CURRENT AWARENESS PAPERS OF THE MONTH

Do heroin overdose patients require observation after receiving naloxone?
Willman MW, Liss DB, Schwarz ES, Mullins ME. Clin Toxicol 2016; online early: doi: 10.1080/15563650.2016.1253846:

Context
Heroin use in the US has exploded in recent years, and heroin overdoses requiring naloxone are very common. After awakening, some heroin users refuse further treatment or transport to the hospital. These patients may be at risk for recurrent respiratory depression or pulmonary edema. In those transported to the emergency department, the duration of the observation period is controversial. Additionally, non-medical first responders and lay bystanders can administer naloxone for heroin and opioid overdoses. There are concerns about the outcomes and safety of this practice as well.

Objectives
To search the medical literature related to the following questions: (1) What are the medical risks to a heroin user who refuses ambulance transport after naloxone? (2) If the heroin user is treated in the emergency department with naloxone, how long must they...
be observed prior to discharge? (3) How effective in heroin users is naloxone administered by first responders and bystanders? Are there risks associated with naloxone distribution programs?

**Methods**

We searched PubMed and GoogleScholar with search terms related to each of the questions listed above. The search was limited to English language and excluded patents and citations. The search was last updated on September 31, 2016. The articles found were reviewed for relevance to our objective questions. Eight out of 1020 citations were relevant to the first 2 questions, 5 of 707 were relevant to the third question and 15 of 287 were relevant to the fourth question. In the prehospital environment, does a heroin user revived with naloxone always require ambulance transport and what are the medical risks if ambulance transport is refused after naloxone? The eight articles were all observational studies done either prospectively or retrospectively. Two studies focused on heroin overdoses and included 1069 patients not transported to the hospital. No deaths occurred in this group. In counting the patients from all eight studies, some of which included non-heroin opioid overdoses, there were 5443 patients treated without transport and four deaths from rebound opioid toxicity. The number needed to transport to save one life (NNT) is 1361. Adverse effects were mostly related to opioid withdrawal. If a heroin user is treated in the ED, how long must the patient stay under observation before being safe for discharge? Five articles addressing the duration of ED observation required for patients treated with naloxone for opioid overdoses. Although a wide range of observation durations were reported, one study supported observing patients for one hour. If after this period the patient mobilizes as usual, has normal vital signs, and a Glasgow Coma Scale of 15, they can be discharged safely.

**Conclusions**

Patients revived with naloxone after heroin overdose may be safely released without transport to the hospital if they have normal mentation and vital signs. In the absence of co-intoxicants and further opioid use there is very low risk of death from rebound opioid toxicity. For those patients treated in the ED for opioid overdose, an observation period of one hour is sufficient if they ambulate as usual, have normal vital signs and a Glasgow Coma Scale of 15. Patients suffering opioid toxicity can be administered naloxone safely by first responders and trained lay people. Programs that train these individuals are likely safe and beneficial, however further research is necessary.

Full text available from: [http://dx.doi.org/10.1080/15563650.2016.1253846](http://dx.doi.org/10.1080/15563650.2016.1253846)

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**Exposures to traditional automatic dishwashing tablets and a comparison with exposures to soluble film tablets reported to the United Kingdom National Poisons Information Service 2008–2015**


**Introduction**

Traditional automatic dishwashing tablets are contained within an external wrapper that requires removal prior to use.
Objective
To determine the toxicity of traditional tablets and to compare this with our previously reported experience of soluble film dishwashing tablets.

Methods
Telephone enquiries regarding traditional tablets were analysed retrospectively for the period January 2008 to December 2015.

Results
Traditional tablets: There were 503 enquiries relating to 492 patients who had been exposed to a traditional tablet. Most involved children aged 5 years or less (87.4%). The majority (78.6%) of patients did not develop symptoms after exposure; 21.1% developed minor (PSS 1) symptoms while one patient developed moderate features. Exposure occurred predominantly as a result of ingestion (n = 476, 96.7%); the most common feature in symptomatic patients (n = 99, 20.8%) was vomiting (70 [14.7%] cases). Significantly (p < 0.0001) more adults (44.9% of 49 adults; 95% CI = 31.9–58.7) were reported with features than children (18.2% of 434; 95% CI = 14.9–22.1). There were five cases of eye contact which resulted in eye pain in two patients and eye irritation in another. Only one of 11 patients exposed dermally developed features (a rash around the mouth).

Comparison with soluble film exposures: The percentage of patients that were reported with clinical symptoms following ingestion of a soluble film dishwashing tablet (31.7% of 473 patients; 95% CI = 27.7–36.0) was significantly greater (p < 0.0001) than that for a traditional tablet (20.9% of 483 patients; 95% CI = 17.5–24.8). Vomiting was the most commonly reported feature and occurred significantly (p < 0.0001) more frequently amongst patients who had ingested a soluble film tablet (25.5%; 95% CI = 21.8–29.6) than a traditional tablet (14.7%; 95% CI = 11.8–18.1).

Conclusions
Exposure to both traditional and soluble film tablets only rarely produced clinically significant symptoms (PSS ≥2). However, ingestion of a soluble film tablet was significantly more likely to result in clinical features than ingestion of a traditional tablet.

Full text available from: http://dx.doi.org/10.1080/15563650.2016.1264588

Modeling the effect of succimer (DMSA; dimercaptosuccinic acid) chelation therapy in patients poisoned by lead

Context
Kinetic models could assist clinicians potentially in managing cases of lead poisoning. Several models exist that can simulate lead kinetics but none of them can predict the effect of chelation in lead poisoning. Our aim was to devise a model to predict the effect of succimer (dimercaptosuccinic acid; DMSA) chelation therapy on blood lead concentrations.

Materials and methods
We integrated a two-compartment kinetic succimer model into an existing PBPK lead model and produced a Chelation Lead Therapy (CLT) model. The accuracy of the model’s predictions was assessed by simulating clinical observations in patients poisoned by lead and treated with succimer. The CLT model calculates blood lead concentrations as the sum of the background exposure and the acute or chronic lead poisoning. The latter was due either to ingestion of traditional remedies or occupational exposure to lead-polluted ambient air. The exposure duration was known. The blood lead concentrations predicted by the CLT
model were compared to the measured blood lead concentrations.

**Results**
Pre-chelation blood lead concentrations ranged between 99 and 150 μg/dL. The model was able to simulate accurately the blood lead concentrations during and after succimer treatment. The pattern of urine lead excretion was successfully predicted in some patients, while poorly predicted in others.

**Conclusions**
Our model is able to predict blood lead concentrations after succimer therapy, at least, in situations where the duration of lead exposure is known.

Full text available from: [http://dx.doi.org/10.1080/15563650.2016.1263855](http://dx.doi.org/10.1080/15563650.2016.1263855)

**Australian taipan (Oxyuranus spp.) envenoming: clinical effects and potential benefits of early antivenom therapy – Australian Snakebite Project (ASP-25)**


**Context**
Taipans (Oxyuranus spp.) are medically important venomous snakes from Australia and Papua New Guinea. The objective of this study was to describe taipan envenoming in Australian and its response to antivenom.

**Methods**
Confirmed taipan bites were recruited from the Australian Snakebite Project. Data were collected prospectively on all snakebites, including patient demographics, bite circumstances, clinical effects, laboratory results, complications and treatment. Blood samples were taken and analysed by venom specific immunoassay to confirm snake species and measure venom concentration pre- and post-antivenom.

**Results**
There were 40 confirmed taipan bites: median age 41 years (2–85 years), 34 were males and 21 were snake handlers. Systemic envenoming occurred in 33 patients with neurotoxicity (26), complete venom induced consumption coagulopathy (VICC) (16), partial VICC (15), acute kidney injury (13), myotoxicity (11) and thrombocytopenia (7). Venom allergy occurred in seven patients, three of which had no evidence of envenoming and one died. Antivenom was given to 34 patients with a median initial dose of one vial (range 1–4), and a median total dose of two vials (range 1–9). A greater total antivenom dose was associated with VICC, neurotoxicity and acute kidney injury. Early antivenom administration was associated with a decreased frequency of neurotoxicity, acute kidney injury, myotoxicity and intubation. There was a shorter median time to discharge of 51 h (19–432 h) in patients given antivenom <4 h post-bite, compared to 175 h (27–1104 h) in those given antivenom >4 h. Median peak venom concentration in 25 patients with systemic envenoming and a sample available was 8.4 ng/L (1–3212 ng/L). No venom was detected in post-antivenom samples, including 20 patients given one vial initially and five patients bitten by inland taipans.

**Discussion**
Australian taipan envenoming is characterised by neurotoxicity, myotoxicity, coagulopathy, acute kidney injury and thrombocytopenia. One vial of antivenom binds all measurable venom and early antivenom was associated with a favourable outcome.

Full text available from: [http://dx.doi.org/10.1080/15563650.2016.1250903](http://dx.doi.org/10.1080/15563650.2016.1250903)
A critical review of the literature to conduct a toxicity assessment for oral exposure to methyl salicylate
Abstract and full text available from: http://dx.doi.org/10.1080/10408444.2016.1236071

Glyphosate epidemiology expert panel review: a weight of evidence systematic review of the relationship between glyphosate exposure and non-Hodgkin's lymphoma or multiple myeloma
Abstract and full text available from: http://dx.doi.org/10.1080/10408444.2016.1214681

Prognostic value of hematological parameters in patients with paraquat poisoning
Abstract and full text available from: http://dx.doi.org/10.1038/srep36235

A systematic review of mancozeb as a reproductive and developmental hazard
Abstract and full text available from: http://dx.doi.org/10.1016/j.envint.2016.11.006

Pregnancy outcomes after maternal varenicline use; analysis of surveillance data collected by the European Network of Teratology Information Services
Abstract and full text available from: http://dx.doi.org/10.1016/j.reprotox.2016.11.010

Focus on cannabinoids and synthetic cannabinoids
Abstract and full text available from: http://dx.doi.org/10.1002/cpt.563
No support for lipid rescue in oral poisoning: a systematic review and analysis of 160 published cases
Abstract and full text available from: http://dx.doi.org/10.1177/0960327116679715

Lung function before and after a large chlorine gas release in Graniteville, South Carolina
Abstract and full text available from: http://dx.doi.org/10.1513/AnnalsATS.201508-525OC

Abstract and full text available from: http://dx.doi.org/10.1016/j.ecoenv.2016.09.001
TOXICOLOGY

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**Developmental toxicity**


**Driving under the influence of alcohol and other drugs**


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**Anticoagulants**


**Warfarin**


**Flecainide**


**Antibiotics**

**Ciprofloxacin**


**Metronidazole**


**Trimethoprim-sulfamethoxazole**


**Vancomycin**


**Anticholinergic drugs**


**Anticoagulants**


**Apixaban**


**Dabigatran**


**Warfarin**

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**Lamotrigine**

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