The interpretation of hair analysis for drugs and drug metabolites

Introduction
Head hair analysis for drugs and drug metabolites has been used widely with the aim of detecting exposure in the weeks or months prior to sample collection. However, inappropriate interpretation of results has likely led to serious miscarriages of justice, especially in child custody cases.

Objective
The aim of this review is to assess critically what can, and perhaps more importantly, what cannot be claimed as regards the interpretation of hair test results in a given set of circumstances in order to inform future testing.

Methods
We searched the PubMed database for papers published 2010-2016 using the terms "hair" and "drug" and "decontamination", the terms "hair" and "drug" and "contamination", the terms "hair" and "drug-facilitated crime", the terms "hair" and "ethyl glucuronide", and the
terms "hair", "drug testing" and "analysis". Study of the reference lists of the 46 relevant papers identified 25 further relevant citations, giving a total of 71 citations.

**Hair samples**

Drugs, drug metabolites and/or decomposition products may arise not only from deliberate drug administration, but also via deposition from a contaminated atmosphere if drug(s) have been smoked or otherwise vaporized in a confined area, transfer from contaminated surfaces via food/fingers, etc., and transfer from sweat and other secretions after a single large exposure, which could include anesthesia. Excretion in sweat of endogenous analytes such as gamma-hydroxybutyric acid is a potential confounder if its use is to be investigated. Cosmetic procedures such as bleaching or heat treatment of hair may remove analytes prior to sample collection. Hair color and texture, the area of the head the sample is taken from, the growth rate of individual hairs, and how the sample has been stored, may also affect the interpretation of results.

**Toxicological analysis**

Immunooassay results alone do not provide reliable evidence on which to base judicial decisions. Gas or liquid chromatography with mass spectrometric detection (GC- or LC-MS), if used with due caution, can give accurate analyte identification and high sensitivity, but many problems remain. Firstly, it is not possible to prepare assay calibrators or quality control material except by soaking "blank" hair in solutions of appropriate analytes, drying, and then subjecting the dried material to an analysis. The fact that solvents can be used to add analytes to hair points to the fact that analytes can arrive not only on, but also in hair from exogenous sources. A range of solvent-washing procedures have been advocated to "decontaminate" hair by removing adsorbed analytes, but these carry the risk of transporting adsorbed analytes into the medulla of the hair therefore confounding the whole procedure. This is especially true if segmental analysis is being undertaken in order to provide a "time course" of drug exposure.

**Proposed clinical applications of hair analysis**

There have been a number of reports where drugs seemingly administered during the perpetration of a crime have been detected in head hair. However, detailed evaluation of these reports is difficult without full understanding of the possible effects of any "decontamination" procedures used and of other variables such as hair color or cosmetic hair treatment. Similarly, in child custody cases and where the aim is to demonstrate abstinence from drug or alcohol use, the issues of possible exogenous sources of analyte, and of the large variations in analyte concentrations reported in known users, continue to confound the interpretation of results in individual cases.

**Conclusions**

Interpretation of results of head hair analysis must take into account all the available circumstantial and other evidence especially as regards the methodology employed and the possibility of surface contamination of the hair prior to collection.

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**Acute lamotrigine overdose: a systematic review of published adult and pediatric cases**


**Context**

Lamotrigine is a broad-spectrum anticonvulsant commonly used to treat seizure and bipolar mood disorders. Evidence from case series and retrospective studies indicate that
lamotrigine overdose is usually benign. However, there are reported cases of cardiac arrest and mortality following lamotrigine overdose. We undertook a systematic review of the literature on lamotrigine overdoses to better understand the clinical severity, the relevance of serum concentrations, and therapeutic interventions for overdose.

**Objectives**
To characterize manifestations of acute lamotrigine overdose, determine if serum concentrations predict poisoning severity, and evaluate the effectiveness of overdose management interventions.

**Methods**
We performed a literature search across eight databases, including Medline, EMBASE, and the Cochrane Library, from database inception to April 2014. Major bibliographic databases were updated on 31 May 2017. Articles were eligible if they described acute or acute on chronic lamotrigine overdose. At least one serum lamotrigine concentration had to be reported for inclusion. Reports on chronic poisoning, studies describing adverse effects of therapeutic use, and animal studies were excluded.

**Results**
We retrieved 6238 records; 48 (51 cases) met the inclusion criteria. Cases primarily involved adults (70.6%). Potentially life-threatening symptoms of overdose included seizures (55%), Glasgow Coma Scale ≤ 8 (20%), hypotension (12%), and wide complex tachycardia (WCT) and cardiac arrest (6%). Among the 25 cases exposed to lamotrigine alone (13 adult; 12 pediatric), 2 adult fatalities occurred (4 g and 7.5 g ingested) and 8 pediatric cases experienced seizures (all children ≤3.5-years-old, 75% without an underlying seizure disorder, ≥ 525 mg ingested). The lowest seizure-associated serum concentration was 3.8 mg/L and 25.6 mg/L for pediatric and adult patients, respectively, suggesting children may be more susceptible to CNS toxicity. Cardiovascular toxicities occurred primarily in adult patients (threshold >25 mg/L). Overdose interventions included benzodiazepines (53%), propofol or barbiturates (14%), NaHCO₃ (20%), lipid therapy (12%), and extracorporeal elimination (10%). NaHCO₃ yielded no response in four of nine cases with conduction delays; however, two of the four cases subsequently responded with lipid therapy.

**Conclusions**
Most cases reporting lamotrigine exposures observed mild or no toxicity; however, large exposures were associated with severe CNS depression, seizures, cardiac conduction delays, wide complex tachycardia, and death. In adults with a serum concentration >25 mg/L, severe toxicity may occur. In patients ≤3.5 years of age, ingestions of ≥525 mg may produce severe CNS depression and seizures.

Full text available from: [http://dx.doi.org/10.1080/15563650.2017.1370096](http://dx.doi.org/10.1080/15563650.2017.1370096)

**Comparison of low dose and standard dose abdominal CT scan in body stuffers**


**Purpose**
Detection of body stuffers is challenging in emergency departments. Because of the small size of baggies, plain radiograph is of little value in most suspects. On the other hand, abdomen CT scan is burdened by high cost and radiation dose. This study was performed to compare the image quality, radiation dose and accuracy of low-dose CT scan in comparison with standard dose.
Material and methods
In this prospective study, suspected body stuffers who were referred to the radiology department underwent two different protocols of abdominal non-contrast CT scan simultaneously: low-dose (with equivalent dose to conventional abdominal x-ray) and standard dose. Standard dose CT scan was considered as the reference. Low-dose CT scans were evaluated for detection of baggies by two radiologists blinded to the result of standard dose CT. Image quality, noise, dose-length product (DLP) and effective dose (ED) compared between two groups.

Results
The study consisted of 40 patients (33.38 ± 7.4 years). Standard dose CT evaluation was positive in 22 patients (55%). In comparison with standard dose CT scan, low-dose group had a sensitivity of 86%, specificity of 100%, PPV and NPV of 100% and 86%. The accuracy of low-dose CT scan for detection of baggies larger than 1 cm was 100%. However, from the 3 cases that could not be detected with low dose protocol, one had CT features suspected for baggies rupture which was intubated and later deceased. Noise average of low-dose protocol, was approximately 7 times greater than standard dose group, while DLP and ED were 9.7 times less.

Conclusion
Low dose CT scan appears to be an appropriate screening method for body stuffers, especially when the baggies are larger than one centimeter. However, in the presence of severe clinical symptoms, a standard dose CT scan will be more helpful due to better image quality especially in suspected ruptured baggies.

Full text available from: http://dx.doi.org/10.1080/15563650.2017.1377220

Suicidal bupropion ingestions in adolescents: increased morbidity compared with other antidepressants

Objective
Bupropion is often categorized as a newer generation antidepressant and assessed with serotonin reuptake inhibitors as a lower risk than older tricyclic antidepressants (TCAs). The objective of this study was to compare outcomes in adolescent suicide from ingestions between bupropion and TCA medications.

Study design
An analysis of the National Poison Data System for exposures coded "suspected suicide" in adolescents (age: 13–19) was undertaken for the years 2013–2016 and included TCAs or bupropion. We compared clinical effects, therapies and medical outcomes.

Results
Over the four-year period there were 2253 bupropion and 1496 TCA adolescent suspected suicide calls. There was a significant linear increase in bupropion ingestions over the four years. Across all years, there were on average 189.2 (95% CI: 58.1–320.4; p = .01) more ingestions of bupropion than TCA. When comparing bupropion to a TCA, ingestions of bupropion were significantly more likely to be accompanied by seizure (30.7% vs 3.9%; p < .01), to be admitted (74.8% vs 61.6%; p < .01) and medical outcomes to be coded as a major outcome (19.3% vs 10.0%; p < .01). The number of cases with death or major clinical outcome for both increased over the four-year period. Ingestions of bupropion were less likely to have hypotension (2.7% vs 8.0%; p < .01) and less likely to be intubated (5.6% vs 16.4%; p < .01) as compared to ingestions of TCA.
Conclusions
Adolescents who overdose on a single medication in a suicide attempt with bupropion have a statistically significant higher incidence of major outcomes and seizures. The risks of bupropion as a potential means of suicidal gesture by overdose must be considered, and weighed against its benefits and side effect profile when choosing an appropriate agent for the treatment of depression in adolescents.

Full text available from: http://dx.doi.org/10.1080/15563650.2017.1377839

DMTS is an effective treatment in both inhalation and injection models for cyanide poisoning using unanesthetized mice

Context
Cyanide (CN) is a metabolic poison, halting ATP synthesis by inhibiting complex IV of the electron transport chain. If exposed at high enough concentrations, humans and most animals can die within minutes. Because time is a crucial factor in survival of CN poisoning, a rapidly bioavailable, nontoxic, easy to administer CN medical countermeasure could improve morbidity/mortality in a mass CN exposure scenario. The most likely route of exposure to CN is via inhalation.

Objective
This study examined the efficacy of a new formulation for dimethyl trisulfide (DMTS), a countermeasure which has shown promise as a treatment for CN poisoning, using both inhalation and injection models of CN exposure.

Methods
We developed a model of acute CN inhalation intoxication, using the highly toxic agent system from CH Technologies for nose-only exposure. Both continuous and discontinuous HCN exposure paradigms were implemented. For comparison, we also utilized a potassium cyanide (KCN) injection model. In all experiments, DMTS was administered as a cyanide countermeasure via intramuscular injection in unanesthetized mice.

Results
We found DMTS administration to be highly protective against both subcutaneous KCN and HCN inhalation toxicity. In the KCN injection model, DMTS afforded protection against 3.73 times the LD50 dose of KCN. In our HCN inhalation exposure model, mice challenged with LC50 HCN doses for the duration of either 10- or 40-minute exposure paradigms demonstrated improved survival in the presence of DMTS treatment (87.5% and 90.0% survival, respectively). Animals in the DMTS treatment groups of both lethal exposure models similarly exhibited improvement in observed toxic signs.

Conclusion
We show that a newly developed formulation of DMTS is efficacious within two lethal CN exposure mouse models (inhalation and injection) and is highly effective by intramuscular injection. Within these HCN studies, we demonstrate efficacy of DMTS in both continuous and discontinuous inhalation exposure models.

Full text available from: http://dx.doi.org/10.1080/15563650.2017.1376749
Synthetic cannabinoid "Black Mamba" infidelity in patients presenting for emergency stabilization in Colorado: a P SCAN Cohort


Background
Use of new psychoactive substances (NPS) has increased over the last decade. During this period, variability of both clinical presentations and chemical compositions of these compounds has increased. Synthetic cannabinoids (SCs) are the most commonly used NPS and there are more than 100 documented unique molecules in this class. "Black Mamba", often associated to ADB-FUBINACA, is the most commonly used SC in Colorado. It has been linked to kidney injury, myocardial toxicity, seizures, and death.

Objectives
We aim to identify the chemical constituents and quantification of eight cases of reported "Black Mamba" use in order to further understand the clinical variability in patients presenting for emergency stabilization.

Methods
We report data from eight cases of reported "Black Mamba" use prospectively captured through the Colorado site of the Psychoactive Surveilance Consortium and Analysis Network (P SCAN). P SCAN is a geographically representative group of academic hospitals that capture clinical presentation, outcome, and biologic samples from patients that present for emergency stabilization following NPS use. Serum and urine samples were analyzed and quantified by liquid chromatography-quadrupole time-of-flight mass spectrometry after a qualitative screen for over 600 unique NPS compounds.

Results
In the reported eight cases, the median age was 28 years old. There were four male and four females. Four patients had agitation/delirium and four patients had chest pain. Normal saline, benzodiazepines and ondansetron were the common treatment provided in the emergency department (ED). Two patients were discharged from the ED and six patients being admitted for emergency observation with a median length of stay (LOS) of six hours. No deaths were reported. Confirmatory testing revealed that only five patients (62.5%) had SCs found in blood or urine samples. Cocaine, NRG-3, 3-methoxyphencyclidine hydrochloride (MeO-PCP), and methamfetamine were identified in other presentations.

Conclusions
The wide range of clinical presentations from "Black Mamba" use may be explained by the wide variability of chemical constituents found by laboratory analysis.

Full text available from: http://dx.doi.org/10.1080/15563650.2017.1357826

Intoxications in the STRIDA project involving a panorama of psychostimulant pyrovalerone derivatives, MDPV copycats


Context
An increasing number of new psychoactive substances (NPS) of different chemical classes have become available through marketing and sale over the Internet. This report from the Swedish STRIDA project presents the prevalence, laboratory results, and clinical features in intoxications involving 11 stimulant pyrovalerone NPS derivatives over a 5-year period.
**Study design**
Case series of consecutive patients with admitted or suspected intake of NPS presenting to Swedish hospitals for emergency treatment from January 2011 to March 2016.

**Patients and method**
Blood and urine samples were collected from intoxicated patients presenting to hospitals all over Sweden. Analyses of NPS and other drugs of abuse were performed by immunochemical and liquid chromatography-mass spectrometry multi-component methods. Clinical data were collected during consultation with the Swedish Poisons Information Centre (PIC), and retrieved from medical records. The study involved analytically confirmed cases with 11 pyrovalerone drugs.

**Results**
During the study period, 114 intoxications were detected that involved any of 11 new pyrovalerone drugs. In addition to these new pyrovalerone derivatives, 3,4-methylenedioxypyrovalerone (MDPV) was detected in 17 of the cases and alpha-pyrrolidinovalerophenone (α-PVP) in 45 cases. Identification was made according to forensic standards and comprised the following substances: 4F-α-PVP, α-PHP, PV8, 4Me-PPP, α-PBP, 4F-PV8, α-PPP, MDPHP, α-PVT, 4Cl-α-PVP, and 4F-α-PHP. The three most frequently detected drugs were α-PBP, MDPHP, and 4F-α-PVP. The age range of patients was 16–66 (median 30) years and 84% were males. The substance concentrations in urine and serum were highly variable, ranging from 1 ng/mL to 300 µg/mL. Poly-drug use was common with only 8 of 114 cases (7%) involving one pyrovalerone drug. The additional substances comprised other NPS and classical psychoactive drugs. The patients showed a variety of clinical signs; agitation, delirium, hallucinations, excessive motor activity, seizures, tachycardia, hypertension, and/or hyperthermia.

**Conclusions**
In analytically confirmed NPS-related intoxications, 11 new pyrovalerone derivatives in addition to MDPV and α-PVP were found. The clinical features were consistent with a sympathomimetic toxidrome, but the urine and serum concentrations were highly variable. The results demonstrated that many novel pyrovalerone stimulants were introduced on the recreational NPS drugs market. Analytical investigations were necessary to obtain this information.

Full text available from: [http://dx.doi.org/10.1080/15563650.2017.1370097](http://dx.doi.org/10.1080/15563650.2017.1370097)

**Clinical predictors of tissue necrosis following rattlesnake envenomation**


**Background**
Rattlesnake envenomation (RSE) causes edema, hemotoxicity and tissue necrosis. Necrosis may result in permanent disability.

**Objective**
To study 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. Inclusion criteria were age ≥18 years and upper extremity (UE) envenomation site. Primary outcome was tissue necrosis, including dermonecrosis, manifesting as bullae. Secondary outcome was amputation.
Results
77 subjects, age 18 to 88 years, met inclusion criteria. Rattlesnake species was unknown in most cases. All received Fab antivenom. 62 (82%) had a digital envenomation. 31 (40.3%) had necrosis. Necrotic area ranged from 0.1 cm² to 14 cm². Procedural interventions, (superficial debridement, dermotomy, surgical exploration, and operative debridement of devitalized tissue) occurred in 25 (32.5%). Five (6.5%) underwent dermotomy and 6 (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 (RR 1.14 95% CI 0.99–1.31 p = 0.09). Time to antivenom did not correlate with risk of necrosis.

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.

Full text available from: http://dx.doi.org/10.1080/15563650.2017.1371311

Carbon monoxide poisoning from waterpipe smoking: a retrospective cohort study

Objective
Waterpipe smoking may increasingly account for unintentional carbon monoxide poisoning, a serious health hazard with high morbidity and mortality. We aimed at identifying waterpipe smoking as a cause for carbon monoxide poisoning in a large critical care database of a specialty care referral center.

Methods
This retrospective cohort study included patients with a history of exposure to waterpipe smoking and carbon monoxide blood gas levels >10% or presence of clinical symptoms compatible with CO poisoning admitted between January 2013 and December 2016. Patients' initial symptoms and carbon monoxide blood levels were retrieved from records and neurologic status was assessed before and after hyperbaric oxygen treatment.

Results
Sixty-one subjects with carbon monoxide poisoning were included [41 males, 20 females; mean age 23 (SD ± 6) years; range 13–45] with an initial mean carboxyhemoglobin of 26.93% (SD ± 9.72). Most common symptoms included syncope, dizziness, headache, and nausea; 75% had temporary syncope. Symptoms were not closely associated with blood COHb levels.

Conclusion
CO poisoning after waterpipe smoking may present in young adults with a wide variability of symptoms from none to unconsciousness. Therefore diagnosis should be suspected even in the absence of symptoms.

Full text available from: http://dx.doi.org/10.1080/15563650.2017.1375115
Metal-on-metal hip joint prostheses: a retrospective case series investigating the association of systemic toxicity with serum cobalt and chromium concentrations
Abstract and full text available from: http://dx.doi.org/10.1007/s13181-017-0629-1

Overdoses with aripiprazole: signs, symptoms and outcomes in 239 exposures reported to the Danish Poison Information Center
Abstract and full text available from: http://dx.doi.org/10.1111/bcpt.12902

Extracorporeal life support and digoxin-specific Fab fragments for successful management of Taxus baccata intoxication with low output and ventricular arrhythmia
Abstract and full text available from: http://dx.doi.org/10.1016/j.ajem.2017.09.031

Post-mortem findings in 22 fatal Taxus baccata intoxications and a possible solution to its detection
Abstract and full text available from: http://dx.doi.org/10.1016/j.jflm.2017.08.016

Reversal of dabigatran-associated bleeding using idarucizumab: review of the current evidence
Abstract and full text available from: http://dx.doi.org/10.1007/s11239-017-1555-4

Detection of tetrodotoxin shellfish poisoning (TSP) toxins and causative factors in bivalve molluscs from the UK
Epidemiologic features and outcomes of caustic ingestions; a 10-year cross-sectional study


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**Medication errors**


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**Nephrotoxicity**


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Nitrobenzene

Nitromethane

Paraffins

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