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ANNUAL MEETING ABSTRACT

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Original Research: Platform Sessions

1. Snake Venom Binding Activity of Expired Antivenoms

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Background: Antivenoms are believed to have limited shelf lives. Research indicates antivenom activity may surpass expiration dates.
Research question: Does binding of antivenom to venom persist after expiration date?
Methods: Fluorescent immunoassays compared binding of antivenom to venom. Ninety-six well plates were coated with venom, incubated with antivenom, and then incubated with biotinylated anti-horse IgG. Streptavidin conjugated to β-galactosidase was added and hydrolysis of substrate generated fluorescence. Plates were analyzed using a fluorescent reader.
Results: Faboterapico Polivalente Antivipmyn Tri antivenoms with expiration dates of 1/00, 3/09, and 10/10 bound *Bothrops jararaca* venom at respective rates of 95, 68, and 73 %, relative to unexpired control. Soro Antibotiopico Laquetico antivenom with an expiration date of 01/00, bound *B. jararaca* venom at a rate of 141 % relative to unexpired control. Faboterapico Polivalente Antivipmyn Tri antivenoms with expiration dates of 1/00, 3/09, and 10/10 bound *Crotalus atrox* venom at respective rates of 115, 73, and 92 %, relative to unexpired control. Soro Antibotiopico Laquetico antivenom with an expiration date of 01/00 bound *C. atrox* venom at a rate of 147 % relative to unexpired control. SAIMR polyvalent antivenoms with expiration dates of 04/98, 04/03, 12/05, and 10/10 bound *Naja naja* venom at respective rates of 81, 81, 93, and 103 % relative to unexpired control. SAIMR Polyvalent antivenom with expiration dates of 04/98, 04/03, 12/05, and 10/10 bound *N. nivea* venom at respective rates of 88, 88, 100, and 106 %, relative to unexpired control.
Discussion: SAIMR antivenom binds *Naja* venom for at least 9 years after expiration. Soro Antibotiopico Laquetico antivenom binds *Bothrops* and *Crotalus* venom for at least 14 years past expiration, demonstrating in some cases, higher venom binding than unexpired antivenom. Faboterapico Polivalente Antivipmyn Tri retained some binding to *Bothrops* and *Crotalus* venoms, but not to the same degree as Soro Antibotiopico Laquetico. However, binding did not differ significantly among all lots of Faboterapico Polivalente Antivipmyn Tri. This study is limited by its in vitro nature and suitability for patient safety was not addressed.
Conclusion: Antivenoms from three manufacturers demonstrated equivalent binding to venom in vitro despite surpassing expiration dates.

2. Trypsin and Rosmarinic Acid Reduce the Toxicity of Eastern Coral Snake (*Micrurus fulvius*) Venom in Mice

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Objective: Since antivenom is expensive and not always available, alternative treatments for toxic bites and stings are needed. The efficacy of trypsin and rosmarinic acid (RA) in treating Eastern Coral Snake (*Micrurus fulvius*) envenomation in a murine model is determined in an in vitro model.
Hypothesis: Both trypsin and RA will reduce the toxicity of Eastern Coral Snake venom.
Methods: Design: randomized controlled blinded study. Subjects: Fifty mice (20–30 g). Study groups: Intraperitoneal injections of (1) 2 mg/kg *M. fulvius* venom (approximately twice the LD50 for mice, n=10), (2) 2 mg/kg *M. fulvius* venom incubated in vitro for 1 h prior to injection with RA at a 1:10 ratio (n=17), (3) 2 mg/kg *M. fulvius* venom incubated in vitro for 1 h prior to injection with 1 mg of trypsin (n=17), (3) 1 mg trypsin IP without venom (n=3), and (4) RA IP without venom (n=3). Mice were observed for 12 h for signs of toxicity. Main outcome: time to toxicity (respiratory distress (respiratory rate<25 breaths/min), loss of spontaneous locomotor activity, or inability to upright self). Statistical analysis: Time to toxicity using Tukey–Kramer honest significant difference and survival to 4, 6, and 12 h using chi-square analysis.
Results: Onset of toxicity: group 1, 120.3 min; group 2, 238.1 min (p=0.15 relative to group 1); and group 3, 319.7 min (p=0.007 relative to group 1). Group 3 but not group 2 survival to 4 h was significant compared to group 1 (p=0.023). Two mice in the trypsin group and one mouse in the RA group survived to 12 h. Mice receiving trypsin alone or RA alone survived to 12 h.
Conclusion: In vitro neutralization of *M. fulvius* venom by trypsin justifies progressing to an in vivo model in future studies.

3. Point of Care Testing in Setting of Nitromethane and Methanol Co-ingestion Will Not Mask True Creatinine, Anion, or Osmolar Gap

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Background: Nitromethane interferes with the Jaffé colorimetric reaction used to measure serum creatinine, potentially mimicking acute kidney injury. This lab interference may confound the clinical management of nitromethane exposure, especially when co-ingested with a toxic alcohol. Bedside point-of-care (POC) testing platforms measure creatinine by an enzymatic method, which may result in more accurate measurements. We further hypothesize that the anion and osmolar gaps remain unchanged in the presence of nitromethane.
Methods: Nitromethane was added to whole blood from healthy volunteers to achieve five concentrations (0, 0.25, 0.5, 1, and 2 mmol/L), and the following tests were performed: creatinine (Jaffé and POC), electrolytes (associated with Jaffé and POC), plasma osmolality, and nitromethane concentration (gas chromatography [GC]). The remaining samples were refrigerated for 7 days and reanalyzed by GC. Anion and osmolar

Mexico entered a total of 235 cases involving 43 agents. One hundred ninety-six (83 %) patients presented with clinical signs of toxicity, while 39 were asymptomatic. The most common clinical presentations were confusion, CNS and respiratory depression, agitation/delirium, or anticholinergic toxidrome. GI decontamination was performed on 44 patients: 37 received gastric lavage and 10 received activated charcoal. Medical treatments, given to 55 patients, were benzodiazepines (44 patients), antipsychotics (11 patients), atropine (7 patients), as well as NAC, calcium, glucose, vasopressors, high-dose insulin euglycemic therapy, and intralipid (1 to 4 patients for each). The most common intoxicants (and number of cases) were synthetic cathinones (42), ethanol (30), antipsychotics (20), sedatives (19), carbon monoxide (12), cannabinoids (12), acid/corrosives (11), and opioids/heroin (6).
Conclusion: These initial data indicate that emerging drugs of abuse, prescription agents, and alcohol are well-represented intoxicants in urban toxicology practice settings worldwide. The increased use of gastric lavage over charcoal represents a trend which markedly differs from the USA and warrants further research. Our experience suggests that an international, web-based registry of bedside medical toxicology consultations is feasible. This project can create opportunities for global collaborative research and education among toxicologists with the ultimate goal of improving the care of poisoned patients worldwide.

51. Capsaicin Cream for Treatment of Cannabinoid Hyperemesis Syndrome

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Background: Cannabinoid hyperemesis syndrome (CHS) is described as cyclical episodes of nausea, vomiting, and abdominal pain associated with chronic and heavy cannabinoid use. The pathophysiology of CHS is poorly understood and published theories fail to explain the involvement of the endogenous cannabinoid system in the development of reported symptoms.
Hypothesis: Topical capsaicin will improve symptoms associated with CHS.
Methods: Prospective, nonblinded, nonplacebo-controlled trial of topical capsaicin preparation (0.075 %) in two patients with CHS. Case 1: A 19-year-old female presents to the emergency department for the third time in 1 week complaining of nausea, vomiting, and severe generalized abdominal pain. She previously underwent negative CT of the abdomen and pelvis, negative transvaginal ultrasonography, negative pelvic exam, and with the exception of mild hypokalemia, negative laboratory values. Further history revealed the patient has frequent and heavy use of marijuana. Her pain completely resolved when placed in a hot shower in the emergency department. She was treated for hypokalemia and when her pain and nausea returned, a trial of topical capsaicin cream was initiated. Her pain decreased from 8/10 to 4/10 and she was subsequently discharged home. Case 2: A 28-year-old man with history of cyclical nausea, vomiting, and abdominal pain for 3 years presents to the emergency department with return of his symptoms. His previous work up includes negative CT of abdomen and pelvis, negative EGD, and cholecystectomy. History revealed frequent and heavy marijuana smoking with improvement of symptoms upon exposure to hot water. A trial of topical capsaicin cream was initiated and the patient reported improvement in symptoms from 8/10 to 3/10. He was then discharged home.
Discussion: Capsaicin's only known receptor, TRPV1, is known to interact with endocannabinoids and plays a role in pain transmission. The results here suggest TRPV1 may play a role in the pathophysiology of CHS as well as indicate a safe and convenient therapeutic option for these often challenging cases.
Conclusion: Topical capsaicin therapy for CHS has potential as both a therapeutic modality and mechanistic probe that merits further investigation.

52. Intravenous Lipid Emulsion Therapy use in the Toxicology Investigators Consortium (ToxIC)

Levine M[1,2], Iwanicki J[3], Leikin JB[4,5], Donovan JW[6], McKay CA[7], Hernandez S[8], et al., for the Management with Intravenous Lipid in Overdose (MILO) investigators
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Background: In May 2012, the Intravenous Lipid Emulsion (ILE) subregistry was created as part of the ToxIC registry. The purpose of this subregistry is to prospectively collect detailed information regarding the use of ILE by toxicologists.
Objective: The primary objective of this interim analysis is to describe the patient characteristics for which ILE is being administered.
Methods: Retrospective review of prospectively collected data.
Results: Between 1 May 2012 through 30 October 2013, 44 patients received ILE. The subregistry analysis was complete on 34 of these patients. The 34 cases were derived from 17 different institutions. Males accounted for 13/34 (38.2 %) of subjects. The median (IQR) age was 48 (34.5–56)years, with the youngest patient being 13 months. ILE was administered most often for nondyhydropyrine calcium channel blockers (n=9), followed by dihydropyridine-class calcium channel blockers (n=5), or the combination of a beta blocker and a calcium channel blocker (n=4). ILE was administered for beta blockers alone in five subjects. Local anesthetics accounted for only three cases of ILE administration. Various other medications accounted for the remaining cases. Bradycardia (HR<50 bpm) was observed in 11/34 (32.3 %), while hypotension (systolic blood pressure <90 mmHg) occurred in 29/34 (85.3 %). Three patients experienced a high-grade AV block prior to ILE administration. Six (17.6 %) patients experienced cardiac arrest prior to implementation of ILE. In total, 10/34 (29.4 %) patients died. Acute kidney injury (creatinine >2.0 mg/dL) was present in 7/34 (20.6 %), while metabolic acidosis (pH <7.2) was present in 14/34 (41.7 %)
Conclusion: In this series of patients who received ILE, the majority of cases involved nonlocal anesthetics. Most patients were in shock and had evidence of abnormal tissue perfusion.

53. Prevention of Neonatal Abstinence Syndrome in the Setting of Intrauterine Baclofen Exposure

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Background: Baclofen is a gamma-aminobutyric acid (GABA) agonist used as a muscle relaxant in the treatment of spasticity. Baclofen is occasionally necessary to continue during pregnancy due to preexisting neurological conditions. Neonatal abstinence syndrome (NAS) including seizures in a benzodiazepine-refractory case has been reported with baclofen and additional information regarding optimal treatment is needed.
Hypothesis: The administration of a baclofen taper shortly after birth will help prevent NAS from intrauterine baclofen exposure.
Methods: A single-patient chart review and review of the literature regarding baclofen exposure during pregnancy and NAS was performed. A 43-year-old female with history of spasticity secondary to a spinal cord injury gave birth to a healthy full-term infant male via spontaneous vaginal delivery. Throughout pregnancy, the mother had received oral baclofen 80 mg daily. In order to mitigate NAS, a baclofen taper was planned after a multidisciplinary meeting. The initial dose was 0.1 mg/kg/day for 4 days, followed by a daily decrease of 0.01 mg/kg/day until discontinuation of the baclofen on the 13th day of life. Daily assessment for NAS was performed using the modified Finnegan NAS scoring system.

Results: Eighty-two modified Finnegan NAS scores were obtained in the first 16 days of life with a mean score of 2.0±2.4. A max NAS score of 9 was observed on the 13th day of life. At no point were there three consecutive NAS scores ≥8, indicating no need for further pharmacological intervention. The infant was discharged 3 days after the taper ended.
Discussion: This study demonstrates the absence of NAS in an infant who received a baclofen taper after intrauterine baclofen exposure from a mother taking 80 mg/day. In addition to the taper, the baby received baclofen through breast milk as well. In fact, baclofen concentrations in milk ranged from 0.28 to 0.38 μg/mL which provided an additional approximate dose of 0.02 mg/kg/day (1/3 diet breast milk).
Conclusion: The administration of a baclofen taper can prevent NAS in the setting of intrauterine baclofen exposure.

54. Baclofen Distribution into Breast Milk—A Potential for Toxicity?

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Background: Baclofen is a gamma-aminobutyric acid (GABA) agonist used as a muscle relaxant in the treatment of spasticity. Baclofen may be used by pregnant and lactating patients but may cause serious toxicity in infants. Other than one case report, there is little data regarding distribution of baclofen into breast milk.
Hypothesis: Nursing infants may be exposed to clinically significant amounts of baclofen when the mother is on oral baclofen.
Methods: A single-patient chart review was conducted. A 43-year-old female with spasticity secondary to a spinal cord injury began supplying breast milk for her baby shortly after giving birth to a healthy full-term infant male. During and after pregnancy, the mother received oral baclofen, 20 mg QID at evenly spaced intervals, between 0600 and 2200 daily. For three consecutive days, breast milk samples were collected at estimated trough (0530) and peak (2400) times. Using high-performance liquid chromatography and tandem mass spectrometry, baclofen concentrations were determined for each sample.
Results: Baclofen mean trough levels were 0.297±0.021 μg/mL and mean peak levels were 0.343±0.033 μg/mL (Table 1).
Discussion: Our patient was taking 80 mg of oral baclofen (20 mg QID) daily and had breast milk concentrations ranging from 0.28 to 0.38 μg/mL. A 3 kg infant consuming 750 mL of breast milk per day would be ingesting approximately 0.075 mg/kg/day, approximately 1/4th the weight-based dose of baclofen (0.29 mg/kg/day) in an average 70 kg adult consuming 20 mg baclofen daily. Infants, however, may have longer elimination half-lives and accumulate baclofen at greater concentrations. Infants may also be more sensitive to the effects of baclofen and exposure to lower amounts of baclofen over time could cause significant toxicity. In our infant-mother pair, the breast milk was initially limited to 1/3 amount of total daily diet (2/3 formula), only after observing for clinical effects and obtaining levels in milk did we increase the ratio to 50 %.
Conclusion: This report adds to the data on baclofen distribution in breast milk. Nursing mothers may have to limit amount of breast milk intake as distribution may be significant.
Table Abstract 54: Baclofen levels

	Day 1	Day 2	Day 3	Mean±SD
Trough level (μg/mL)	0.32	0.29	0.28	0.297±0.021
Peak level (μg/mL)	0.38	0.32	0.33	0.343±0.033

55. Aspirin-Associated Fanconi Syndrome: Is it an Occult Phenomenon?

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Background: Fanconi syndrome is a generalized transport defect within the proximal renal tubules which leads to inappropriate urinary losses of glucose, amino acids, bicarbonate, uric acid, phosphate, potassium, and other organic compounds. It may be inherited or acquired following exposure to certain xenobiotics. The medical literature has a few case reports of aspirin (ASA) intoxication leading to its development.
Research question: In cases of ASA toxicity, what proportion of patients develop laboratory findings consistent with Fanconi syndrome?
Methods: This is a retrospective review at a tertiary care hospital in an urban setting. All cases from 2001 to 2011 with ASA concentrations >30 mg/dL were reviewed for proximal tubule renal dysfunction (either elevation of creatinine on presentation that resolved prior to discharge or development of an elevation during hospital stay), an associated glucosuria (within the renal threshold level of 160–180 mg/dL or greater than expected based on serum glucose levels), and proteinuria.
Results: One hundred three patients in 108 independent encounters had ASA levels >30 mg/dL and were analyzed for elevations in creatinine, proteinuria, and glucosuria. Nine cases were identified to meet the study criteria. The average age was 25.8±9.9 years. Women accounted for 66.7 % of all identified cases. Mean ASA concentration was 59.8±20.4 mg/dL. The mean maximum serum glucose was 142.6±30.1 mg/dL, while the mean maximum urinary glucose was 237.5±174.7 mg/dL. Mean proteinuria was 128.6±75.6 mg/dL, while mean pH was 7.4±1.1.
Discussion: A proposed mechanism for Fanconi syndrome involves covalent bonding of salicylate or its metabolites to the mitochondria of the proximal tubular cells, altering its function and leading to energy-dependent dysfunction of active transporters. Though the study was limited by the retrospective design, restriction to a single center and a small number of events fitting the definition of Fanconi syndrome, the findings consistent with Fanconi syndrome in patients with ASA overdoses suggests ASA's role in the development of renal tubular dysfunction.
Conclusion: Fanconi syndrome was found in 8.7 % of patients, but further studies in a larger scale may provide better understanding regarding the frequency or risk factors for the development of this syndrome following ASA overdose.

56. Transient Fanconi Syndrome Following Salicylate Overdose

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Background: Fanconi syndrome is a generalized transport defect within the proximal renal tubules leading to inappropriate urinary losses of glucose, amino acids, bicarbonate, uric acid, phosphate, potassium, and other organic compounds. It may be inherited or acquired following exposure to certain xenobiotics.
Hypothesis: We hypothesized that salicylates may lead to Fanconi syndrome.
Methods: This is a single-patient chart review. A 15-year-old previously healthy female reportedly ingested 65 g of aspirin in a self-harm attempt. Within 5 h, she experienced nausea, vomiting, abdominal pain, and decreased hearing. Her initial vital signs were a heart rate of 118 beats per minute, respiratory rate of 20 breaths per minute, blood pressure of 137/93 mmHg, and a temperature of 36.1 °C. She was empirically started on an infusion of 5 % dextrose containing 150 mEq of sodium bicarbonate at 200 mL/h. Activated charcoal was also given. Initial laboratory values included: creatinine-1.06 mg/dL, potassium-3.3 mmol/L, bicarbonate-21 mmol/L, a pH of 7.47, and an initial salicylate concentration of 72 mg/dL. Over the next 3 days, she developed acute renal failure.
Results: Creatinine peaked at a level of 1.21 mg/dL. Her urinalysis was notable for elevated protein at 100 mg/dK, glucose was greater than 500 mg/dL despite normal serum glucose concentrations, rising urinary pH and the presence of red blood cells.
Discussion: There is limited data on the role of salicylate intoxication as a cause of proximal tubular dysfunction in humans and it is not previously