squared), and antidepressants (+9.7 % absolute, $P = 0.009$ chi-squared).

Discussion: ToxIC continues to grow in the number of cases and participating sites. Many patterns in type of, and reason for a toxicological consultation, as well as general agent class appear similar across years. However, even in this short time period, this descriptive analysis still identified trends for the most common agent classes and illustrated the influence of event characteristics on temporal changes.

Conclusion: Consideration of the type of exposure (single or multiple agent) and characteristics of participating sites, including relative reporting completeness, need to be considered in future analyses.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

105. Opiate and Sedative-Hypnotics/Muscle Relaxants: Trends in Two Important Drug Classes as Reported to the ToxIC Registry, 2010–2014

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Background: Opioids (OPIs) and sedative-hypnotic/muscle relaxants (SEDs) are two of the most common agent classes reported to the Toxicology Investigators Consortium (ToxIC). Recent review of the relative proportion of total agents has appeared to show a decline in both OPIs and SEDs over time. However, as almost one third of the Registry cases reported an exposure to more than one agent, it is important to parse out the relative influence of multiple vs. single agent exposures, as well as other factors, to explain any observed crude changes.

Research Questions: What changes in toxic events involving OPIs and/or SEDs have occurred over the initial 5 years of reporting to the ToxIC Registry?

Methods: This descriptive analysis included all ToxIC Registry cases reported over the period January 1, 2010 through December 14, 2014. Summary descriptive statistics calculated included relative frequencies and chi-square for linear trend.

Results: Linear tests based on the percentage of total agents indicated a downward trend for SEDs ($P < 0.001$ chi-square) and no trend for OPIs ($P = \text{NS}$ chi-square). In contrast, among single-agent poisonings only, significant positive trends appeared for OPIs only (+28.1 % absolute, $P < 0.001$ chi-square). In the OPI class (% 5 years, P for trend chi-square), the most frequently agents reported in single agent events were heroin (2.5 %, $P < 0.0001$), methadone (1.3 %, $P = 0.012$), and oxycodone (1.1 %, $P = \text{NS}$). Clonazepam, alprazolam, and lorazepam were the most common agents reported in the SED class (range 0.7–1.5 %). Benzodiazepines as a group (4.4 % single agent cases) demonstrated a positive trend ($P = 0.033$ chi-square). However, no individual SED agent demonstrated a significant trend over this 5-year time period.

Discussion: As the Registry continues to increase in size and accumulated data years, the ability to identify stable estimates of trend will improve. Not only by using simple descriptive analysis but also via modeling to determine the influence of other case and site characteristics.

Conclusion: ToxIC Registry cases involving an OPI or SED demonstrated significant positive increases in their relative proportion of single agent poisonings for the individual agents heroin and methadone, and for the sub-class benzodiazepines.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

106. Predicting Adverse Events Based Upon a Drug's Molecular Target Profile

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Background: Clinical trials do not identify all adverse events (AEs) that will eventually be associated with a drug following market introduction. A new software tool generates target AE (TAE) profiles from the public FDA Adverse Event Reporting System (FAERS) database. Unlabeled AEs from the TAE profile warrant consideration for an enhanced pharmacovigilance program.

Methods: A software tool integrates publicly available FAERS data with bioinformatics data. The tool translates a drug into its molecular targets and then associates the adverse events to the targets generating a TAE profile. Drug to molecular target mapping uses DrugBank, PubChem, UniProt, NCI Nature, Reactome, and BioCarta. Many oncologic tyrosine kinase inhibitor (TKI) drugs inhibit VEGF receptors (VEGFRs). A molecular TAE profile was created for VEGFR. Potential unlabeled AEs were identified using disproportionality analysis (PRR ≥ 1.25 ; case count ≥ 100). The profile, therefore, creates a list of potential AEs for post-market surveillance.

Results: The VEGFR TAE profiles identify disproportionality for the following selected AEs (PRR): venous (pulmonary embolism, 1.65) and arterial thromboembolic events (CVA, 1.9), left ventricular dysfunction (cardiac failure congestive, 2.7), infections (pneumonia, 1.9), renal dysfunction (acute renal failure, 2.0), vascular dysfunction (edema peripheral, 1.8), neuropathy (peripheral, 2.2), and interstitial lung disease (PRR 1.6). AEs related to skin, CNS, and hypertension are not included as these are universally labeled.

Conclusion: Molecular target analysis hypothesizes a number of AEs for VEGFR inhibitors that are not universally found on the labels of VEGFR inhibiting drugs. Drugs that inhibit VEGFR that do not include these AEs in their proposed label may warrant enhanced pharmacovigilance. Marketed drugs may warrant a post-market review for these AEs.

107. Current Treatment Recommendations and Clinical Outcomes of Sodium Bicarbonate Therapy on Sodium Channel Blocking Agents through the ToxIC Registry

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Background: In April 2015, a ToxIC subregistry was initiated to study the use of sodium bicarbonate by toxicologists as an antidote for sodium channel blockade as evidenced by QRS widening on the ECG.

Hypothesis: Treatment recommendations and clinical outcomes regarding sodium bicarbonate use are variable.

Methods: Using the ToxIC Registry, a prospective observational study of sodium bicarbonate use was performed using a 21-question survey.

Results: Nine completed cases were collected from April until November 2015 encompassing four sites. Six patients were male and three were female; mean age was 29 years. Five cases were attempts at self-harm. First agents listed were amitriptyline, nortriptyline, carbamazepine, bupropion, and an unknown agent. Sodium bicarbonate was initiated for a QRS of 105–151 ms. Services recommended sodium bicarbonate for a range of 100–120 ms. Eight patients received sodium bicarbonate boluses and infusions; one case received boluses only (primary agent was bupropion). All services used 150 mEq/L as the concentration of sodium bicarbonate infusion. Duration of infusion was unknown in one case; the remaining durations ranged from 8 to 48 h. The average change from maximal QRS to minimal QRS on sodium bicarbonate was 26.4 ms (± 19.9 ms). One patient had ventricular tachycardia prior to the administration of sodium bicarbonate treated successfully with defibrillation. No other therapies were given and no other dysrhythmias were reported while on sodium bicarbonate. The QRS range was 86–116 ms when sodium bicarbonate was stopped. Two cases had rewidening of the QRS (106 and 130 ms at 8 and 24 h, respectively) and sodium bicarbonate was reinitiated only for the case of rewidening to 130 ms. The sole reported complication reported was one case of QTc widening >500 ms.

Discussion: Although there were a small number of cases, sodium bicarbonate was used for multiple agents with an average reduction in QRS of 26.4 ms and there were no dysrhythmias reported.

Conclusions: Sodium bicarbonate was frequently used in combination of bolus and infusion administration with a wide range in duration of infusion with a low rate of complications.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

108. A Death-Like Slumber, Toxic Outbreak of AB-FUBINACA

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Background: Synthetic cannabinoids (SCB) continue to evolve and elude both law enforcement and medical personnel treating SCB intoxication. We report a case series of four patients exposed to AB-FUBINACA, a third generation SCB, confirmed by drug specimen and urine analysis.

Case Series: All reported ingesting the same capsule of white powder marketed as “Molly.” Urine was analyzed by LC/MS-MS for 12 synthetic cannabinoid metabolites including AB-FUBINACA. All patients ingested at the same time, and presented 10–12 h later to a local ED. The four patients presented here were deemed critical and transferred to a tertiary care center. Case #1: A 21-year-old male with no PMH was found unresponsive in bed 10 h post-ingestion. Bystander CPR was initiated—an AED advised and administered defibrillation twice for ventricular tachycardia. The patient achieved ROSC and was intubated by EMS. The patient had an unexplained core temperature of 31.6 °C and was hypotensive, 80/49. He was comatose and had 3 mm fixed pupils. There was no hyperreflexia or clonus, and no posturing. Blood pressure was supported with norepinephrine and therapeutic hypothermia initiated. The patient had a successful outcome and was discharged from hospital within 8 days of cardiac arrest with no neurologic sequelae. Case #2: A 20-year-old male, no PMH, presented 12 h post-ingestion with sedation and altered mental status. He had a seizure at 14 h post-exposure, refractory to benzodiazepine therapy. Patient required intubation and sedation with propofol to control seizure. The patient had normal vital signs with normal reflexes on propofol. Pupils were 6 mm sluggishly reactive. The patient was extubated the following day and discharged on hospital day #3 with normal neurologic function. Cases #3 and 4: An 18-year-old female and 19-year-old male presented 12–14 h post-ingestion with significant sedation but vital signs were within normal limits. Both patients were significantly sedated but received no medical intervention, were monitored for 24 h, and discharged in good health.

Discussion: AB-FUBINACA toxicity was variable among this cohort, ranging from sedation to severe hypothermia, ventricular tachycardia, and refractory seizure.

Conclusion: Therapeutic hypothermia may be considered in the setting of SCB-related cardiac arrest.

109. Teaching Effective Opioid Prescribing through a Simulation Curriculum

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Background: In response to mortality from opioid overdose more than quadrupling in the USA from 1999 to 2010, the American College of Emergency Physicians (ACEP) created a clinical policy in 2012 to guide responsible prescribing by emergency medicine (EM) physicians.

Objective: This study aims to develop an educational curriculum that decreases the number of opioid prescriptions written by EM residents not endorsed by the ACEP clinical policy.

Methods: This is a pre-post study design. Residents in the EM program at the University of Massachusetts were consented for participation. A didactic and simulation curriculum regarding the ACEP Clinical Policy was delivered during residency conference, in time earmarked for toxicology (2 h).

Opioid prescriptions written by this group for patients on ED discharge were recorded for a 3-month period before, and after, the intervention. The medication, formulation, and quantity of each prescription were recorded, then cross-matched with the patient chart to determine the diagnosis for which the patient received the medications. Prescriptions written for acute low back pain or chronic non-cancer pain were not endorsed by the ACEP clinical policy.

Results: A total of 1507 prescriptions for oxycodone were written by the residents ($n=28$) during the study period; 794 (53 %) before and 713 (47 %) after the educational intervention. In the pre-intervention period, 70 prescriptions were written for acute low back pain and 88 prescriptions were written for chronic non-cancer pain. Post intervention, there were 60 prescriptions written for acute low back pain and 66 prescriptions written for chronic non-cancer pain. In total, there were 158 (19.9 %) inappropriate prescriptions written by residents pre-intervention, and 126 (17.7 %) prescribed post-intervention ($p=NS$, Chi-square).

Discussion: The total number of oxycodone prescriptions written by EM residents after participation in the curriculum not endorsed by the ACEP clinical policy were reduced compared to the pre-intervention period; however, the difference was not significant.

Conclusion: In this study, a brief educational intervention did not result in greater adherence to the ACEP Clinical Policy with respect to opioid prescribing for low back pain and chronic non-cancer pain. However, the ACEP Clinical Policy was directly applicable to a minority of patients in the sample.



Medical Toxicology Foundation

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110. Elder Toxicology: Characterizing Intentional Pharmaceutical Exposures in the Aged Population Using the ToxIC Registry

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Background: The ageing and elderly (age ≥ 65 years of age) represent 15 % of the US population. Comprising 40 % of all hospitalizations, they are the most medicated age group and one that is at high risk for overdose. Little has been published characterizing the clinical details of intentional pharmaceutical exposures in the aged.

Hypothesis: We hypothesize that greater age confers greater risk of death from overdose.

Methods: Data from the ACMT ToxIC database were obtained from January 1, 2010 to October 1, 2015. We performed age-specific queries with respect to intentional pharmaceutical exposures and extracted all available clinical data points from all aged patients. For the purposes of analysis, age groups were defined as "aging" (age 66–89 years) and "elderly" (age >89 years).

Results: Of 3288 intentional pharmaceutical exposures, 2355 occurred in patients >18 years of age. Of these, 145 (6.2 %) occurred in the ageing group, 9 (0.4 %) in the elderly. There were 90 (62.1 %) exposures involving single agents in the ageing, compared to 8 (88.9 %) in the elderly. Adverse drug reaction or medication error occurred in the ageing and elderly populations 49 (33.7 %) and 4 (44.4 %) times, respectively.

Compared to the ageing group, elderly exposures were slightly more often from self-harm (29 vs 33.3 %) and resulted in greater ICU admissions (20 vs 33.3 %) and usage of vasopressors (9 vs. 22 %). Of the 209 total agent exposures, cardiovascular agents were the primary agent of concern in 49 (23.4 %) of cases, followed distantly by acetaminophen, benzodiazepines and opiates (22, 22, and 17 cases, respectively). Digoxin was responsible in over 1/3 of cardiovascular agent toxicities. Despite similar need for toxicological treatment (ageing 77.9 %, elderly 66.7 %), death was more common in elderly exposures (2 vs 11 %).

Discussion: Using the ACMT ToxIC Database, we offer the characterization of the single largest bedside toxicology database with respect to pharmaceutical exposures in the aging and elderly population.

Conclusion: While limited by a small sample size, increased age appears to confer increased risk for significant illness and death from intentional exposure. Further study regarding variables contributing to exposure and death in this population may prove beneficial.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

111. Elder Toxicology: Characterizing Unintentional Pharmaceutical Exposures in the Aged Population Using the ToxIC Registry

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Background: Comprising the most medicated population in the US healthcare climate, the aged may be at the greatest risk for unintentional pharmaceutical exposures and adverse drug events.

Hypothesis: Morbidity and mortality from unintentional pharmaceutical exposures increases with age.

Methods: Data from the ACMT ToxIC database were obtained from January 1, 2010 to October 1, 2015. We performed age-specific queries with respect to unintentional pharmaceutical exposures and extracted all available clinical data points from all aged patients. For the purposes of analysis, age groups were defined as "aging" (age 66–89 years) and "elderly" (age >89 years).

Results: Of 1383 unintentional pharmaceutical exposures, 545 occurred in patients >18 years of age. Of these, 138 (25.3 %) occurred in the ageing, while 12 (2.2 %) victims were elderly. Adverse drug reactions occurred with similar frequency between groups (11.6 vs. 16.7 %), while the frequency of medication error was doubled in the elderly group (8.7 vs. 16.7 %). Single and double agent exposures were most common and similar between age groups (ageing, 75 [54.3 %] and 37 [26.8 %]; elderly, 6 [50 %] and 4 [33.3 %], respectively). However, ICU admission and toxicological treatment were more often required in the aging population (15.9 vs. 8.3 %), despite similarity in chronicity of exposure between groups (i.e., acute vs. acute-on-chronic). Of the 238 total agent exposures, cardiovascular agents were the primary agent of concern in 64 (26.9 %) cases, followed distantly by anti-diabetic agents (22 or 10.2 %) and anti-depressants (19 or 8.8 %). Digoxin was responsible for 19 (29.6 %) of

cardiovascular agent toxicities. Unintentional pharmaceutical exposure resulted in death in 4 of 138 patients in the aging group. No deaths were reported in the 12 patients >89 years of age.

Discussion: Using the ACMT ToxIC Database, we offer the characterization of the single largest bedside toxicology database with respect to pharmaceutical exposures in the aging and elderly population

Conclusion: While limited by a small sample size, toxicity from unintentional pharmaceutical exposure results primarily from cardiovascular and anti-diabetic agents, with medication error more common in the elderly population. Although death is uncommon, toxicological treatment is often required for unintentional pharmaceutical exposures in the aged.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

112. Massive Acetaminophen Overdose: What Are We Recommending?

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Background: While the toxicological management of routine acetaminophen (APAP) overdose is well described, the approach to massive acetaminophen overdose is less well defined. Various case reports hint at modified approaches to the massive APAP overdose, but no controlled trials exist with respect to toxicological management.

Research Question: In the absence of clinical trial data, what approaches to massive APAP overdose are medical directors of Poison Control Centers recommending?

Methods: Contact information for the Medical Directors (MedD) of the Nation's 57 Poison Control Centers (PCC) was obtained from the American Association of Poison Control Centers. Of these, 25 sites were randomly selected for a phone-based survey. Two clinical scenarios were posed to select MedDs and they were questioned regarding their management recommendations. Scenario #1: a single ingestion of 7500 mg of APAP with a 4-h post-ingestion APAP concentration of 165 mcg/mL. Scenario #2: a single ingestion of 40,000 mg of APAP with a 4-h post-ingestion APAP concentration of 530 mcg/mL, lactate 1.5 mmol/L, and normal AST.

Results: Of the 25 sites selected, 16 medical directors participated in the survey. In response to scenario #1, 10 MedDs recommended IV N-acetylcysteine (NAC) using the 21-h, three-infusion rate approach. Fifteen recommended continuation of NAC until specific lab targets were met, but only 12 would re-check an APAP level prior to NAC termination. With respect to scenario #2, answers varied substantially. Half of MedDs would change the recommended approach, using either modified IV infusion rates or transition to oral NAC. Defined triggers for modification were equally gestalt based and level-specific, with definitions of massive overdose ranging from serum levels of 450 to >1000 mcg/mL. While only one PCC had a defined trigger for HD recommendation, most MedDs had personal thresholds for recommendation. No PCC had a specific written protocol for massive APAP overdose.

Discussion: While limited by a small number of survey participants, these data help illustrate what those who did respond might recommend in these unusual cases.

Conclusion: In this small phone-based survey of the Nation's PCC MedDs, while there was general agreement towards management of routine APAP overdose, recommendations for massive overdose were widely variable.

113. Endotracheal Intubation for Toxicologic Exposures: a Retrospective Review of Toxicology Investigators Consortium (ToxIC) Cases

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Background: Endotracheal intubation remains a cornerstone of early resuscitation of the poisoned patient, but little is known about which substances are associated with intubation.

Research Question: Our objective was to describe exposures to substances reported to the American College of Medical Toxicology (ACMT) Toxicology Investigators Consortium (ToxIC) that were managed with intubation between 2010 and 2014.

Methods: We performed a retrospective review of cases managed with endotracheal intubation in the ACMT ToxIC Registry from January 1, 2010 through December 31, 2014. Descriptive statistics were used to describe exposures.

Results: A total of 2724 exposures to substances were managed with endotracheal intubation. Intubated patients were 52 % male and 82 % adults. For all ages taken together, the most common known single substance exposures managed with intubation were sedative hypnotics (9.8 %), antidepressants (8.7 %), and opioids (8.0 %). The most common single ingestions associated with intubation in various age group were as follows: opioids (<2 years old), alpha-2 agonists (2–6 years old), antidepressants (7–18 years old), sedative-hypnotics (19–65 years old), and cardiac medications (>65 years old). Multiple substances were involved in 29.0 % of exposures. The most common substances involved in single and multiple substance exposures managed with intubation varied by age group. Most patients were managed with supportive care. Decontamination and elimination processes were rare.

Discussion: Knowledge of substances commonly involved in exposures managed with intubation may inform poisoning prevention.

Conclusion: Exposures to substances reported to the ToxIC registry and managed with intubation varied by age group.



This research was performed in collaboration with the ACMT Toxicology Investigators Consortium.

114. Partnership Building in Pediatric Environmental Health Through a Monthly Webinar Series

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Background: In 2014, the Agency for Toxic Substances and Disease Registry (ATSDR) announced a competitive renewal of the national Pediatric Environmental Health Specialty Unit (PEHSU) Program, established in the late 1990s to provide a network for education, consultation, and referral in children's environmental health. Two cooperative agreements were awarded: to the American Academy of Pediatrics (AAP) for PEHSU operations in federal Regions 1–5 in the eastern US; and to the American College of Medical Toxicology (ACMT) for Regions 6–10 in the western US (PEHSU West).

Hypothesis: A webinar series will engage PEHSU members and partners. **Methods:** As part of its multifaceted effort to engage the PEHSUs and national partners, and to expand the educational reach of the Program, ACMT initiated a monthly webinar series for each of the five PEHSUs in the western Regions 6–10. ACMT created a schedule of 1-h webinars for the first 20 months of the 5-year cooperative agreement and requested that each of the 5 PEHSUs in Regions 6–10 volunteer one of their subject-matter experts (SMEs) to present a total of four webinars: two grand rounds, one journal club, and one case conference. ACMT staff reviews the scientific content prior to presentation, and then moderates the webinars, hosted via the WebEx platform (Cisco Systems, Santa Clara, CA).

Results: The webinars to date have focused on a variety of common issues that arise in children's environmental health (climate change, e-cigarettes, endocrine disruptors, hydraulic fracturing, leukemia, and marijuana). SMEs present the subject matter and then engage in a moderated question-and-answer session with, for the first 6 months, a mean of 98 (range, 41–203) attendees, who include national PEHSU members as well as partners at ATSDR and EPA. Attendees have obtained free CDC CME credits, and 82 % have ranked the education as 4 or 5 of 5. These recorded webinars reside online at the redesigned PEHSU website [pehsu.net], and some presentations will become the basis for instructional designer-facilitated online courses on the PEHSU National Classroom webpage.

Conclusion: A national PEHSU webinar series, held monthly via teleconference, serves to engage PEHSU members and as the basis for enduring education.



This presentation was supported by the ACMT Pediatric Environmental Health Specialty Unit (PEHSU) network. The ACMT PEHSU network is funded (in part) by the cooperative agreement FA1N: U61TS000238 from the Agency for Toxic Substances and Disease Registry (ATSDR).

115. Fatal Bupropion Overdose with Status Epilepticus and a Wide-Complex Rhythm

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Background: Bupropion is an atypical antidepressant that inhibits reuptake of dopamine and serotonin.

Methods: This is a single patient chart review. A 35-year-old woman, weighing 59 kg, presented to the emergency department (ED) approximately 4 h after intentional ingestion of 90 tablets of 150 mg extended release bupropion and an unknown amount of methylphenidate. The patient was seizing upon EMS arrival, which resolved after 2 mg of intravenous (IV) lorazepam. ED vital signs were significant for HR, 125/min and BP, 163/80 mmHg. She was somnolent, offered confused responses to questions, but localized to pain. She was diaphoretic, and her pupils were 3 mm, equal and reactive.

Results: She had a metabolic acidosis with pH, 7.23; anion gap, 23; and arterial lactate, 12 mmol/L. Her initial EKG was notable for sinus tachycardia and QT, 473 ms. While in the ED, she had a 30-s generalized tonic-clonic seizure that self-resolved, after which she was treated with another 2 mg IV lorazepam. Her post-ictal period lasted less than 10 min, and she returned to her presenting mental status. She was admitted to the medical intensive care unit, but within a short time, developed status epilepticus and was intubated. She developed wide-complex bradycardia and hypotension requiring vasopressors. Asystolic arrest occurred twice, for 5 min and then 60 min, with return of spontaneous circulation. IV sodium bicarbonate (200 mEq) was administered. Extracorporeal membrane oxygenation, intravenous lipid emulsion infusion, and continuous renal replacement therapy were initiated. After 24 h, though, her examination was consistent with brain death and care was withdrawn.

Discussion: The sodium channel blockade exhibited by bupropion, manifested as QRS widening and cardiovascular collapse, was delayed in onset, likely due to the extended release preparation ingested. Sodium bicarbonate and intravenous lipid emulsion therapy administration are controversial in bupropion toxicity, but have the potential for benefit. Although severe toxicity is not uncommon with large doses of bupropion, death is rare.

116. Hyperglycemia Without Evidence of Acute Pancreatitis in a Patient with a Massive Metformin Overdose

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Background: Large metformin ingestions have been rarely associated with hyperglycemia. The mechanism of hyperglycemia is unknown but has been previously postulated to be associated with metformin-induced pancreatitis.

Hypothesis: Hyperglycemia associated with massive metformin overdose is not associated with acute pancreatitis.

Methods: This is a single case report. A 62-year-old female with a history of diabetes, cardiovascular disease, hypertension, and depression presented with vomiting 2 h after a single ingestion of 270 g of metformin in a suicide attempt. Vital signs were initially normal and initial laboratory results showed a blood glucose of 245 mg/dL, lactate of 6.9 mMol/L, and BUN 18 mg/dL and creatinine 1.4 mg/dL. Liver function tests, coagulation studies, troponin, ethanol level, acetaminophen level, and salicylates level were normal. The patient became hypotensive requiring several vasopressors and was started on a bicarbonate infusion and CVVH for her lactic acidosis. Her blood glucose 6 h after ingestion increased to 566 mg/dL at which time her labs showed an elevated anion gap metabolic acidosis with a pH of 6.91, bicarbonate 15 mMol/L, and lactate 11.2 mMol/L.

Results: Given previous hypotheses of metformin-induced pancreatitis as the etiology of hyperglycemia during acute metformin overdose, a serum lipase was checked and was normal. The

patient was treated with IV insulin with improvement in blood glucose. She continued to become more hypotensive and acidemic. The patient's lactate level increased to 36 mMol/L, pH decreased to 6.65, and glucose was 145 mg/dL just prior the patient's cardiac arrest, after which she expired.

Discussion: Hyperglycemia associated with massive metformin overdoses has been reported but is rare. Metformin's mechanism of action and pharmacokinetics do not offer any direct explanation of hyperglycemia and thus authors have proposed that hyperglycemia may be due to metformin-induced pancreatitis. Our case report of a massive metformin overdose with associated hyperglycemia and normal serum lipase does not support this alternative theory.

Conclusion: Hyperglycemia associated with massive metformin overdose does not appear to be related to metformin-induced pancreatitis in this single case report.

117. Integrating OSHA into Medical Toxicology Training

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Background: The 2012 Core Content of Medical Toxicology requires medical toxicology fellows (MTFs) to be trained in occupational assessment and prevention. ACGME Program Requirements for Graduate Medical Education in Medical Toxicology requires MTFs be provided with experience in evaluating and managing patients with workplace and environmental exposures and in workplace evaluations. We present a case illustrating the collaboration between a medical toxicology fellowship, poison center (PC), and state Occupational Safety and Health Administration (OSHA) to provide hands-on experience in occupational toxicology to their MTFs.

Hypothesis: Medical toxicology fellowship and PC partnership with OSHA may help MTFs meet requirements for evaluating occupational toxicological exposures outlined in the Core Content of Medical Toxicology and by ACGME.

Methods: Our PC has a Memorandum of Understanding (MOU) to refer occupational exposure calls to state OSHA. In April 2015, a hydrogen sulfide (H₂S) exposure at an asphalt refinery plant resulted in one death, one serious injury requiring intubation and prolonged hospitalization, and one traumatic brain injury. Our PC referred these cases to state OSHA. Our toxicology service provided inpatient and subsequent outpatient evaluations to surviving patients.

Results: Our MTFs coordinated with state OSHA and participated in on-site workplace investigations. The state OSHA officers expressed that MTFs helped improve their efforts by providing education on the mechanism of toxicity of H₂S, assistance in clinical and toxicological data interpretation, and providing a different perspective in workplace interviews. MTFs obtained better understanding of toxicological exposure risk in the workplace, improved their ability to assess occupational exposures for inpatient consults and outpatient referrals, and how government agencies try to protect workers from these risks. Both the OSHA officers and MTFs expressed interest in future collaboration.

Discussion: Partnership between medical toxicology fellowships, PCs, and federal occupational agencies such as OSHA may help fulfill core content objective requirements and also provide MTFs hands on education in the role of government agencies and policies in medical toxicology, workplace hazard evaluation and risk management, and insight into pre-hospital exposure scenarios.

Conclusion: Collaboration with state OSHA has helped our MTFs meet objectives in the medical toxicology curriculum for occupational assessment and prevention.

118. *Veratrum* Steroidal Alkaloid Toxicity Following Ingestion of Foraged *Veratrum parviflorum*

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Background: Steroidal alkaloids are found in the *Veratrum* genus of plants. Their toxicity manifests as gastrointestinal symptoms followed by a Bezold-Jarisch reflex: hypopnea, hypotension and bradycardia. We present a case of accidental poisoning from *Veratrum parviflorum* mistaken for the edible *Allium tricoccum* (ramps, wild leeks).

Hypothesis: *V. parviflorum* contains cardiotoxic *Veratrum* steroidal alkaloids and does not respond to digoxin immune Fab.

Methods: This is a two-patient chart review. A 27-year-old man and his 25-year-old wife presented to the emergency department (ED) with nausea and vomiting after foraging and ingesting what they believed to be wild leeks from the Appalachian Trail in Georgia, USA. We used high performance liquid chromatography and high resolution electrospray ionization time of flight tandem mass spectrometry to extract steroidal alkaloids from the foraged plant and patients' serum.

Results: The man and woman had BP 87/40, HR 53 and BP 88/40, HR 50, respectively, after antiemetics and fluid resuscitation. They were alert and awake and EKGs showed sinus bradycardia. Ten vials of digoxin immune Fab were given due to concern for cardiac glycoside toxicity. Laboratory analysis showed undetectable digoxin levels in both patients. Their symptoms resolved 12 h after arrival and they were discharged within 34 h. The plant was identified by local botanists as *V. parviflorum* at a later time. Steroidal alkaloids were extracted and identified from the plant. At the time of this abstract, quantification of steroidal alkaloids from the plant and a method to extract and measure serum steroidal alkaloid concentrations were being developed.

Discussion: Steroidal alkaloids have been previously isolated from *Veratrum californicum* and *Veratrum album* and toxicity has been reported mainly from *V. album* species. This is the first reported case of *Veratrum* toxicity from *V. parviflorum* with identified steroidal alkaloids. A prior study shows some cross reactivity between *Veratrum* steroidal alkaloids and the digoxin assay but no digoxin immune fab binding. These patients may benefit from supportive care with atropine and vasopressors.

Conclusion: In patients presenting with cardiotoxicity after ingestion of wild plants in the Southeastern USA, consider *V. parviflorum* toxicity and treat supportively.

119. Ambient Temperature and Mortality Risk from Sympathomimetic Drugs of Abuse

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Background: Sympathomimetic drugs increase mortality in animals in the settings of higher ambient temperatures. Cocaine has been

shown to increase the risk of death in humans as the ambient temperature increases. Two threshold temperatures (31.1 and 24 °C) have been proposed previously in the American Northeast beyond which risk of death increases cocaine use. There are no prior human studies looking at ambient temperature and mortality with other sympathomimetic drugs.

Objective: This study aims to determine an association between mortality from sympathomimetic drugs and temperature.

Methods: This was a retrospective chart review study of fatality cases from the Georgia Bureau of Investigation (GBI) and the Fulton County Medical Examiner's Office that were certified as an accidental drug-related deaths between 2003 and 2014. We included accidental drug death cases involving cocaine, amphetamines, and MDMA. At the time of this abstract, we were able to analyze only Fulton County sympathomimetic drug deaths. Air temperature was collected from weather station data from the North American Land Data Assimilation System (NLDAS) that corresponded to the time and zip code of cases. We compared the average temperature on the day of death and for a week preceding the death. We estimated logistic regressions as part of a case-crossover analysis to estimate any changes in the risk of death associated with a temperature anomaly.

Results: Between January 1, 2003, and December 31, 2014, there were 1559 accidental deaths due to drugs in the Fulton County ME database. Sympathomimetic drugs contributed to over half the cases. We found that the average temperature on day of death was higher compared to the day a week before the death but the difference was statistically insignificant. Results from the logistic regression showed that the percent excess risk of death for a 1 °F increase in average temperature was 17 %, but this result was statistically insignificant.

Discussion: We do not see a relationship between mortality and temperature at this point in our study. We plan to analyze GBI data and do subgroup analyses of the sympathomimetic drugs.

Conclusion: Mortality due to sympathomimetic drugs does not increase with increased temperature.

120. Layperson Naloxone Administration: Pulp Fiction Style

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Background: As the numbers of opioid-related deaths have increased, initiatives for harm reduction have included the adoption of layperson naloxone administration programs.

Hypothesis: Layperson naloxone delivery may result in unexpected complications.

Case: We report a severe complication following improper naloxone administration. A bystander discovered an unresponsive 22-year-old male who overdosed on heroin and injected naloxone into the left anterior chest wall using a 3.8-cm, 22-gauge needle as demonstrated in the widely known movie "Pulp Fiction." During this process, the needle broke off inside of the patient's chest and he was subsequently taken to the hospital. Upon hospital arrival, he was mildly tachycardic, normotensive, and in no distress. Diagnostic studies included the following: (1) EKG showing sinus tachycardia; (2) CXR demonstrating a curvilinear foreign body over the sternum projecting retrosternally; (3) bedside ultrasound showing penetration of the needle into the pericardium without evidence of a pericardial effusion; (4) CT chest confirming pericardial involvement and a small left pleural effusion. Following diag-

nostic evaluation, he was taken to the operating room for transesophageal echocardiogram, wound exploration, foreign body removal, and tube thoracostomy. On post-operative day 1, he developed pleuritic chest pain with EKG suggestive of pericarditis. Repeat transthoracic echocardiogram revealed interval development of a large pericardial effusion which required pericardial drain placement with 400 mL bloody output over the next 24 h. The pericardial drain was removed on hospital day 3 and chest tube was removed on day 5. The patient recovered uneventfully. The bystander was not trained in naloxone use.

Discussion: Layperson naloxone administration is widely accepted, felt to be safe, and reduces mortality following opioid overdose. To our best knowledge, there are no prior reports of adverse events from the delivery technique when given by a layperson. We report improper administration that resulted in pericardial and pleural injury requiring operative interventions.

Conclusion: Our case adds to the body of knowledge regarding layperson naloxone delivery. As naloxone availability increases, vigilance is needed for unintended complications and educational material needs to be tailored to prevent these complications.

121. Toxic Malingering: the Work Excuse Worth Poisoning for

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Background: Toxic malingering is the feigning of illness for purposes of "secondary gain," usually involving neuropsychological symptoms following an alleged toxic exposure. We present six cases of documented exposures to CO, Hg, Pb, HF, ethylene glycol (EG), and diesel with characteristics that represent self-induced non-occupational exposures and malingering behavior.

Case Series: Six patients undergoing Independent Medical Examination (IME) were identified during the period 1999–2015, each filed workers' compensation claims for toxic exposure. Education ranged from incomplete high school education to college degree. Patients presented with acute symptoms which persisted 1–4 months. Five of six cases were male. All cases had access to the claimed substance within the workplace. One case (Hg) had a known psychiatric history. Three cases claimed inhalation, one ingestion, ocular and dermal exposure. Most patients were evaluated by multiple providers (average = 7, range 1–20) prior to diagnosis. Exposures were documented by blood concentrations of CO, Hg, Pb, and EG. Clinical findings appeared to support ocular diesel exposure and dermal HF exposure. Evaluation by non-medical toxicologists supported claimed exposures, although none required medical treatment, except the EG case. Industrial hygiene evaluation failed to confirm a plausible workplace exposure in any case, except diesel. Evaluation of time course of the alleged exposures and half-life of the substance ruled out workplace exposures. Cases CO, Hg, and Pb demonstrated blood concentrations not consistent with prolonged absence from the workplace. HF demonstrated signs of self-injury (interpreted as HF findings) weeks following exposure. The diesel case claimed progressive blindness.

Discussion: Toxic malingering in our cases is represented by multiple toxic substances. Features that differentiate these cases from symptom exaggeration include the appearance of self-administration of a toxic substance and the length of symptom complaint for the purpose of gaining workers' compensation benefits. Careful evaluation of the toxicokinetic and industrial hygiene data led to the conclusion that malingering behavior was the most likely explanation based upon reported history and findings.

Conclusion: Malingering is uncommon and difficult to diagnose in clinical practice. The diagnosis of toxic malingering requires careful analysis of reported workplace exposure, toxicokinetics, and physical findings of the implicated substance.

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