Abstracts of the 2011 International Congress of the European Association of Poisons Centres and Clinical Toxicologists, 24–27 May 2011, Dubrovnik, Croatia

1. GHB and its Analogues

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Discussion: Gamma-hydroxybutyrate (GHB) and its precursors gamma-butyrolactone (GBL) and 1,4-butanediol (BD) are three compounds that emerged as recreational drugs among young people during the 1990s, mostly in some parts of Europe, the USA and Australia. GHB, BD and GBL are normally consumed as liquids but GHB also exists in crystalline form. Chemically GHB is a short-chained fatty acid, GBL is the corresponding lactone and BD is a diol. The precursor chemicals GBL and BD are rapidly converted to GHB in the body when ingested. They act completely as GHB within the organism. Furthermore, GHB can be easily manufactured from GBL and BD. The precursors are widely used in the chemical industry as solvents and are commercially available. The sodium salt of GHB, sodium oxybate is manufactured and licensed as a pharmaceutical drug for the treatment of narcolepsy. GHB, GBL and BD are used as recreational drugs due to their ability to induce euphoria, relaxation and anxiolysis. These drugs have several names among the users such as “Liquid ecstasy, G, GHB, Gamma-O, Blue Verve or Gobbe (swe)”. The mechanism of action of GHB is similar to that of alcohol, barbiturates, and benzodiazepines. GHB is classified as a narcotic in most countries (Schedule II of the Convention on Psychotrophic Substances) while GBL only in a few countries. Use of GHB and GBL is generally low but there is evidence of some sub-populations, settings and geographical areas, where it is commonly used, such as gay nightclubs in the UK and the USA. In other areas, such as in the Nordic countries it is more often used in private settings for purposes of recreation, bodybuilding and as a sleeping aid. Abuse of GHB is often mixed with other illicit drugs such as amphetamine, cannabis or cocaine, many times due to its strong ability to induce sleep. GHB has a steep dose-response curve where even a small increase in dose may cause nausea, vomiting, muscular jerks, hallucinations, amnesia and impaired consciousness. Both GHB and GBL are difficult to dose correctly with unpredictable effects, so, when consumed, an overdose is easily achieved. Patients with overdose may present with hyperactivity, ataxia, confusion and aggression but also when larger amounts are taken deep coma, hypothermia, bradycardia and respiratory depression may be present. Severe overdose may finally lead to death, mainly due to hypotension, hypoperfusion and hypoxemia. The depressant effect of GHB on the central nervous system is potentiated by alcohol, opiates and other sedative or anesthetic drugs. Most overdoses are accidental and account for a substantial proportion of acute emergencies admitted to hospitals related to illicit drugs. Pharmacologically, GHB acts mainly on benzodiazepine receptors in a dose-dependent manner. GHB acts at specific GHB receptors and at GABAB receptors. Small doses of GHB seem to increase the release of dopamine, while larger doses inhibit the release. GHB also inhibits norepinephrine release, increases the serotonin turnover and possibly increases endogenous opioid concentrations. The amount of GHB taken for recreational use is highly individual and development of tolerance is rapid. GHB is normally consumed as a liquid from a PET bottle where a cap normally contains around 2–3 g or 1 centiliter. Normal dosage is 0.5 to 1 g to achieve relaxation, 2–3 g for euphoria and 4–6 g for sleep. GHB dependence develops rapidly with regular consumption. Physical dependence may be seen already after 3 to 6 months of regular use. Finally, the users may be highly addicted with need for intake of GHB every 3 hours. In cessation of drug abuse GHB abstinence may present which is a severe clinical condition. GHB abstinence needs treatment in hospital for at least 3 weeks. First line treatment of abstinence is benzodiazepines in very high doses. Conclusion: Additional measures within the European Community and other countries seem to be necessary to control availability of the GHB precursors GBL and BD, to prevent further abuse of GHB.

2. Recent Advances in the Management of Opioid Toxicity

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Introduction: Opioid analgesic use is a significant cause of recreational, iatrogenic and deliberate self-poisoning in the community. Acute opioid analgesia toxicity commonly results in the toxidrome of reduced conscious state, bradypnoea and miosis and may result in death due to primary respiratory arrest. The application of basic or advanced life support measures to improve ventilation and oxygenation may be life-saving if administered in a timely fashion and should precede any antagonist therapy administration. Discussion: Opioid antagonists, such as naloxone, are well-known to effectively reverse the effects of opioid toxicity by competitive antagonism of opioid receptors in a dose-dependent manner. Naloxone is a relatively short-acting pure opioid antagonist (half-life less than 1 hour), widely used in the pre-hospital setting to reverse the effects of recreational opioid intoxication, in particular that related to heroin use. Longer acting antagonists such as naltrexone and nalmefene are also available but are not routinely used or recommended in the acute poisoning setting. Many patients presenting with suspected heroin intoxication are managed in the pre-hospital setting by paramedics administering naloxone by various routes with patients often refusing hospital transport. Recent recreational use and therapeutically abuse of prescription opioid analgesics seems to be increasing with a concurrent increase in the risk of adverse events related to the availability of these agents. As a result, it is important to be aware that when assessing patients with opioid toxicity, the toxic agent should be identified, the route of administration ascertained and the formulation of the drug confirmed. In view of the short duration of action of naloxone, reversal of acute opioid toxicity from a long-acting or sustained-release opioid analgesic without a prolonged period of observation may result in recurrence of toxicity that may require further antagonist administration by continuous infusion and/or ongoing respiratory support. Naloxone has a high first-pass metabolism with minimal oral bioavailability. As a result, it is administered by the intravenous (IV), intramuscular (IMI) or subcutaneous routes. Subcutaneous administration of naloxone is dose-dependent. Peak blood concentrations occur more quickly with IV administration but clinical response to IV and IMI have been reported as comparable when a larger IMI dose is used. In an attempt to reduce the risk of needle stick injuries to health care workers, particularly in the pre-hospital setting, a number of authors have reported success with intranasal (IN) naloxone administration in reversing opioid toxicity. Naloxone is best administered IN using a mucosal atomiser device (MAD) which achieves maximal exposure of the nasal mucosa to the drug. Intranasal drug administration is limited by the concentration and volume that can be delivered. Less than 1 mL is recommended as the maximum volume to each nares to prevent liquid escaping the nasal passage. The standard naloxone concentration for IV administration is 400 micrograms per mL. Using this concentration, 2.5 mL would need to be given to each nares to deliver 2 mg of naloxone. Studies reporting positive effects for IN naloxone have used higher concentrations of the drug (2 mg/mL) allowing for smaller volume administration to the nasal mucosa. Pharmacokinetic comparison of 2 mg doses of naloxone, using the 400 micrograms/mL concentration, by IV, IMI, IN routes to volunteers revealed bioavailability of 36% and 4% for the IMI and IN routes respectively. As a result, although positive clinical effects have been reported with the standard naloxone concentration by the IN route, higher concentration solutions are preferred to ensure more reliable absorption of naloxone. While IN administration of naloxone shows promise, further study is required to ascertain effectiveness, dosing and safety. Complications of opioid antagonist therapy include the induction of acute opioid withdrawal states, which may be induced by overzealous therapeutic administration of naloxone and with the use of other antagonists, such as oral naltrexone in attempts to undertake rapid opiate detoxification. Opioid-induced non-cardiogenic pulmonary oedema has also been described after naloxone administration, particularly in patients with significant hypoxemia and respiratory depression. Opioid antagonists’ administration has been reported to be safe in isoalted cases and case series of treatment of altered mental state in other acute poisoning scenarios (e.g. clonidine, valproic acid). To date, there is no good evidence to suggest that the use of opioid antagonists at non-opioid-induced sedative drug poisoning results in reliable improvements in mental state. Supportive care remains the mainstay of treatment for these situations. Finally, the role of oral naltrexone, such as extended-release naloxone for out-of-hospital management of presumed opioid overdose, Acad Emerg Med 1998; 5:293–9. 2. Barton ED, Colwell CB, Wolfe T, et al. Efficacy of naloxone in treating opioid overdose in the prehospital setting. J Emerg Med 2005; 29:265–71. 3. Kerr D, Dietze P,

3. Hallucinogens - Disturbances of Perception, Mood and Thought

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Background: Hallucinogenic drugs (psychedelics), e.g. psilocybin-containing mushrooms and peyote cactus, have been used for several thousand years in religious, ritual and spiritual contexts to produce sensory distortions. The modern era started in 1943 with Albert Hofmann, who was unintentionally exposed to lysergic acid diethylamide (LSD) and experienced hallucinations. LSD was later marketed as the drug Delysid, used to treat several psychiatric disorders, including alcohol and opioid withdrawal. Development of new hallucinogenic drugs was frequently used to develop model psychoses. A large number of scientific papers on LSD were published in this period. From the early 1990s onwards, several reports of LSD use were favorable, but reversed from that point to the present. The term hallucination is derived from the Latin word alucinari, meaning 'to wander in mind or talk idily'. Objective: To provide a brief overview of the hallucinogens. Results: Hallucinogens are distinguished from other substances that produce hallucinations by inducing distortions of perception, mood and thought as a primary effect in the presence of an otherwise clear sensorium. Hallucinations are subjectively experienced sensations in the absence of an appropriate stimulus, which are regarded by the individual as real. Illusions on the other hand are distorted perceptions of objects based in reality, so called misinterpretation of a real external, sensory experience. Hallucinogens have been divided into different classes; frequently occurring ones are, for example, phenethylamines (amphetamine), mesylamines (ergolines), tryptamines (indolylamines), arylcycloalkylamines (arylhexamines), piperazines, cannabinoids, belladonna alkaloids and tropane alkaloids. In all these classification attempts, an additional miscellaneous group has always been needed, consisting of, for example, Salvia divinorum and kava kava. Differences in chemical structure these substances produce similar cognitive effects supporting the fact that most of these drugs are acting on several serotonergic receptors. The central reason for this is that serotonin is a neurotransmitter involved in a wide range of human behavior and brain functions. The use of recreational drugs remains common, particularly amongst those who frequent the night-time economy (e.g. pubs/bars, nightclubs, discotheques). In addition to the use of classical recreational drugs, such as MDMA (‘ecstasy’), cocaine, ketamine and amphetamines, over the last five to ten years there has been increasing use of ‘novel psychoactive substances’ (nps), sometimes known as ‘legal highs’.

4. Novel and Emerging Drugs: A Chemical Overview for the Toxicologist

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Objective: To give a simple overview of the chemistry of novel psychoactive substances that are currently being marketed on the Internet. The United Kingdom has set up a national database of substances called ‘ highs’. These are either single chemical substances that are related to existing drugs of abuse or herbal materials which contain psychoactive natural products that have been adulterated with psychoactive compounds. These materials are outside of the UK 1971 Misuse of Drugs Act and the synthetic drugs are probably produced as close structural drug-analogues specifically to fall outside of this legislation but to retain the psychoactive qualities of the parent compound. In April 2010 the UK government took the decision to control certain illegal highs related to the natural product cathine and these included methylone, methedrone. This was quickly followed by the control of the related cathinone synthetics, cathinone and cathine. All these are analogues of cathine, a plant-derived natural product from the popular stimulant Catha edulis (Celastraceae), which is used socially by various communities in the United Kingdom. Each novel substance is part of a drug category being similar to that of established drugs such as MDMA and cocaine. Although some individuals may probably produce as close structural drug-analogues specifically to fall outside of this legislation but to retain the psychoactive qualities of the parent compound.

5. Novel and Emerging Recreational Drugs: A Clinical Toxicology Perspective

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Background: The use of recreational drugs remains common, particularly amongst those who frequent the night-time economy (e.g. pubs/bars, nightclubs, discotheques). In addition to the use of classical recreational drugs, such as MDMA (‘ecstasy’), cocaine, ketamine and amphetamines, over the last five to ten years there has been increasing use of ‘novel psychoactive substances’ (sometimes known as ‘legal highs’).

Discussion: The market for novel drugs is rapidly changing and the majority of novel drugs that have become available over the last few years fall into the following classes or groups of drugs: piperazines, phenethylamines work as partial agonists of 5HT2A-receptors found in vast amounts in the serotonergic receptors, mainly as partial agonists on the differences in chemical structure these substances produce similar cognitive effects supporting the fact that most of these drugs are acting on several serotonergic receptors. The central reason for this is that serotonin is a neurotransmitter involved in a wide range of human behavior and brain functions. The use of recreational drugs remains common, particularly amongst those who frequent the night-time economy (e.g. pubs/bars, nightclubs, discotheques). In addition to the use of classical recreational drugs, such as MDMA (‘ecstasy’), cocaine, ketamine and amphetamines, over the last five to ten years there has been increasing use of ‘novel psychoactive substances’ (sometimes known as ‘legal highs’).
choose to purchase and use these novel substances, others will be exposed to them when they are mis-sold a novel substance instead of the classical drugs that they had intended to purchase from a dealer. The challenge for the toxicologist was related to the specialist interest in novel recreational drugs in addition to the identification of the compounds, is trying to determine the true pattern of acute toxicity associated with use of these substances. Firstly, the data above, the individual presenting with acute recreational drug toxicity may not be aware that they have taken a novel drug. Secondly, the healthcare professional treating the patient may not have been aware of the potential for the compounds to have resulted in acute toxicological reactions. Thirdly, routine toxicological screening of biological samples (blood, urine) are not usually performed on the majority of patients presenting with acute recreational drug toxicity. Not only are detailed analytical results often not available, but the use of these novel drugs is often not recorded in healthcare databases.

6. New Drugs of Abuse: Acute Intoxication by Smoking Herbal Products Containing Synthetic Cannabinoids

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Objective: "Herbal" mixtures are advertised via the internet as legal alternatives to cannabis in several European countries. Since 2008 various synthetic cannabinoids ('herbal cannabis', 'eaph', 'eaph', 'herbal cannabis', 'herbal cannabis' and/or hypokalaemia were reported. Furthermore, consumption of JWH-081, JWH-250 and JWH-122 was associated with shaking, acute psychosis, generalized seizures, myoclonus, muscle jerking, muscular pain and moderate hypokalaemia of 2.9 mmol/L. Conclusions: Symptoms were similar in most cases to severe cannabis intoxication, but the occurrence of seizures and pronounced hypokalaemia is alarming. Since the synthetic cannabinoids found here act as cannabimimetics and show much higher affinity to the CB1 receptor than Δ9-THC, they should be significantly more potent. Interaction effects cannot be excluded, since in the third of the presented cases at least 2 synthetic cannabinoids were detected. Development of dependence and tolerance was described after continued abuse of a product containing CP-47,497-C8 and JWH-018. Therefore especially cannabis naive users may be ruled out that these substances are 'legal highs' or alternatively "legal highs" or 'legal highs'.

Abstracts

199

8. Novel and Emerging Recreational Drugs: Routes of Supply and the Role of the Internet

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Background: The availability and patterns of use of the novel and emerging recreational drugs has been accompanied by changes in legislation to control these drugs, but also by changes in their availability and sources of supply. Discussion: In the latter part of the 20th century, the commonest drugs used recreationally included cocaine, ketamine and amphetamines including MDMA ('ecstasy'). Typically these drugs were sourced from street level drug dealers and they became controlled under relevant international and national legislation. In addition to these therapeutic drugs there has been an increase in the use and availability of novel and emerging recreational drugs (referred to as 'legal highs') over the last 5 to 10 years in Europe and many other areas of the world. This, together with the increase in the use of the Internet has changed not only the patterns of substances being used recreationally, but also the methods by which they are sourced and supplied. There have been a few studies that have assessed the sources of novel and emerging recreational drugs. These studies have shown that, although street level drug dealers are a source for some users, the Internet and street 'head shops' are increasingly important, particularly when the drugs first become available. These studies have also suggested that the sourcing of drugs is age dependent. For example, use of the Internet to source drugs is uncommon in those aged under 16-18 years, probably as they do not have banking/credit cards. Thus, the Internet is one of the main routes for younger users to access these drugs. There are many hundreds of websites that sell novel and emerging recreational drugs to users. A number of
9. The European Early Warning System: Responding to Novel and Emerging Recreational Drugs

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Objective: The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) provides the European Union and its Member States with ‘objective, reliable, timely and evidence-based information on all aspects of drug problems’ including drugs of abuse. The Centre collects data on various drug-related issues, such as drug use, drug treatment and drug policy. The data are used to inform the EMCDDA’s work on developing policies and strategies to address drug-related issues in Europe. The Centre also produces reports and publications on drug-related topics, including the European Early Warning System (EWS), which aims to improve information and data on drug trends at European level. The EWS monitors changes in drug use and drug-related problems, and highlights emerging trends and developments in the field of drug policy.

Conclusions: The EWS provides a valuable resource for policymakers, educators, and researchers who are interested in understanding drug trends and developments in Europe. The results of the EWS are used to inform the work of the EMCDDA and other organizations that are involved in drug policy and research. The EWS is an essential tool for anyone who is interested in understanding drug trends and developments in Europe.
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James DA1, Potts S 2, Thomas SHL 1, Chincholkar VM 1, 2-Diphenylmethylpiperidine (2-DPMp) and butahydroxybutyric acid (GHB) increased from 2.2% in 2007 to 3.1% in 2009. The ratio of mono- to poly-intoxications ranged from 3 hours to 1 week. Undesirable psychiatric symptoms and dizziness. Ketamine abusers often present with upper gastrointestinal symptoms, the commonest of which was epigastric pain. Pyloric negative gastritis was the most common histopathological finding. Abstinence from ketamine abuse could lead to relief of symptoms. A syndrome of cytostasis and contracted bladder could be associated with ketamine abuse. Secondary renal damage could occur in severe cases which might be irreversible, rendering patients dependent on dialysis. The duration and frequency of abuse apparently correlated with the severity of the symptoms and degree of damage to the urinary tract. The prevalence of drivewayed drivers among non-fatal driver casualties was on the increase and ketamine was most frequently detected as a cause of suicide. Conclusion: Drug abuse in young adults has become a very serious problem. Ketamine was most frequently taken throughout the whole study period. Poisonings by Brugmansia species were quite frequently registered in 2000 (19%) and moderate (6.2% versus 17.1%) and severe symptoms (3.2% versus 5.5%) and resulted more frequently in death (0.2% versus 0.4%). In total, 13 deaths (10 in mono-intoxications, 3 with amphetamine derivatives and 3 with inhalation of butane/propane) due to PSA were observed (all between 2000 and 2006). From 169 severe PSA, 39 were seen with GHB, 30 with PCP, 25 with ketamine and 14 with derivatives. Conclusions: The observed rise of PSA was probably caused by the simultaneous increase in all exposures registered by the PIC Erfurt from 2000 to 2009. While the abuse of other substances like benzodiazepines or GHB changed with time. Although no deaths due to PSA were observed in the last three years, the contribution of substance abuse to severe poisonings remained high in comparison to all exposures.

12. Clinical Features Associated with Recreational Use of ‘Ivy Wave’ Preparations Containing Desoxypipradrol

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Objective: In August 2010 the UK National Poisons Information Service received many enquiries relating to a recreational ‘legal high’ called ‘Ivy Wave’. Although previously reported to contain methylene-dioxyamphetamine (MDMA) and dimethylamphetamine 85.4%, followed by ecstasy (15.6%), methamphetamine (14.9%), cocaine (9.3%) and cannabis (9.0%). The most common symptoms of ketamine abuse were muscle toxicity. Analysis is not available for all cases, but available data indicate the availability of solid forms (up to 40 mg/capsule). A higher risk of voluntary intoxication with the capsule form (p < 0.001). Conclusion: Despite a higher risk of voluntary intoxication with the capsule form, there are no other differences between the two forms in this type of poisoning. As a result of this the French Health Authorities have decided to stop the prospective study concerning suicide attempts with methadone.

15. Risk Assessment of Moderate to Severe Alcohol Withdrawal - Predictors for Seizures and Delirium Tremens in the Course of Withdraw

Eyer F 1, Schuster T 2, Pfä recycling (8%), chest pain (4%), raised creatine kinase (62%) and aggression (each 4%). Tachycardia (73%), palpitations (58%), insomnia (46%), agitation (38%), paranoia (23%), anxiety (15%), restlessness and aggression (4%) Tachycardia (73%), palpitations (8%), chest pain (4%), raised creatine kinase (62%) and movement abnormalities (e.g. dystonia, hemiballismus and akathisia, 27%) were also observed. Marked livido reticularis was seen in one patient; this had not resolved completely after two days. Analysis of a sample of the ‘Ivy Wave’ product associated with the Edinburgh cases confirmed the presence of desoxypipradrol (2-diphenylmethylylpyrerpine, 2-DPMp) but not MDPV or other active compounds. Biological samples from these Edinburgh cases all contained desoxypipradrol. Conclusion: Ivy Wave exposure was associated with marked psychiatric and neurological effects, together with cardiovascular features and evidence of muscle injury. It is not available for sale in the UK, but when performed confirmed the presence of 2-DPMp. The reported psychiatric features resemble those described in Ireland after exposure to ‘whack’, also found to contain 2-DMPp with fluorotropacocaine. In response to this apparent increasing recreational use, an import ban for 2-DMPp was introduced in the UK on 4th November 2010. References: 1. Kavanaugh P, McNamara S, Angelov D, et al. The Characterization of ‘Legal’ Highs’ Available from Head Shops in Dublin. http://www.addictionireland.ie/fileupload/publications/08_Consensus_Report.pdf (accessed 15 November 2010). 2. Herbert JX, Daly F, Tracey JA. ‘Whacked!’ BMJ letters Published 15 July 2010 http://www.bmj.com/ content/341/bmj.c5564.full.reply BMJ el 238830 (ac- cessed 15 November 2010). Imports of Desoxypipradrol (2-DMPp, 2-Benzhydroxypropyridine, 2-Diphenylmethylylpyrerpine). http://www.homeoffice. gov.uk/publications/drugs/drug-licences/desoxypipradrol/ (accessed 15 November 2010).

13. Poisonings Due to Substance Abuse Reported to the Poisons Information Centre Erfurt Liebreau G, Prasa D, Hentschel H, Deters M. Poisons Information Centre, Erfurt, Germany

Objective: The aim of the study was to evaluate characteristics of all poisonings due to substance (ethanol excluded) abuse (PSA) reported to the Poisons Information Centre Erfurt (PIC Erfurt) in a one-year period. Methods: A retrospective analysis of PSA-related inquiries to the PIC Erfurt was undertaken for the year 2008. All commercial available (3.2% versus 5.5%) and resulted more frequently in death (0.2% versus 0.4%). In total, 13 deaths (10 in mono-intoxications, 3 with amphetamine derivatives and 3 with inhalation of butane/propane) due to PSA were observed (all between 2000 and 2006). From 169 severe PSA, 39 were seen with GHB, 30 with PCP, 25 with ketamine and 14 with derivatives. Conclusions: The observed rise of PSA was probably caused by the simultaneous increase in all exposures registered by the PIC Erfurt from 2000 to 2009. While the abuse of other substances like benzodiazepines or GHB changed with time. Although no deaths due to PSA were observed in the last three years, the contribution of substance abuse to severe poisonings remained high in comparison to all exposures.

14. Suicide Attempts with Methadone in France: A 2 Year National Survey Since the Availability of Capsules in 2008

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Background: Before 2008, methadone was used in France for opiate substitution was only available as syrup. In 2007 the French Health Authorities permitted the sale of capsules (up to 40 mg/capsule). A national survey was performed in order to evaluate the modification of poisonings (suicide attempts) induced by such a new pharmaceutical form. Methods: A prospective study was set up (April 15, 2008 [availability of capsules in France] - April 15, 2010) with the analysis of suicide attempts managed by the French Poison Centres. Results: Forty-five cases of suicide attempts with the 2 different forms of methadone were reviewed (syrup 90 patients, capsules 45 patients). Comparison shows that patients were provided to enable an easy clinical application. However, the Poisons Information Centre Erfurt continued to receive reports about such a new pharmaceutical form.

Clinical Toxicology vol. 49 no. 3 2011

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prevalence of structural brain lesions (OR 5.8; 95% CI: 2.6–12.9; p < 0.001). The c-index of this prediction model was 0.81 (95% CI: 0.74–0.87). Conclusion: In this large retrospective cohort, some easily determinable parameters at admission may be useful to predict a complicated course of alcohol withdrawal regarding occurrence of WS or DT. Using the provided nomograms, clinicians can estimate the percentage likelihood of patients developing either WS or DT after stopping their alcohol consumption during their course of withdrawal. Prevalence of structural brain lesions in the patient’s history does strongly warrant a careful observation of patients.

16. Usefulness of Animal Data for Poison Centres: Kupfer (HE) - Swiss Toxicological Information Centre, Zurich, Switzerland


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18. Respiratory Depression Related to Buprenorphine and Diazepam Combination in Rats: Study of the Pharmacodynamic Interaction

Vodovar D1, Alahadd H2, Risède P, Baud FJ1,2. Mégabran B1,2
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**Objective:** Buprenorphine (BUP) is responsible for ceiling respiratory effects; however, deaths due to asphyxia were attributed to BUP/benzodiazepine (BZD) co-ingestion. When experimentally administered alone, BUP did not induce deleterious respiratory effects. Our objective was to study the pharmacodynamic interaction between BUP and diazepam (DZP) on rat ventilation. **Methods:** In Sprague-Dawley rats, we studied the respiratory effects (using plethysmography and arterial gases) of DZP (20 mg/kg SC/BUP [30 mg/kg IP] association [4 groups: solvent (SV)/SV, DZP/BSV, SV/BUP, DZP/BUP; n = 8/group]. Reversion of DZP/BUP effects was analyzed following the pre-administration of specific opioid-receptor (naloxonazine [NLZ] [mu-antagonist]; naltrindole [delta-antagonist]; norbinaltorphimine [kappa-antagonist]) and GABA antagonists (flumazenil [FLZ] [GABA-A-antagonist]; scopolene [GABA-B-antagonist]) [2 groups for each antagonist: SV/DZP/BUP and antagonist/DZP/BUP; n = 6/group] at doses, time, and route of administration allowing complete receptor blockage. Comparisons were performed using ANOVA for repeated measurements followed by Bonferroni post-tests. **Results:** DZP/BUP combination resulted in a significant early-onset short-duration respiratory depression: PaCO₂ increase (p < 0.01) and minute volume decrease (VE, p < 0.001). The effect was additive (p < 0.05) and significant when regarded VE (p < 0.001). Like DZP/SVT group (p < 0.05), DZP/BUP group (p < 0.001) resulted in a significant tidal volume (VT) decrease in comparison to the SV/VT and SV/BUP groups (p < 0.001). VT decrease was compensated in the DZP/SVT group by an increase in the respiratory frequency (f), in comparison to the SV/VT group (p < 0.05), corre- sponding to a decreased expiratory time (TE) (p < 0.01), which was not observed in the DZP/BUP group. Like BUP alone, DZP/BUP combination resulted in a significant increase of the inspiratory time (TI, p < 0.001), compensated by a significant decrease in TE (p < 0.05); f was significantly decreased in the DZP/BUP group when compared to the DZP/BSV (p < 0.001) and SV/BUP groups (p < 0.05). However, although not significant, TE decrease was less marked with the association. Only NLZ and FLZ significantly reversed PaCO₂ (p < 0.05) and VE (p < 0.01), while FLZ significantly increased f (p < 0.05) and significantly decreased VT (p < 0.05). **Conclusion:** DZP/BUP combination is responsible for an early-onset and short-duration respiratory depression, related to the combination of a significant VT decrease, a significant f increase, and TE decrease; and GABA-A-receptors are the pharma- dynamic interaction between both molecules.


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**Objective:** Translational toxicology involves the move- ment of potential antidotes from basic mechanistic research at the bedside in animals to a marketed therapeutic. Because poisonings are infrequent, the clinical development of antidotes is fraught with complex multi-center trials and many tribulations involving technology transfer. Academic scientists often conduct basic mechanistic work with antidotes, but until recently have not been frequently involved in further drug development. The development of 4-methylpyrazole (4MP) as an antidote for toxic alcohol poisonings, particularly methanol and ethylene glycol (EG), acts as an interesting case study. **Methods:** Early mechanistic research established that both methanol and EG poisonings were mediated through alcohol dehydrogenase (ADH), to formaldehyde and glycolaldehyde respectively, then by formaldehyde and aldehyde dehydro- genases to formic acid, the proximate toxicant for methanol, or to glycolic acid, which produces the clinical symptoms. ADH activities can be further metabolized to oxalic acid, which is poorly soluble in the presence of calcium and leads to the formation of calcium oxalate crystals, which is the primary mechanism for the renal toxicity of EG. Antidotol treatment of these poisonings up to the 1970s included empirical doses of ethanol to compete for ADH, reducing toxic metabolite formation. However, several issues were brought up on its own problems, including the erratic kinetics and adverse effects of ethanol per se. **Results:** The story of 4MP began with its synthesis in the late 1960s, followed by studies of its activity in animals and its inactivity in human subjects. The goal at the time was to inhibit ADH in order to diminish the adverse metabolic effects of ethanol, thus advancing the therapy of alcoholism. The key mechanistic study for its therapeutic efficacy, reported in 1975, showed that 4MP could reverse and totally prevent methanol toxicity in animals by completely inhibiting the accumulation of formate. Translational work in the early 1980s defined the effective doses and plasma levels in the animal model, where 4MP levels above 9 μM were sufficient to prevent accumulation of formate. Further studies in the early 1980s showed that treating EG poisoning in animals, and in fact was superior to the use of ethanol. Although this basic research in animals was not immediately productive in treating methanol and EG poisoning in humans, translation of 4MP as a marketed drug in the US was slow for a number of reasons, including the difficulties inherent in conducting clinical toxicology research, a lack of interest to fund these types of studies by the National Institutes of Health and the lack of drug development by the pharmaceutical industry except for diseases that would make a lot of money. Although studies progressed slowly in the US through the 1980s, it was already being used with apparent success to treat several cases of EG poisoning in France. Thus, a major event in the development of 4MP in the US was passage of the Orphan Product Act (indirectly aiding its development in Europe also). This act led to the funding of Phase 1 studies that examined the safety and metabolism of 4MP and that eventually led to the liaisons with the drug company-sponsored clinical efficacy trials (the META study) in both methanol and EG poisoned-patients. Soon after completion of these trials, 4MP was approved by the FDA in the US, first for treatment of EG and a few years later for methanol, the latter at exactly 25 years after it was shown efficacious in animals. **Conclusion:** Development of 4MP in clinical toxicology, even as organ products, is not easy. Among the problems that are encountered include the need for a suitable drug source (Good Manufacturing Practice-certified for human use), an inability to attract seed money, difficulty with recruiting centers for the necessary multi-center trials, technology transfer issues, and the need for long of time and patience (30 years from discovery of 4MP activity until it reached the market as fomepizole). Advancement of fomepizole for the treatment of methanol and EG poisoning only became possible after research showing the specific role of metabolites in producing the toxicities. Beyond the strong mechanistic research, other aspects that helped fomepizole reach the market was its undeniable preclinical efficacy, an evident therapeutic need, investigator perseverance, and pure luck (such as the Orphan Product act, timing of scientific collaborations, and development of innovative drug companies).

20. Advances in Understanding Sodium Hydroxide Eye/Skin Penetration: In Vitro and Ex Vivo Studies

**Mathieu L¹, Burgfer F², Fosse C², Lat E³, Hall A⁴, Shreve C⁴, Moura R⁴, Sénéchal C⁴, Larose R⁴, Piché R⁴, Lavoie S⁴, Côté D⁵, Grenier A⁶, Adam P⁷, Gagné P⁸, Mongeau P⁸, Lavoie A², Caron F², Thibault M², ¹PREVOR Laboratory, Valmondois; ²BIO-EC Laboratory, Longjumeau, France; ³Toxicology Consulting and Medical Translating Services Inc., Laramie, Wyoming; ⁴Colorado School of Public Health, Denver, Colorado; ⁵Department of Dermatology, University of California San Francisco; ⁶Department of Medicine, San Francisco, California, US

**Objective:** Sodium hydroxide (NaOH) is a common corrosive substance, causing severe eye/skin burns. Knowledge is lacking about eye/skin penetration speed as shown by pH evolution and histological damage. In vitro and ex vivo experiments were performed and models were validated. Results: NaOH penetration was simulated through a semi-permeable cellophane membrane. NaOH (100 μL) was placed on the membrane surface and pH was measured in presence of a receiving compartment simulating the skin (9 g/L saline solution). Different NaOH concentrations were tested. Ex vivo: 41 human skin explants were exposed to 50% NaOH (30 μL); controls had no exposure. Histological sampling was done at various times from 1 minute to 24 hours. Alterations were evaluated by optical microscopy in stratum corneum, basal epidermis, and papillary and reticular dermis. Results: In vitro experiments were in accordance with the European classification, depending on NaOH concentration: 0.1 molar did not induce significant pH changes and did not produce signs of penetration. Penetration of NaOH concentrations >1 molar was <2 minutes. Penetration of 50% NaOH was complete in approximately 1 minute. Ex vivo: At 1 minute, stratum corneum alterations were seen; at 4 minutes, lesions reached the stratum corneum basal layer; at 30 minutes, the stratum corneum was totally altered. After 2 hours, no cells remained viable in the epidermis and papillary dermis. Conclusion: The in vitro model mimics the irritating corrosive danger of a chemical agent in accordance with European regulations. NaOH burning in the ex vivo model corresponds with the expected split-thickness splash clinical lesions. Direct effects of corrosion were rapid, lesions progressed quickly, and severe tissue destruction was observed. Similar ex vivo studies have been done with hydrofluoric acid (HF) and sulfuric acid (H₂SO₄). The ex vivo model will lend itself to graduated rating scale development and confirmed the need for urgent and effective decontamination to prevent or minimize the severity of concentrated NaOH chemical burns.

22. Assessment of QT Prolongation in High-Dose Droperidol Administration Using Continuous 12-Lead Holter Recording

**Calvo C¹, Dowses M¹, Elster GK², Shirani M², ¹Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle; ²School of Medical Practice, University of Newcastle, Newcastle, New South Wales, Australia

**Objective:** There are concerns about the safety of droperidol and international drug regulatory bodies have removed it or restricted its use because of concerns about Torsade de Pointes and QT prolongation. However, there is little evidence to support cardiac drug interactions. We performed an analysis of the state of knowledge in an attempt to accurately measure QT interval changes following the administration of droperidol using continuous 12-lead Holter recordings. **Methods:** We undertook a prospec- tive study of the implementation of intravenous droperidol for the sedation of emergency department patients with acute behavioural disturbance. In addition to obtaining standard 12-lead electrocardiograms (EGC) we used continuous 12-lead Holter recordings (Mortara Instrument, Inc.) to obtain serial QT measurements for 4 to 8 hours after droperidol administration. Patients with acute behavioural dis- turbance were given 10 μg/kg IV or an additional dose of 10 μg after 15 min, if required. A continuous 12-lead Holter recorder was attached when the patient was settled. Recordings were reviewed using Mortara software (E-scribe) to obtain high-resolution digital 12-lead ECGs which were then imported into another program E-scribe...
23. Poisoning by Serotonin Reuptake Inhibitor Antidepressants: A Ten Year Study
Savie P1, Gavrylo C2, Nisse P3, Garnier R4, Pulce C5, National Coordination Committee for Toxicovigilance, France

**Objective:** Selective serotonin reuptake inhibitor (SSRI) and serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants have largely replaced traditional tricyclic antidepressants (TCA). The severity of acute SSRI/SNRI poisoning is usually regarded as low. The aim of this study was to compare the severity of poisonings with different SSRI/SNRI antidepressants commercially available in France. **Methods:** All parasuicide poisonings involving SSRI/SNRI as a unique agent reported to the French poison and toxicovigilance centers (2000–2009) were analyzed. Age, gender and symptoms were collected. The "cardiac signs" were defined as the presence of arrhythmia, tachycardia (>100 bpm), bradycardia (<60 bpm) or cardiac conduction disorders, and "severity" by the presence of bradycardia, apnea, acute respiratory distress syndrome (ARDS), circulatory collapse or coma. **Results:** The risk of severe poisoning was low. A notification bias is likely, as severe and deadly cases are usually recorded to the poison and toxicovigilance centers of Angers (Dr Harry), Bordeaux (Dr Chasseur), Lille (Dr Mathieu-Nolf), Lyon (Dr Descotes), Marseille (Dr Hayek), Nancy (Dr Pravier), Paris (Dr Renault), Rennes (Prof Verger), Strasbourg (Dr Flesch) and Toulouse (Dr Cabot).

24. Alcohol-Based Hand Rubs Exposure: Retrospective Study from the French Poison and Toxicovigilance Centre
Savie P1, Richard P2, Lagarde L3, Gagnon V4, Garnier R5, Pulce C5, National Coordination Committee for Toxicovigilance, France

**Objective:** To limit the transmission of influenza A(H1N1) virus, the use of alcohol-based hand rubs (ABHR) by the general public was reinforced in 2009. The French Health Products Safety Agency requested the French Committee of Toxicovigilance to assess the risk of adverse effects related to these measures. **Methods:** All poisonings involving ABHR reported to the French poison and toxicovigilance centers (PTV) from January 1, 2000 to December 31, 2009 were analyzed. Each PTV completed a standardized collection sheet. Detailed analyses of symptomatic cases were performed. Among the 1,105 cases which occurred in 2009, 263 showed symptoms; 15 were excluded (ABHR poorly identified, absence of causality). The analysis therefore concerned 248 cases continuing ABHR at the time of the PTV. **Results:** The characteristics of poisoning cases according to the main circumstances were: home accident, 180 cases with: male 51%, median age 2.5 months–84 years, ingestion of less than 500 mg/kg by volume or oral exposure (41.5%); only symptoms of irritation except in 12 cases with: drunkenness, agitation, drowsiness, confusion, without severe signs; professional exposure, 25 cases (in a hospital or in laboratories). 20 cases with: ingestion: more than 500 mg/kg by volume; or oral exposure (97.5%); 1 case with: female 11 cases, median age 77 (12–86); ingestion 12 cases (storage outside of the original container, dementia, misuse or product used by mistake), absence of severe signs; suicide attempt, 11 cases (alcohol beverage associated in 5 cases) with: ingestion: 7 cases, median age 37 (15–80), coma 4 cases; alcohol consumption, 5 cases (in hospital 3 cases) with: ingestion: male 4 cases, median age 36 (30–38), absence of severe signs of alcoholic intoxication. **Conclusion:** This retrospective study has shown an increase of ABHR exposure cases since 2000, parallel to the use of these products. Symptoms depended primarily on circumstances (route of exposure, estimated dose). The risk of severe poisoning was low.

25. Acute Hemolysis and Hemolytic Uremic Syndrome following N-Acetylcysteine Overdose
Mulins ME, Vitokovitsky IV, Division of Emergency Medicine, Washington University School of Medicine, St Louis, Missouri, US

**Case report:** A 21-year-old woman (70 kg) took an overdose of acetylsalicylic acid (ASA) and ethanol (EtOH) after allegedly texting a suicide note to a friend. Her [ASA] was >200 mg/L with a serum [EtOH] of 163 mg/dL. The ED physician ordered intravenous (IV) N-acetylcysteine (NAC). A 21-year-old woman (70 kg) took an overdose of acetaminophen (APAP) and ethanol (EtOH) after allegedly texting a suicide note to a friend. Her [APAP] in the ED was 200 mg/L with a serum [EtOH] of 163 mg/dL. The ED physician ordered IV NAC. A 21-year-old woman (70 kg) took an overdose of acetaminophen (APAP) and ethanol (EtOH) after allegedly texting a suicide note to a friend. Her [APAP] in the ED was 200 mg/L with a serum [EtOH] of 163 mg/dL. The ED physician ordered IV NAC. A 21-year-old woman (70 kg) took an overdose of acetaminophen (APAP) and ethanol (EtOH) after allegedly texting a suicide note to a friend. Her [APAP] in the ED was 200 mg/L with a serum [EtOH] of 163 mg/dL. The ED physician ordered IV NAC.

26. A Case Report of Trimethoprim/Sulfamethoxazole Induced Hypoglycemia
Nichols SD1, Godara G2, Wiegand T3, 1Department of Pharmaceutical Care, Portland, 2Department of Medicine, Maine Medical Center, Portland, Maine, 3Department of Emergency Medicine, Strong Memorial Hospital, The University of Rochester Medical Center, Rochester, New York, US

**Objective:** Trimethoprim/sulfamethoxazole (TMP/SMX), a dihydrofolate reductase inhibitor antibiotic, is widely used for a variety of infections in the United States. Despite being an older medication, there are still misconceptions about its safety profile. A lesser known effect (ADR) of this medication is hypoglycemia, usually occurring 1.5 h - 10 days after therapy initiation. We present a case of severe symptomatic

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**Table 1. Parasuicidal cases with a unique antidepressant agent**

<table>
<thead>
<tr>
<th>INN</th>
<th>n</th>
<th>With symptoms</th>
<th>Cardiac signs (%)</th>
<th>Seizures (%)</th>
<th>Severity (%)</th>
<th>Deaths (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>citalopram</td>
<td>719</td>
<td>44.4</td>
<td>4.8</td>
<td>1.7</td>
<td>1.3</td>
<td>0.1</td>
</tr>
<tr>
<td>duloxetine</td>
<td>52</td>
<td>57.7</td>
<td>3.9</td>
<td></td>
<td>0</td>
<td>1.9</td>
</tr>
<tr>
<td>escitalopram</td>
<td>314</td>
<td>44.3</td>
<td>6.1</td>
<td>0.6</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>fluoxetine</td>
<td>859</td>
<td>40.3</td>
<td>2.0</td>
<td>0.2</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>fluvoxamine</td>
<td>75</td>
<td>4.0</td>
<td>0.0</td>
<td>0.2</td>
<td>2.7</td>
<td>0.6</td>
</tr>
<tr>
<td>mirtazapine</td>
<td>120</td>
<td>50.8</td>
<td>6.7</td>
<td>0.8</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>paroxetine</td>
<td>1,418</td>
<td>44.7</td>
<td>2.8</td>
<td>0.2</td>
<td>0.6</td>
<td>0.15</td>
</tr>
<tr>
<td>venlafaxine</td>
<td>964</td>
<td>49.3</td>
<td>11.2</td>
<td>3.2</td>
<td>2.7</td>
<td>0.6</td>
</tr>
<tr>
<td>sertraline</td>
<td>294</td>
<td>5.5</td>
<td>3.9</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5,265</td>
<td>45.6</td>
<td>4.9</td>
<td>1.1</td>
<td>1.2</td>
<td>0.15</td>
</tr>
</tbody>
</table>

**Table 1.**

*INN: International Non-proprietary Names; *amitriptyline, *citalopram.*
hypoglycemia after initiation of TMP/SMX. Case report: An 84-year-old female with history of anemia, hypothyroidism, hypertension and diabetes was admitted for hypoglycemia. In reviewing her medications she had had a recent dose increase in her glipizide with improved blood sugar control to 120–150 mg/dL (6.7–8.3 mmol/L). Two days after this dose increase the patient was started on TMP/SMX, one double-strength (DS) every 12 hours for lower extremity cellulitis. An additional two days later the patient was found minimally responsive with blood sugars of 21 mg/dL (1.2 mmol/L). After initial normalization of her glucose the patient had recurrent episodes. TMP/SMX was continued 12 hours after admission and subsequent blood sugars normalized without further treatment. Conclusion: Risk factors for TMP/SMX induced hypoglycemia include renal dysfunction, advanced age, diabetes mellitus, co-administration of a sulfonylurea, malnutrition, hepatic dysfunction, sepsis and higher medication dosage. The mechanism is secondary to a SMX-induced sulfonylurea-like effect in the pancreas. SMX directly binds to K-ATP channel in pancreatic islet β-cells thereby stimulating insulin release. SMX-induced hypoglycemia has been seen in non-diabetic and diabetic patients. Our patient had many risk factors for this drug toxicity: advanced age, malnutrition, decreased renal function and diabetes although the primary contributing factors were most likely the patient’s renal insufficiency and lack of dose-adjustment of TMP/SMX. We used the Naranjo adverse drug reaction probability scale to calculate the probability of ADR. The Naranjo score was 4 indicating “possible” ADR. The risk of this toxicity can be minimized by: adjusting dose for renal dysfunction, cautious use in elderly, AIDS and diabetic patients and careful monitoring of glucose when co-administered with a sulfonylurea.

27. Pediatric Battery Button Exposures Fernández MC 1, Roth B 2, Villarreal CL 1.

South Texas Poison Center, University of Texas Health Science Center, San Antonio, Texas; 2 University of Texas Southwestern, Dallas, Texas, US

Objective: Button batteries are often easily accessible in many households where younger children may encounter them and ingest them intentionally in their normal course of environmental exploration. In addition to their potential to cause airway or gastrointestinal obstruction, battery buttons may also carry the potential to cause serious direct tissue injury through electrical and caustic burns that may sometimes lead to tissue perforation and scarring. Because of the potential for serious injury, invasive removal procedures are sometimes performed, particularly for cases of retention or obstruction. We sought to examine the features of pediatric button battery ingestions in order to better characterize the potential clinical risks. Methods: We retrospectively analyzed data collected on a total of 1341 button battery ingestions related to battery button ingestions in children under 6 years in age reported to six poison centers in the USA during the ten-year period from the year 2000 through 2010. Results: Of the reported exposures identified, 52% occurred in males and 48% in females. Age at exposure was 2 years old (IQR: 1–4 years). The most common forms of ingestion were: 38% swallowing the battery, 30% with the hands and 32% placing it in the mouth. With respect to clinical outcomes, 92% were symptomatic (Table 1). Of those presenting with symptoms, 64% were evaluated in the ED, 12% were admitted for observation and 24% were discharged home. Hypothyroidism, hypertension, dysarthria, nausea, vomiting and diarrhea were the most common symptoms. Conclusion: Battery button ingestions are a common and potentially serious pediatric exposure. tabletop. A follow-up phone call and medical record review (when available) was attempted for each case. Results: There have been ten cases of toxicity directly reported to the NSW Poisons Information Centre in the period October 2008 to October 2010. Symptoms reported were gastrointestinal in nature with severe abdominal cramping, nausea, vomiting and diarrhoea. The complaints occurred in five of these patients. No sequelae have been identified. The other Australian Poisons Information Centres reported a further nine cases in 2008–2009. All presented with similar symptoms, with two of these cases observed in hospital. Most cases involved use of the product incorrectly diluted. Conclusion: Sodium chlorite has the risk of significant morbidity, particularly when used outside the ‘recommended dose’. This case series and unlawful therapeutic claims prompted the Australian Therapeutic Goods Administration to act in mid-2010 and a number of Australian websites have now ceased to operate and those remaining have had to remove all therapeutic claims. This resulted in hospitalisation of five of these patients. No sequelae have been identified. The other Australian Poisons Information Centres reported a further nine cases in 2008–2009. All presented with similar symptoms, with two of these cases observed in hospital. Most cases involved use of the product incorrectly diluted. Conclusion: Sodium chlorite has the risk of significant morbidity, particularly when used outside the ‘recommended dose’. This case series and unlawful therapeutic claims prompted the Australian Therapeutic Goods Administration to act in mid-2010 and a number of Australian websites have now ceased to operate and those remaining have had to remove all therapeutic claims. Further public protection is still required as it is being marketed in a common drop formulation (with no written therapeutic claims) and it lacks child-resistant packaging.

Clinical Toxicology vol. 49 no. 3 2011
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30. Prolonged Psychosis from Omega Conotoxin Toxicity
Obafemi AO, Roth B.
University of Texas Southwestern, Dallas, Texas, US

Background: Omega conotoxin is a peptide from the venom of the marine snail Conus geographus. It has an estimated analgesic effect of 100 to 1000 times that of morphine, thought to act by calcium channel blockage. By targeting these channels, it has a very low toxicity. We report a case of severe adverse drug reaction related to an idiosyncratic mechanism, characterized by low incidence but high mortality.¹⁻²

Objective: Toxic Epidermal Necrolysis (TEN) is a severe adverse drug reaction related to an idiosyncratic mechanism, characterized by low incidence but high mortality.¹⁻²

Case Report: A 74-year-old female was admitted to the Rehabilitation Unit (RRF) with a diagnosis of Left hemiparesis after surgery of the knee. She had been taking citalopram 20 mg/day was started at a Neurosurgery Institute. The patient was discharged 4 months after delivery with a diagnosis of Paroxetine toxicity. No drug levels were obtained. She had Apgar scores of 8, 8, and 10 at 1, 5, and 10 minutes respectively. Ten minutes after birth, the baby became hyperactive. Muscular rigidity attenuated with diazepam 0.8 mg/day. Electroencephalogram and routine laboratory tests were normal. Symptoms resolved over the following 14 days, when the infant was discharged. Citalopram and desmethylclozepam levels at 31 hours of age were 73 ng/mL and 26 ng/mL respectively (normal adult levels <200 ng/mL). Citalopram and desmethylclozepam levels decreased to 20 ng/mL and 8.5 ng/mL respectively at 98 hours of age, to 18 ng/mL and 6.5 ng/mL respectively at 146 and 218 hours of age to <10 ng/mL at 338 hours of age. Conclusion: Both drug levels and time-course of symptoms suggest that neonatal clozepam toxicity is the most probable diagnosis. The extended duration of symptoms may be related to the prolonged half-life of citalopram: in adults, citalopram’s half-life is about 33 to 37 hours, but in infants it may be much higher due to the poor glucuronidation capacity during the first months of life. Citalopram blood levels, when available, are very helpful for the definitive diagnosis, as they help distinguish between citalopram toxicity and withdrawal syndrome.

34. Neonatal Paroxetine Toxicity Related to Serum Concentrations Eleftheriou G1, Butera R2,3, Radice S4,5, Clementi E4,5, Cattaneo D1, Manzo L2, Farina ML3
1Poison Control Centre and Teratology Information Service, Ospedali Riuniti, Bergamo; 2Poison Control Centre, IRCCS Maugeri Foundation and University of Pavia; 3Neonatal Pathology Unit, Ospedali Riuniti, Bergamo; 4Laboratory for Mother and Child Health, IRCCS Fondazione degli Infermi, Milan; 5Laboratory of Analytical Toxicology, IRCCS Foundation Policlinico San Matteo, Pavia, Italy

Objective: Late gestational exposure to serotonin reuptake inhibitors (SSRI) with long half-lives, like citalopram, can be associated with a neonatal toxicity syndrome in immediate onset at birth or soon after birth and sometimes may be confounded with neonatal withdrawal syndrome. We report a case of neonatal toxicity in a newborn in utero exposure to citalopram. Case report: A 3860 g infant boy was born after an uneventful normal pregnancy, required no treatment. Neonatal paroxetine toxicity was suspected due to citalopram delivery during weeks gestation. The mother had a positive history of major depression and she had been taking citalopram 20 mg daily for several months. The day before delivery she had taken 8, 8, and 10 at 1, 5, and 10 minutes respectively. Ten minutes after birth, the baby became hyperactive. Muscular rigidity attenuated with diazepam 0.8 mg/day. Electroencephalogram and routine laboratory tests were normal. Symptoms resolved over the following 14 days, when the infant was discharged. Citalopram and desmethylclozepam levels at 31 hours of age were 73 ng/mL and 26 ng/mL respectively (normal adult levels <200 ng/mL). Citalopram and desmethylclozepam levels decreased to 20 ng/mL and 8.5 ng/mL respectively at 98 hours of age, to 18 ng/mL and 6.5 ng/mL respectively at 146 and 218 hours of age to <10 ng/mL at 338 hours of age. Conclusion: Both drug levels and time-course of symptoms suggest that neonatal clozepam toxicity is the most probable diagnosis. The extended duration of symptoms may be related to the prolonged half-life of citalopram: in adults, citalopram’s half-life is about 33 to 37 hours, but in infants it may be much higher due to the poor glucuronidation capacity during the first months of life. Citalopram blood levels, when available, are very helpful for the definitive diagnosis, as they help distinguish between citalopram toxicity and withdrawal syndrome.

35. Neonatal Paroxetine Toxicity
Eleftheriou G1, Butera R1,2, Radice S4,5, Clementi E4,5, Cattaneo D1, Manzo L2, Farina ML3
1Poison Control Centre and Teratology Information Service, Ospedali Riuniti, Bergamo; 2Poison Control Centre, IRCCS Fondazione Maugeri and University of Pavia; 3Clinical Pharmacology Unit, University Hospital Luigi Sacco, Milan, Italy

Objective: Neonatal withdrawal syndrome following in utero exposure to paroxetine is a well known condition but it is not always associated with serotonin toxicity, as both hyper- and hypoperinergic states can result in similar symptoms in newborns. We report a case of paroxetine toxicity in a newborn after in utero exposure to paroxetine and olanzapine. Case report: A 3060 g male was born at 38 weeks of gestation to a 32-year-old mother treated with paroxetine 20 mg and olanzapine 5 mg once daily. Apper scores were 8 at 30 minutes and 5 minutes. At birth the infant was cyanotic, failed to show respiratory effort and was ventilated for 30 seconds. After 1 hour, he was bradycardic, hypotonic and with opisthotonic posturing; at 6 hours, convulsions ensued and lorazepam bolus was administered. The patient was discharged 5 days after delivery with

31. Accidental Benzodiazepine Hydrochloride (Tantum Rosa) Poisoning Due to Ingestion of a Single Oral Dose
Petrides G, Obafemi AO, Weiner J1,2,3, Lukačić I4,5,2,3, Wibo W4,5,2,3, Corring M6,7,8,9, Wibo B10,11,2,3
1Poison Control Centre and National Toxicology Information Centre, IRCCS Maugeri Foundation and University of Pavia, Pavia, Italy

Objective: Benzodiazepine hydrochloride (BH) is a non-steroidal anti-inflammatory drug currently administered for relief of painful/inflammatory conditions. BH is usually available as a topical solution or sachets (mouthwash, dermal cream, vaginal irrigation), or as suppositories or pills. It is well absorbed from the gastrointestinal tract with an elimination half-life of 13 hours. Side-effects including neurological symptoms are reported during therapy, incorrect use and abuse. We report a Pavia Poison Centre (PPC) case series of side-effects due to erroneous ingestion of BH. Case series: From January 1st 2009 to October 2010, PPC registered 13 cases (approximately 1.2 cases/month) of BH wrong-use due to ingestion of Tantum Rosa® (BH 500 mg/sachet), normally intended for vaginal irrigation. In most cases the incidence was calculated as approximately 0.5 cases/month. Such an increase seemed to follow the drug re-classification as over-the-counter and the consequent confounding advertising campaign. All patients declared that they had misunderstood the indication and thought the drug had to be consumed orally. All of them denied recreational purposes. Seven patients ingested one sachet diluted in a glass of water; six ingested a variable quantity after direct dissolution (one sachet in 1000 millilitres of water). All patients were female (age 25–87 years) with a mean age of 56 years; four were admitted with reduced range of motion in the joints. Other signs and symptoms within the following month. Other signs and symptoms within the following month.

References: 1. Levin T, Petrides G, Weiner J, et al. Intractable delirium associated with ziconotide. The mechanism of the delirium is unknown. 2. Obafemi A, Roth B. Omega conotoxin is a peptide from the venom of the marine snail Conus geographus. It has an estimated analgesic effect of 100 to 1000 times that of morphine, thought to act by calcium channel blockage. By targeting these channels, it has a very low toxicity. We report a case of severe adverse drug reaction related to an idiosyncratic mechanism, characterized by low incidence but high mortality.¹⁻²

1. Levin T, Petrides G, Weiner J, et al. Intractable delirium associated with ziconotide. The mechanism of the delirium is unknown. 2. Obafemi A, Roth B. Omega conotoxin is a peptide from the venom of the marine snail Conus geographus. It has an estimated analgesic effect of 100 to 1000 times that of morphine, thought to act by calcium channel blockage. By targeting these channels, it has a very low toxicity. We report a case of severe adverse drug reaction related to an idiosyncratic mechanism, characterized by low incidence but high mortality.¹⁻²

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no symptoms and normal laboratory values. Cord blood levels of paroxetine and olanzapine at the time of delivery were 17.2 ng/mL and 4.6 ng/mL, respectively; neonatal serum concentrations at 24 h of age were 10.2 ng/mL and 4.5 ng/mL, respectively (adult therapeutic range, 10 to 100 ng/mL, and 10 to 50 ng/mL, respectively). Conclusion: There is an ongoing debate about whether the adverse effects seen in some neonates are due to a paroxetine withdrawal syndrome, or are due to toxicity. In our case, other causes explaining the observed clinical picture (e.g. peripartum asphyxia, CNS infections or metabolic disorders) were excluded. Neonatal serum concentrations of paroxetine in the typical adult therapeutic range and the onset of the symptoms immediately after birth render the hypothesis of serotoninergic syndrome more plausible. The time interval between birth and the first symptoms and the time-course of symptoms. Normal or low plasma concentrations of paroxetine may be associated with serotoninergic perinatal complications in susceptible infants when exposed to paroxetine during late pregnancy. A definitive differential diagnosis between paroxetine toxicity and withdrawal syndrome is possible only if neonatal paroxetine blood levels are available. References: 1. Koren G, Matsui D, Emsen A, et al. Is maternal use of selective serotonin reuptake inhibitors in the third trimester of pregnancy harmful to neonates? CMAJ 2005; 172:1457–9.

36. Brimonidine Eye Drops in Young Infants Hermanns-Clausen M 1, Koch I 1,2,3.

Objective: Brimonidine is a relatively selective alpha-2 adrenergic agonist. The drug lowers intraocular pressure via a reduction in aqueous humor production, and via an increase of uveoscleral outflow. Brimonidine is not structurally similar to clonidine. Small children are especially susceptible to adverse effects of the drug, but brimonidine is still used also for children <6 months old. There is controversy about the use of naloxone as an antidote for brimonidine. Case series: Case 1: A nine week old boy (5.6 kg) was given 1 drop of brimonidine 0.1 percent into the right eye in hospital because of a congenital glaucoma. Within 30 minutes he developed hypopnoea (8/min) with irregular breathing pattern, restlessness, decreased muscle tone, and a sunken fontanelle. On admission in the Children's hospital he was somnolent (GCS 7) and pale. Miosis was noted. The application of naloxone failed to improve the symptoms. A continuous infusion of naloxone was without positive effect. The patient recovered within 12 hours. Case 2: After topical treatment with 2 drops brimonidine 0.2% a two month old infant developed within 90 minutes irritability, moaning, somnolence and periodic breathing similar to Cheyne-Stokes respiration. The patient recovered within 12 hours. Naloxone was not applied. Conclusion: Topical brimonidine therapy for glaucoma was associated with severe systemic side effects in young infants after only one drop of a 0.1% brimonidine solution. Naloxone was only given in one patient but was without any effect. Especially in small infants therapy with brimonidine eye drops should be initiated only under medical care because of the potential for serious side effects such as those reported here.

37. Poisoning Caused by Fire Lighters: A Ten Year Analysis of French Poison Control Centres’ Data Flesch F 1, Savici P 2, Sinno-Tellier S 3, Manel J 1, Daoudi J 2,3,4.

1Poison Control Centre, Strasbourg; 2Toxicovigilance Centre, Grenoble; 3Poison Control Centre, Nancy; 4French Institute for Public Health Surveillance (InVS), Saint Maurice, France

Table 1. Summary of cases of poisoning caused by fire lighters

<table>
<thead>
<tr>
<th>Liquid</th>
<th>Solid</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 1394)</td>
<td>(n = 2743)</td>
</tr>
</tbody>
</table>

Cases between April and September (Summer months)

<table>
<thead>
<tr>
<th>Child</th>
<th>Adult</th>
<th>Sex ratio male/female</th>
<th>Place of ingestion</th>
<th>Symptoms</th>
<th>Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 4 years</td>
<td>&gt; 19 years</td>
<td></td>
<td>home</td>
<td>cough</td>
<td>90%</td>
</tr>
<tr>
<td>1,125 (80.7%)</td>
<td>140 (10.0%)</td>
<td>1.7</td>
<td>family garden</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>1,358 (68.9%)</td>
<td>2,716 (90.0%)</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingestion:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>736 (52.8%)</td>
<td>328 (12.0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Objective: At the meeting of the Limitation Working Group in July 2006, Germany reported on accidents with lamp oils and grill lighters. French Poison Control Centre (PCC) data concerning all hydrocarbon and liquid fire lighter (LFL) ingestions were analyzed and the report was transmitted to the Ministry of Health in 2007. The aim of this study was to compare exposure to LFL with exposure to solid fire lighters (SFL). Methods: SFL and LFL recorded in the French national database of substances and products were selected and cases of poisoning were collected in the French national database of toxic exposures (FNDTE) and catalysed. Results: Among the 1,240,792 cases recorded in the FNDTE between January 1999 and January 2009, 1394 cases were related to LFL (0.11%) and 2743 (0.22%) to SFL. Table 1 summarizes the main results. Discussion: Children were concerned in more than 80% of the exposures to fire lighters, which occurred almost exclusively at home. Between April and September exposures to LFL were more frequent (68% versus 44% for SFL), mainly in the family garden (8% versus 3% for SFL) where LFL are more often used to light barbecues. Considering the LFL exposures, symptoms were 4.4 more frequent and the number of the hospitalizations 4.5 times greater. Eighty-nine cases of aspiration pneumonia were observed with the LFL, 6 and none with the SFL. Conclusion: Although SFL exposures are twice as frequent as LFL exposures, no case of pneumonia was observed with the SFL. The French Commission for Consumer Safety recommended in July 2009 that SFL be used preferentially in fire-places, barbecues and stoves.

38. Too Much of a Good Thing: Dosing Errors with Infant Vitamin D3 Supplements Casey PB, Cassidy N, Tracey JA.

National Poisons Information Centre, Beaumont Hospital, Dublin, Ireland

Objective: Since May 2010 it has been the policy of the Irish Department of Health & Children that all infants, from birth to 12 months, be given a daily supplement of 5 micrograms (200 IU) of vitamin D3, to prevent deficiency. The impact of this policy on enquiries to the National Poisons Information Centre (NPIC) about infant vitamin D overdose was reviewed. Methods: All enquiries to the NPIC about vitamin D overdose in infants aged from birth to 12 months, from January 2005 to October 2010 inclusive, were extracted from the NPIC enquiries database. Data was collected on the age of the patients, circumstances of poisoning, vitamin D dose administered, and the treatment advised. Results: There were no enquiries before 2009. Since then the NPIC received enquiries related to infant vitamin D3 overdose in infants; 8 incidents occurred in the five months after the policy was introduced, compared to four in the preceding 17 months. Patient ages ranged from 6 weeks to 36 weeks (median 6 weeks). Nine of these 12 cases were due to therapeutic error, where a parent had administered an excessive dose on a single occasion (5 cases), repeatedly over periods of 2–10 days (3 cases), or chronically (for 6 weeks in 1 case). Two infants were given an acute overdose because of problems with the dropper or bottle dropper-top, and one case involved accidental ingestion by a 9-month old child. Four infants had received the European tolerable upper intake of 1000 IU vitamin D3 per day and 6 had exceeded it. Four infants who had received excessive doses repeatedly were referred to hospital to check for hypercalcaemia. Conclusion: These cases demonstrate that poisoning centres can rapidly detect the unintended consequences of public health measures. They suggest that parents have problems with the dosing instructions and method of administration for infant vitamin D3 supplements, leading to acute or chronic overdose. The dosing instructions should be revised to prevent further accidents occurring. References: 1. Herbert JX, Tracey JA. The toxicological impact of two public health protection measures in Ireland. J Toxicol Clin Toxicol 2003; 41:495.


1Department of Emergency Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA; 2Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, US

Objective: To describe hyponatremia in patients using levamisole-adulterated cocaine. Cocaine is often “cut” with other agents to expand the volume and quantity available. Levamisole-adulterated cocaine is increasingly prevalent, up to 70% containing levamisole. Levamisole, previously used as an immunomodulator, has been shown to cause hyponatremia.

We present three cases of unexplained hyponatremia associated with levamisole-adulterated cocaine use. Case series: A 26 year old man presented with chest pain after insufflating cocaine and drinking beer; serum sodium: 120 mEq/L. A 39 year old man with history of daily cocaine use presented with chest pain, myalgias and shortness of breath; serum sodium: 113 mEq/L. A 57 year old man with untreated non-insulin dependent diabetes presented with malaise; serum sodium: 124 mEq/L. Laboratory values and pertinent physical findings are presented in Table 1. Workup for possible etiologies including medications and thyroid disease,

Table 1. Laboratory values and physical findings for patients presenting with hyponatremia

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Serum Sodium (mEq/L)</th>
<th>Urine Osm (mOsm/L)</th>
<th>Urine Osm (mOsm/L)</th>
<th>Serum Osm (mOsm/L)</th>
<th>Physical examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>120</td>
<td>45</td>
<td>&lt;10</td>
<td>105</td>
<td>Tachycardia: 104 beats/min, Blood pressure: 183/97</td>
</tr>
<tr>
<td>39</td>
<td>113</td>
<td>135</td>
<td>&lt;10</td>
<td>234</td>
<td>Normal na, no dehydration, Heart rate: 70 beats/min</td>
</tr>
<tr>
<td>57</td>
<td>124</td>
<td>262</td>
<td>&lt;10</td>
<td>262</td>
<td>Tachycardia: 120 beats/min, Blood pressure 102/68</td>
</tr>
</tbody>
</table>

Abstracts 207

Clinical Toxicology Vol. 49 No. 3 2011

40. Delayed Acute Liver and Renal Failure After Deliberate Chloroform Inhalation Eyer F, Felgenhauer N, Murgan I, Zilker T. Toxicological Department, Technische Universität, Munich, Germany Objective: Since the use of chloroform has been widely banned, acute overdoses are rare. We report on a case of acute deliberate chloroform inhalation in which severe liver and renal failure developed after a latency of 50 hours. Case report: A 42-year-old depressive female was admitted after she had deliberately inhaled 250 mL of pure chloroform that was soaked in a towel. She woke spontaneously after 7 hours with nausea and dizziness. At admission, the patient was awake (GCS 15), vital signs were stable and physical examination was unremarkable besides a skin degradation lesion on the left shoulder. Blood gas analysis, ECG and laboratory were normal at admission and the following day. Quantitative toxicological analysis revealed a chloroform concentration in plasma of 3.9 mg/L and 0.2 mg/L some 10.5 hours and 32 hours after exposure, respectively. There were no signs of cardiotoxicity or cardiotoxicity. About 50 hours after exposure, the patient developed oliguric renal injury, hepatic failure (ALT 10943 U/L, AST 16936 U/L, bilirubin 5.5 mg/dL, LDH 10362 U/L) and severe coagulopathy (INR 3.5, fibrinogen 165 mg/dL). The patient was transferred to our ICU and received vitamin K, fresh frozen plasma and intravenous antecedent treatment with acetaminophen, as phenoxyethanol is highly reactive. The toxic metabolite of chloroform - depletes hepatocellular glutathione. Hepatotoxicity peaked about 60 hours after exposure and the patient developed anoxic tubulo-toxic renal failure with renal replacement therapy. Due to ensuing hepatic encephalopathy I and severe coagulopathy, we were prepared for high-urgency liver transplantation. However, both the clinical and clinical-chemical data improved with time: In the next 24 hours during symptomatic and antecedent treatment, thus liver transplantation could be circumvented. Intermittent haemodialysis was required for another week and the patient finally made a full recovery with restored renal and hepatic function 21 days after her suicidal attempt. Conclusion: Life-threatening sequelae after chloroform inhalation may occur with remarkable clinical latency. Beside antecedent therapy with acetaminophen, frequent re-evaluation of the clinical as well as the laboratory condition of the patient is thus required and patients are to be transferred early to specialized toxicological units where urgent liver transplantation is feasible.

41. Acetaminophen (Paracetamol) Exposures: A Profile of Life-Threatening and Fatal Outcomes Kenzelkop E1,2, Green JL2, Dart RC1,2
1Pittsburgh Poison Center, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania; 2Rocky Mountain Poison and Drug Center, Denver Health, Denver; 3University of Colorado, Denver, Colorado, US Objective: Exposures to acetaminophen (paracetamol) alone or in combination with other pharmaceuticals are the most common exposures managed by poison information centers in the United States. Most exposures described are those that are life-threatening or fatal. This project profiles the life-threatening and fatal acetaminophen exposures as reported to American poison information centers. Methods: A retrospective study of all acetaminophen exposures searched from 2000–2007 for all human exposures to acetaminophen alone or in combination with other pharmaceuticals. Descriptive statistics were used to characterize the data. Results: An initial total of 616,395 exposures to acetaminophen were identified. Life-threatening outcomes accounted for 13,016 (2.1%) exposures and there were 1,217 (0.2%) fatalities. Acetaminophen in combination with another drug was the most frequent type of exposure. Fifty-five percent of the fatalities compared to 92.5% of the life-threatening exposures. Intentional exposures for substance abuse purposes or self-harm were responsible for 87.2% of the fatal outcomes and 89.9% of life-threatening exposures. In fatal outcomes 36.4% had an acute-on-chronic or chronic (duration of exposure that exceeds 8 hours) component to the exposure; in life-threatening exposure patients 26.0% were acute-on-chronic or chronic exposures. Females accounted for 63.4% of the fatalities and 60.7% of life-threatening exposures. Less than 0.9% of fatal and life-threatening occurrences occurred in individuals less than 12 years of age; adults over 20 years of age accounted for 87.4% and 92.9%, of life-threatening and fatal outcomes. The majority of fatal and life-threatening exposures involved multiple pharmaceuticals, not just acetaminophen. Fatal and life-threatening exposures were more likely to occur in adults and fatalities were rare in children less than 12 years of age. Chronic exposure to acetaminophen was slightly more common among patients with fatal outcomes.

42. The Role of a Poisoning Centre in Pharmacovigilance Ulmeau CE, Petran ME, Ulmeau AI, Nivescu GV, Daepledic Poisoning Centre, Emergency Clinical Hospital for Children "Gregorie Alexandrescu", Bucharest, Romania Objective: To demonstrate the role and the means of pharmaco-vigilance, management and handling of data. Case report: Dentiocalmin, a product used as a local anesthetic, analgesic and anti-septic in dental practice contains lidocaine, menthol and phenol and does not produce toxic side effects. The first clinical case with Dentiocalmin poisoning was reported in 2005 in a 3 year old boy who died as a consequence of seizures and acute respiratory failure. Between 2005–2008 600 suspected cases were handled in the centre; 3 cases with an acute mortality were reported. The majority (94%) of patients recovered, but confirmed benzylecgonine and levamisole by gas chromatography-mass spectrometry for ADR information, Credits: From February to July 2010, 104 suspected drug reactions were reviewed, involving 124 agents. Sixty-eight patients were included in the study. Seventeen patients (25%) were admitted because of the ADR. Of all ADRs reported 23% were severe or life-threatening. Of the 56 patients contacted, four first found out about the ADR after they received the letter. 80% found the card useful, with 50% carrying the card in their wallet. 52% patients had shown or were intending to show the letter to their doctors. Only 2 (4%) had shown it to their pharmacist. 63% would like the letter sent directly to their doctor. The majority (94%) would recommend this system to other hospitals. Of the 49 discharge summaries available, the ADR was documented in 80% and 92% for general practitioners and other consumers. Current methods are being improved to further facilitate communication of ADR information between health care professionals and their patients in acute and ambulatory settings. References: 1. Zhang M, Holman CD, Preen DB, et al. Repeat adverse drug reactions causing hospitalization in older Australians: a population-based longitudinal study 1980–2003, Br J Clin Pharmacol 2007; 63:163–70. 2. Second National Report on Patient Safety: Improving Medication Safety: Australian Council Safety Quality Health Care, 2002. Available at: http://www.safety.nationalfoundation.org.au/publishing.nsf/Content/F0FD7424D1F2F5DDCA2571C6000854F5/$file/med_saf_rept.pdf [accessed 19 Nov 2010]

43. Adverse Drug Reactions - Is The Patient in the Loop? Graudins LV1, Hopper IK2, Fary RJ3, Lord J1
1Pharmacy Department, Alfred Health, Melbourne; 2Clinical Pharmacology, Alfred Health, Melbourne; 3Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia Objective: Adverse drug reactions are common, and may cause readmission. Our aim is to develop a best practice model based on published standards, incorporating our existing method of communication about adverse drug reactions (ADR) experienced during hospitalisation. Methods: Each ADR report is reviewed fortnightly by a multi-disciplinary ADR committee, which sends a letter and card detailing ADR advice to patients and/or their doctors. Patients were contacted by telephone to assess the value of this process. The hospital’s consumer group was consulted on the format of the letter. Patients’ discharge letters were assessed for ADR information. Results: From February to July 2010, 104 suspected drug reactions were reviewed, involving 124 agents. Sixty-eight patients were included in the study. Seventeen patients (25%) were admitted because of the ADR. Of all ADRs reported 23% were severe or life-threatening. Of the 56 patients contacted, four first found out about the ADR after they received the letter. 80% found the card useful, with 50% carrying the card in their wallet. 52% patients had shown or were intending to show the letter to their doctors. Only 2 (4%) had shown it to their pharmacist. 63% would like the letter sent directly to their doctor. The majority (94%) would recommend this system to other hospitals. Of the 49 discharge summaries available, the ADR was documented in 80% and 92% for general practitioners and other consumers. Current methods are being improved to further facilitate communication of ADR information between health care professionals and their patients in acute and ambulatory settings. References: 1. Zhang M, Holman CD, Preen DB, et al. Repeat adverse drug reactions causing hospitalization in older Australians: a population-based longitudinal study 1980–2003, Br J Clin Pharmacol 2007; 63:163–70. 2. Second National Report on Patient Safety: Improving Medication Safety: Australian Council Safety Quality Health Care, 2002. Available at: http://www.safety.nationalfoundation.org.au/publishing.nsf/Content/F0FD7424D1F2F5DDCA2571C6000854F5/$file/med_saf_rept.pdf [accessed 19 Nov 2010]
poison control centers during 2000 to 2009 were identified. Demographics, dose, co-ingestants, symp-
toms, and medical outcome were abstracted from each exposure case. Univariate analyses were used to identify significant potential risk factors. Results: A total of 506 cases of levetiracetam exposures were reported during the study period. Median age was 29.5 years (interquartile range: 8.0 years, 50.0%); females were 572 (45.8%) cases. In 478 of 506 cases (94.9%) cases resulted in major or moderate toxicity, respectively. Minor, minimal or no effects were reported in 388 (76.7%) cases. Multiple substance ingestions and suicidal intention were strongly asso-
ciated with major toxicity or death. There were no cases of major toxicity in children aged 6 years or less. In only one of 18 (5.6%) cases with major toxicity reported was exposure to levetiracetam only. Conclusion: Exposure to levetiracetam was safe in the vast majority of cases.

45. Aphasias: An Unusual Effect from Bupivacaine Regional Anesthesia
Morrissey RP 1,2,3, Moore SW 4, Borys DJ 1,

Objective: Focal neurological deficits have rarely been described as complications of intrathecal and retro-
bulbar local anesthetic administration. We describe a patient who developed expressive aphasia after regional bupivacaine infusion. Case report: A 48-year-old woman with chronic neck pain received 28 mg bupivacaine as a cervical median nerve branch block in preparation for radiofrequency neurotomy. Shortly after the infusion she complained of shortness of breath and the sensation of tongue swelling so the procedure was aborted and she was turned from prone to supine. She developed hypotension with systolic pressure below 80 mm Hg and a pulse oximetry value below 50% saturation. She was treated with 500 ml saline boluses and required an additional 500 mL intravenous saline bolus, and diphenhydramine intravenously for a suspected allergic reaction. She was then transported to the emergency department and manifested aphasia en route. On arrival, her vital signs had improved: blood pressure 147/28 mm Hg; pulse 108/min; respiratory rate 16/ min; oral temperature 36.4 degrees Celsius; oxygen saturation 99% on room air; and capillary glucose 93 mg/dL. The patient remained awake and alert at all times. The patient was admitted to the ICU for further workup. CT and MRI of the head demonstrated a left frontal infarction. She was weaned from mechanical ventilation over the course of the next four days and her aphasia slowly resolved. She was discharged home one week later with no residua.

Objective: Experience to date suggests that patients with Clostridium difficile infection (CDI) are at increased risk for another Clostridium difficile infection (CDI) and hence for quinolone prophylaxis. We describe a case of recurrent CDI and Clostridium difficile infection (CDI) with an unusual presentation. Case report: An 83-year-old Caucasian male with a history of chronic atrial fibrillation and recent stroke was admitted to the hospital with a 3 day history of fever, nausea and vomiting. Physical examination revealed tachycardia and hypotension. Laboratory findings included: white blood cells 22,000, AST 1500 U/L, ALT 750 U/L, creatinine 1.4 mg/dL, bilirubin 1.7 mg/dL, potassium 4.7 mg/dL, sodium 133 mEq/L, chloride 99 mEq/L, bicarbonate 14 mEq/L, calcium 8.3 mg/dL, creatine kinase 7800 U/L, myoglobin >1000 mg/dL, troponin I 10 ng/mL, troponin T 0.05 ng/mL, BUN 70 mg/dL, creatinine 1.4 mg/dL, lactate 10.7 mg/dL. An ECG demonstrated sinus tachycardia with normal QRS. The patient was treated with 500 mL saline bolus and vasopressin starting at 0.05 units/min and naloxone 10 mg drip and norepinephrine starting at 0.05 micrograms/min. Over the course of 30 minutes, the patient’s blood pressure increased to 114/80 mmHg and heart rate decreased to 90 beats/min. The patient was stabilized and transported to the ICU for further management.

46. Rhabdomyolysis and Hepatits in a Patient with Prostate Cancer Being Treated with High Dose Ketconazole and Concurrent Simvastatin Therapy
Jang DH 1,2,3, Hoffman RS 1,2,3,

Objective: HMG-CoA reductase inhibitors such as simvastatin are associated with rhabdomyolysis through a decrease in Coenzyme Q10 concentration. Ketconazole is a potent inhibitor of CYP3A4 which is responsible for the metabolism of simvastatin. We report a case of rhabdomyolysis and hepatitis related to concomitant simvastatin and ketconazole use.

Case report: A 77 year-old man with a history of hormone therapy to prostate cancer, hypertension, and dyslipidemia presented to the hospital with progressive weak-
ness over 2 weeks. He had obtained a prescription refill that included ketocenoazole 400 mg TID, hydrocor-
toine, and simvastatin three weeks prior. Approximately one week after the refill, he complained of generalized muscular weakness and dark colored urine. Physical examination revealed diffuse muscle weakness most pronounced proximally, a normal neurologic examination and no evidence of spinal cord compression. The aspartate transaminase and alanine aminotrans-
ferase were 1500 U/L and 750 U/L respectively (normal <48 and 40 U/L, respectively) and the creatine kinase was 6400 U/L. The urine was red, cloudy, and stained positively for myoglobin. He was admitted and received supportive care with discontinuation of simvastatin. The patient’s transami-

48. Electroconvulsive Therapy for Severe Refractory Neuroleptic Malignant Syndrome
Livshits Z1,2, Larocque A3, Schwartz DR1, Papadopoulos J3, Ying P1,2, Nelson LS1,2

Objective: To describe the management of severe refractory Neuroleptic Malignant Syndrome (NMS) likely due to rapid escalation of clozapine dosage. Case report: An 18 year-old man with bipolar disorder, presenting for 6 to 3 days of temperatures of 38.9–

39.4°C and confusion. One week prior to his hospitalization, the patient developed fever, sedated, and with a loss of appetite. He was admitted to the hospital for further evaluation. On admission, the patient was noted to be alert but morbidly obese, with a body mass index of 45.2 kg/m². He was afebrile, had a malar flush, and his blood pressure was 140/80 mmHg. His heart rate was 90 beats/min, respiratory rate was 20 breaths/min, and oxygen saturation was 98% on room air. His physical examination was significant for a soft, non-tender abdomen with normal bowel sounds. His neurologic examination was notable for a right-sided Babinski sign. Laboratory studies revealed a white blood cell count of 12,500 cells/µL, hemoglobin of 12.6 g/dL, and platelet count of 246,000/mm³. His creatinine was 0.8 mg/dL, blood urea nitrogen was 17 mg/dL, sodium was 139 mEq/L, potassium was 5.0 mEq/L, and bicarbonate was 26 mEq/L. His aspartate aminotransferase and alanine aminotransferase were 150 U/L and 75 U/L respectively. His liver function tests were significant for a total bilirubin of 1.2 mg/dL, direct bilirubin of 0.8 mg/dL, alkaline phosphatase of 573 U/L, and aspartate aminotransferase of 260 U/L. His serum creatine kinase was 10,500 U/L. His electrolytes were within normal limits. His chest X-ray was unremarkable. His electrocardiogram was significant for tachycardia with no other significant findings. A head CT scan was unremarkable.

47. Use of Naloxone and Vasopressin to Treat Prolonged Hypotension Following Vasartan
Jang DH1,2, Nelson LS1,2, Hoffman RS1,2

Objective: Angiotensin II receptor blockers (ARBs) such as valsartan are commonly used to treat hypertension. The Angiotensin II receptor blockers (ARBs) vasartan and irbesartan were 5 mg/kg, 10 mg/kg, and 20 mg/kg respectively. She was transferred to the emergency department 30 minutes after ingesting 25 tablets of valsartan (80 mg) that was her stepfather’s medication. Concurrently, approximately 12 days prior, he started clozapine and increased the dose from 100 mg to 125 mg the day prior to the ingestion. Other medications included: metformin, astatase, allopurinol. His initial vital signs were: BP 120/ 70 mmHg; HR 105/min; RR 18/min; T 38.9°C; SpO2 98%. Over the course of the next two days, the patient became progressively more hyperthermic (T 40.4°C), confused, and agitated. He had a whole body tremor without rigidity and/or hyperreflexia. The patient was nonverbal, somnolent, sedated, paralyzed, and actively cooled with an external cooling device. Within 48 hours of hospitalization, the patient displayed autonomic instabilty, with fluctuating blood pressures. When intermittently weaned off sedation, lead rigidity was present, and broncromisie was administered unsuccessfully for a diagnosis of NMS. He had a normal CT and MRI of the brain, lumbar puncture with negative viral and bacterial cultures, and an unremark-

Abstracts 209

Clinical Toxicology vol. 49 no. 3 2011

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therapeutic options, in a patient with recalcitrant NMS.


49. Status Epilepticus After Chronic Topical Use of Camphor Cream

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Introduction: Camphor is a pleasant smelling cyclic ketone of the hydro aromatic terpene group. The mechanism by which camphor produces toxicity is unknown. It is known that camphor commonly complain of mucous membrane irritation, nausea, vomiting, and abdominal pain. Generalized tonic-clonic convulsions are often the first sign of significant toxicity and can occur soon after ingestion. Central nervous system depression is commonly seen, such as headache, dizziness, confusion, agitation, anxiety, hallucinations, myoclonus, and hyporeflexia.

Objective: The aim of the study is to describe a unique case of generalized tonic-clonic convulsions, after one week of dermal applications of camphor cream in an elderly patient. Case report: A 66-year old female was brought to the University Clinic of Toxicology in Skopje, with status epilepticus, after several generalized tonic-clonic seizures. On arrival, the patient was somnolent, with severe headache, hypertensive (149/90 mm Hg), with partial amnesia, relaxed muscles, a small amount of blood in the mouth and a specific odour. Five minutes later, during standard examination, the patient developed another generalized tonic-clonic seizure. 10 mL diazepam was given intravenously to stabilize the patient, and a few minutes later the patient woke up. Heteroanamnesis taken from her husband showed that she had had another similar convulsion ten days previously, EEG, CT and MRI taken previously, did not show any abnormalities. The specific smell, repeated seizures and especially the dermal application of camphor cream, suggested poisoning with camphor. The toxicological examination showed a positive result.

After excluding the camphor cream, the patient did not manifest further seizures. Conclusion: Chronic topical use of camphor cream can result in serious toxicity. References: 1. Manoguerra AS, DeVane CL, Wax PM. Other biological specimens and CT scan were normal. Further blood samples for olanzapine showed 35 micrograms/L, on Day 15 and 7 micrograms/L on Day 43. Discussion: LAO is a pamoate salt of olanzapine, administered by intramuscular injection with an intended slow release of olanzapine during several weeks. Olanzapine plasma level was 7.1 micrograms/L at H4.4 with 5 mg by oral route and 5 fold more with 5 mg by intramuscular route. After LAO injection (150–300 mg) olanzapine levels went from 4.2 to 73.2 microgram/L, some cases up to 600 microgram/L, returning to therapeutic range within 24–72 hours; half-life was 30 days. Objective: To present a case of neuroleptic malignant syndrome in patients with schizophrenia treated with LAO. The toxicological examination showed a positive result. After excluding the camphor cream, the patient did not manifest further seizures. Conclusion: Chronic topical use of camphor cream can result in serious toxicity. References: 1. Manoguerra AS, DeVane CL, Wax PM. Other biological specimens and CT scan were normal. Further blood samples for olanzapine showed 35 micrograms/L, on Day 15 and 7 micrograms/L on Day 43. Discussion: LAO is a pamoate salt of olanzapine, administered by intramuscular injection with an intended slow release of olanzapine during several weeks. Olanzapine plasma level was 7.1 micrograms/L at H4.4 with 5 mg by oral route and 5 fold more with 5 mg by intramuscular route. After LAO injection (150–300 mg) olanzapine levels went from 4.2 to 73.2 microgram/L, some cases up to 600 microgram/L, returning to therapeutic range within 24–72 hours; half-life was 30 days. Objective: To present a case of neuroleptic malignant syndrome in patients with schizophrenia treated with LAO.


After excluding the camphor cream, the patient did not manifest further seizures. Conclusion: Chronic topical use of camphor cream can result in serious toxicity. References: 1. Manoguerra AS, DeVane CL, Wax PM.

51. Foveal Damage in 10 out of 30 Cases of Visual Disturbance in Poppers Users

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Objective: To update the regulation of poppers in France. The French Health Products Safety Agency requested the French Committee of Toxicovigilance for the analysis of cases reported to the French poison centres. The discovery of cases with visual disturbance during this 1st study justified a complementary inquiry targeted on this new risk. We report the results of this 2nd study. Methods: A retrospective study collected all cases of poppers inhalation exposure reported to the French Poison and Toxicovigilance centres between 1999 and May 2010. Cases resulting from direct ocular contact with poppers were excluded. Results: 829 cases of inhalational exposure to poppers were identified and 30 with VD appearing a few minutes to a few days after inhalation. The two main complaints were visual acuity deterioration and the presence of ‘‘floaters and phosphenes’’ (light or flashing spots, dazzling flashes, in 50% of the cases). Fundoscopy showed a yellow dot or stain in the fovea in 10 of the 11 investigated cases. High resolution optical coherence tomography showed damage of cones in the external segment of the fovea (9 cases). The involved poppers were butyl nitrile in 2 cases, isopropyl nitrile in 6, and n-propyl nitrile in 4; the nature of the remaining 18 poppers was unknown. Inhalation of poppers was associated with alcohol intake in 8 cases, with cocaine in 2, and a combination of the 2 in a further case. Conclusion: Three previous cases have been described. In the first reported: visual acuity deteriorating was associated with yellow dots in the fovea in 2 cases and with damage to the foveal external segment in one. Poppers users (and all other physicians) should be informed of this retinal toxicity, and the latter, of the investigations to be conducted.

52. An Unusual Cause of Intestinal Lymphoma in a Teenager

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Objective: To present a case of intestinal lymphoma in a previously healthy teenager, caused by an unusual environmental exposure. Case report: A 15-year-old male teenager presented with 5 days of diarrhea, cough, and one year of fatigue and weight loss. Past medical history was significant for asthma, anemia non-responsive to iron supplements, and facial acne. Physical examination was only remarkable for facial acne, with heavy make-up. Chest radiograph demonstrated severe, diffuse, coarse intestinal lymph nodularity bilaterally. High-resolution computed tomography of the chest demonstrated: bilateral patchy interstitial infiltrates, areas of ground glass opacity, honeycomb pattern, and subcortical lymphadenopathy. Flexible bronchoscopy demonstrated blood-tined secretions in the trachea. Laboratory evaluation demonstrated normocytic non-hemolytic (Coombs negative) anemia (Hgb: 9.4 mg/dL), and elevated acute phase reactants (ESR: 90 mm/hr, CRP: 138 mg/L). Viral and fungal serologies were negative. Bacterial, mycobacterial, and fungal cultures from blood and broncho-alveolar lavage fluid were negative. Flow cytometry with leukaemia/lymphoma panel was negative for malignancy. Urine chloride was normal, and the genetic testing for cystic fibrosis and alpha-1-antitrypsin deficiency were negative. Lupus panel, ANCA antibodies, and complement levels were normal. Tuberculin skin test was negative. Inquiry about environmental exposures revealed the use of more than twelve 30-gram containers of facial make-up within the past 2 years, to cover her facial acne. The active ingredients were: titanium dioxide and zinc oxide; the inactive ingredients included: silica, calcium silicate, soil minerals, mica, and iron oxides. Lung biopsy demonstrated sub-pleural foci of alveolar lipoproteinosis, with granular eosinophilic debris, prominent cholesterol clefts, and mild chronic interstitial inflammation, consistent with the clinical diagnosis of acute silica-proteinosis. This raised suspicion for pulmonary sarcoidosis, and the patient was started on systemic corticosteroids; she became afebrile, her symptoms resolved, and her hemoglobin normalized (12 g/dL) within four weeks of the initial presentation. Conclusion: To our knowledge, this is the first case of acute silicosis reported in a pediatric patient, and it should raise awareness about the risks associated with excessive use of powder make-up containing silica. References: 1. Greenberg DA, Klauber MS, Fernandes J. Silicosis: A Review. Dis Mon 2007; 53:394–416.

53. Carbon Monoxide Poisoning Caused by Waterpipe Smoking

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Objective: Waterpipe smoking is an old tradition in the Middle East that has been considered quite harmless. The use of waterpipes is spreading among young Europeans, but with a different pattern of smoking habits which was described. One case is described. Case report: A 25-year-old woman was admitted to the emergency department complaining of headache. Clinical examination showed post-confoundal confusion, misos, clonus of the arms; intravenous anzazen was given. BP was 110/70 mmHg, HR 95 bpm, SpO2 100%. ECG showed normal sinus rhythm with 171 beats/min. Trocure was 6.2 mmol/L and lactate 2.6 mmol/L. In the follow-up, he presented delirium, no verbal contact; awoke at 11h6; discharged at 13h0 with oral clozapam 10 mg daily dose. Olanzapine level (HPLC) on H16 was 36 mmol/L, valproate level 58 mmol/L, alcohol and other known drug abusers were absent.

Due to the heterogeneity and limited number of known cases, a prospective study should be performed to better characterize this adverse effect and identify its risk factors.
woked up. The patient presented at the emergency room 1.5 hours after smoking. She was then confused, answered questions with delay, and complained of headache. An arterial carboxyhaemoglobin (a-COHB) sample, taken 40 minutes after smoking, showed 21%. She was treated with 100% normobaric oxygen and the a-COHB had dropped to 1.8% at 8 hours post smoking. At follow-up she displayed no sequelae. 2, A 27 year old man was admitted to a hospital in a habit of smoking a waterpipe on his balcony. This time he was smoking inside in a friend's apartment. After the session he felt dizzy and cold, and soon thereafter he became unconscious. During transportation to hospital he awoke. At the emergency room he complained of headache and was unable to lift his arms and legs from the stretcher. The immediately measured a-COHB level was 32%. The patient was treated with intravenous oxygen and was discharged two days later in good condition. Conclusion: Waterpipe smoking involves a risk of severe carbon monoxide poisoning. Several explanatory factors contribute: a higher CO content per smoke volume compared to cigarettes due to incomplete combustion, a much larger volume of each waterpipe inhalation because of a low and comfortable smoke temperature, and probably, a more intense way of smoking among young European. References: 1. Lim BL, Lim GH, Seow E. Case of carbon monoxide poisoning after smoking shisha. Int J Emerg Med 2009; 2:121–2. 2. Patil Y, Patil RH, Ghodke GH. Carbon monoxide poisoning associated with narghile use. Emerg Med J 2010; 27:406.

54. Cerebral Venous Thrombosis Following Exogenous Thyroxine Consumption

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Objective: Cerebral venous thrombosis (CVT) is a rare complication of primary hyperthyroidism. We report the first case, to our knowledge, of CVT following exogenous thyroxine poisoning. Case report: A 27 year-old man presented to the Emergency Department (ED) immediately following a generalization tonic-clonic convulsion. He later reported that for approximately four weeks he was taking Veterinary thyroxine 0.8 mg tabs purchased on the Internet up to three times daily for weight loss. He discontinued their use five days prior to presentation because of headache. Vital signs were: BP 154/77; pulse 169/min; respirations 35/min; temperature 37°C. O2Sat, 82–85%. An AGB on supplemental O2 revealed: pH 7.46, PCO2 23 mmHg, PO2 181 mmHg. The patient was intubated for airway protection. Co-oximeter analysis of the arterial blood specimen was empirically treated for methemoglobin with methylene blue (0.7 mg/kg) intravenously. No improvement in his cyanois was noted. Fourteen hours later, on arrival to the tertiary care center, he was still cyanotic and received methylene blue 2 mg/kg intravenously with only mild improvement in his cyanois. Two hours later, cyanois recurred and three oximeters revealed a methemoglobin level of 13%. He remained cyanotic with continually elevated methemoglobin levels that slowly trended down reaching 10% on day four, 5% on day five, and 2% on day six. His ICU course was complicated by hemolysis, pneumonia, and renal failure. His glucose-6-phosphate dehydrogenase (G6PD) deficiency screening and family history were negative for G6PD deficiency. Following three weeks of supportive measures, the patient was discharged home. The material safety data sheet for this Octane Booster listed only "petroleum distillate NOS" under hazardous components, failing to identify an agent with oxidizing potential. Review of the literature regarding refractory methemoglobinemia highlights dapsone and aniline as common causes. In one proposed mechanism, aniline’s metabolite, phenylhydroxylamine (PHA), rapidly metabolizes to nitrosobenzene, oxidizing a molecule of hemoglobin to methemoglobin. Nitrosobenzene is then reduced back to PHA with the electron donor NADPH and NADPH oxidase. Dapsone also requires NADPH and is thereby competitively inhibited by aniline metabolism. The company was contacted and the chemical mixer reported that aniline was used as a stabilizer in this product. Conclusion: Aniline-induced methemoglobinemia may be prolonged and may not completely resolve with one dose of methylene blue.

55. “Octane Booster” Ingestion Causing Refractory Methemoglobinemia

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Objective: Methemoglobinemia generally resolves rapidly with methylene blue therapy. We report refractory methemoglobinemia following ingestion of an automotive fuel additive. Case report: A 26 year-old man presented to a rural hospital with cyanois and altered mental status after ingesting 250 mL of Klotz Octane Booster. Vital signs were: pulse, 140/min; respirations, 45/min; BP, 130/50 mmHg; and room air O2Sat, 82–85%. An AGB on supplemental O2 revealed: pH 7.46, PCO2 23 mmHg, PO2 181 mmHg. The patient was intubated for airway protection. Co-oximeter analysis of the arterial blood specimen was empirically treated for methemoglobin with methylene blue (0.7 mg/kg) intravenously. No improvement in his cyanois was noted. Fourteen hours later, on arrival to the tertiary care center, he was still cyanotic and received methylene blue 2 mg/kg intravenously with only mild improvement in his cyanois. Two hours later, cyanois recurred and three oximeters revealed a methemoglobin level of 13%. He remained cyanotic with continually elevated methemoglobin levels that slowly trended down reaching 10% on day four, 5% on day five, and 2% on day six. His ICU course was complicated by hemolysis, pneumonia, and renal failure. His glucose-6-phosphate dehydrogenase (G6PD) deficiency screening and family history were negative for G6PD deficiency. Following three weeks of supportive measures, the patient was discharged home. The material safety data sheet for this Octane Booster list only "petroleum distillate NOS" under hazardous components, failing to identify an agent with oxidizing potential. Review of the literature regarding refractory methemoglobinemia highlights dapsone and aniline as common causes. In one proposed mechanism, aniline’s metabolite, phenylhydroxylamine (PHA), rapidly metabolizes to nitrosobenzene, oxidizing a molecule of hemoglobin to methemoglobin. Nitrosobenzene is then reduced back to PHA with the electron donor NADPH and NADPH oxidase. Dapsone also requires NADPH and is thereby competitively inhibited by aniline metabolism. The company was contacted and the chemical mixer reported that aniline was used as a stabilizer in this product. Conclusion: Aniline-induced methemoglobinemia may be prolonged and may not completely resolve with one dose of methylene blue.

56. Eight Orelanilin Mushroom Intoxications with Acute Kidney Injury after the Ingestion of Curtinellus orellanus

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Objective: Mushroom intoxications can be categorised into 13 specific syndromes.1 The gastrointestinal syndrome, the amatoxin syndrome and the phalloidin syndrome are the most frequent syndromes. The other syndromes concern clinically relevant mycotoxins and moulds.2 Severe orelanilin intoxication is very infrequent and there exist only a few case series describing this rare entity.3 Hence a case series of severe orelanilin intoxications is presented. Methods: In this retrospective analysis the clinical course and long-term outcome of eight patients with orelanilin syndrome intoxication was evaluated. Results: All patients (four men, 44–74 years of age) were members of a German tourist group who vacationed in Norway. Hunting mushrooms, they all mistook Curtinellus orellanus for the edible mushroom, the chanterelle. They all developed gastrointestinal symptoms, headache and myalgia. They went to see a physician (7 ± 1 days later. All developed acute renal insufficiency (serum creatinine 27–14 mg/dL). Five patients required diuretics and required renal dialysis. In addition, 6 patients were treated with steroids and N-acetylcysteine. The duration of their hospital stay was from 7 to 33 days. At present, none of the patients were treated by chronic hemodialysis. In the other 5 patients renal function has not fully recovered resulting in advanced chronic kidney disease. Treatment with steroids and N-acetylcysteine did not affect outcome. Conclusion: Orelanilin is a nephrotoxic substance that can cause severe renal tubular damage. Due to the infrequency of this syndrome and the long latency between the ingestion of the mushrooms and the emergence of symptoms the syndrome is difficult to diagnose. Therapy is symptomatic and depends on the severity of the acute kidney injury. Steroids and N-acetylcysteine are of questionable value in chronic kidney disease is a frequent long term outcome. There is no specific antidote. References: 1. Flammer R, Herget-Rosenthal S, Borys DJ. Mushroom poisoning – A review. In: Flammer R, Borys DJ, editors. Mushroom Poisoning – A Review. 1. ed. Basle, Switzerland: Schwabe Verlag, 2003. 2. Annual Reports of GIZ-Nord Poisons Centre, 1996–2007.

57. Survival Despite Lethal Level of Methemoglobin

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Background: Many substances are known to cause methemoglobinemia including foods, drugs, and ni- trates. The concentration of methemoglobin usually correlates with severity of symptoms. Patients are rarely symptomatic with methemoglobin fractions below 15%, whereas patients with fractions greater than 25% are generally reported to be symptomatic. Methemoglobin is 70%–80%. Case report: A 38 year old male and a 42 year old male, both previously healthy, presented to the emergency department 2 hours after ingesting mushrooms which they suspected to be bluish-gray as well. He was evaluated and placed on a ventilator. Repeat methemoglobin level had risen to 86%. He was given a second dose of methylene blue. Nine hours after ingestion, his vital signs had improved and his methemo- globin level dropped to 29%. The next day, he was extubated and had a methemoglobin level of 0.8%. He was discharged from the hospital after 4 days. On arrival to the ED, the 42 year old male vomited and appeared to be bluish-gray as well. He was evaluated and found to have a methemoglobin level of 19%. Following a dose of methylene blue, he was admitted to the hospital overnight. His methemoglobin level was 70%–80% before being discharged. Later, a home visit revealed the men had purchased a meat seasoning and had used 1 teaspoon per pound of pork. The label was written in Chinese lettering, and it was determined to be potassium nitrate (saltpeter). Conclusion: Consumption of potas- sium nitrate “meat seasoning” provides enough oxidant stress to cause potentially lethal levels of methemoglobinemia. Reports of multiple fatalities have been successfully treated with rapid supportive care and methylene blue therapy. Poison control centers should be aware

Clinical Toxicology vol. 49 no. 3 2011

Abstracts 211
that food additives or seasonings may contain potassium nitrate or other nitrates.

58. Fatal Suicidal Poisoning by Injection of Vipera lebetina Snake Venom

Background: Snake bites are quite common in Azerbaijan. The most frequent are Vipera lebetina bites. More than 100 cases are registered annually. However no medical reports about intravenous injection of Vipera lebetina poison exist in the literature. We report a case of fatal suicidal envenomation by Vipera lebetina snake venom. Case report: A 54 year old man with a past medical history of attempted suicidal poisoning with barbiturates occurring 2 months previously was admitted to the emergency department of the toxicological center 3 hours after deliberate intravenous injection of Vipera lebetina snake venom. On arrival the patient was comatose. His vital signs were BP 70/30 mmHg, HR 128 beats/min, RR 28/min, Temp 35.7°C, O₂ saturation 93% on room air. Initial laboratory tests showed leukocytosis - 20,700/mm³ and mild anemia (hemoglobin level 6.8 g/dL). Treatment was started with intravenous fluid infusion, corticosteroids and vasopressors. The patient received 3 doses of vepirine polyvalent antivenin. One hour later the patient presented severe gastrointestinal bleeding (recent coffee-ground vomiting and melena). Bleeding from the injection sites and development of vast hematomas were also observed. Blood tests showed thrombocytopenia (30,000/mm³), severe hypocalcemia (5 mg/dL), prothrombin time prolonged to 17 seconds, an activated partial thromboplastin time prolonged to 66 seconds, fibrin split products were 45 mg/mL. Due to gastrointestinal bleeding and coagulopathy the patient received a transfusion of 2 units of red blood cells and 2 units of fresh frozen plasma. Despite aggressive supportive treatment the patient died 3.5 hours after admission. The patient’s past medical history revealed no severe systemic disease. At postmortem examination, the stomach contained bile and a large amount of necrotic material. The alimentary tract showed fresh bleeding from numerous ulcers, which were also observed macroscopically. The postmortem examination revealed no significant cardiovascular abnormalities. The cause of death was concluded to be acute poisoning by Vipera lebetina snake venom.

59. Overdose of Methimazole

Objective: The acute toxicity of organic thiourea antithyroid drugs is considered to be low. There are few reports about adverse effects due to therapeutic use, human poisoning cases were not known up to now. Firstly, the aim of the study was to evaluate cases of acute overdose. Secondly, we present the lethal course of a chronic overdose. Case series: 69 cases of accidental and intentional overdose (27 single, 42 multiple drug ingestions) with methimazole were reported to the PIC Erfurt from January 1994 to October 2010. Children and adults were involved in 24 and 45 cases, respectively. Female gender of patients predominated (40 f, 20 m, 9 not registered). Children and adults ingested 2.5 to 5000 mg (0.2 to 85 mg/kg) and 2.5 to 12,500 mg (0.04 to 179 mg/kg), respectively. All patients with acute overdose were asymptomatic or had nonspecific symptoms. Only one case with gastrointestinal complaints was reported after ingestion of 60 mg/d for 5 days. Case report: An 84-year-old woman with diabetes mellitus was treated with methimazole 5 mg/d for a long period. Despite chronic renal failure, the daily dose was not changed. She complained of gastrointestinal discomfort for weeks before and was admitted in a generally grave condition. Clinical features and laboratory findings showed severe hypothyroidism. In addition, marked chronic heart failure was diagnosed. High doses of thyroid hormones were administered in addition to symptomatic treatment. The patient developed severe myxedema coma as a consequence of decompensated hypothyroidism. She died two days after admission.

Conclusion: No specific poisoning symptoms are expected after a single overdose of methimazole. It is unknown whether hormonal status will be changed when a very high dose is ingested. In such cases, we recommend control of thyroid-stimulating hormone and thyroid hormones a few days after ingestion. In chronic overdose, hormone synthesis may be depressed dramatically resulting in a life-threatening hypothyroidism. Reference: 1. Bartalena L, Bogazzi F, Martino E. Adverse effects of thyroid hormone preparations and antithyroid drugs. Satt F 1996; 15:53–63.

60. Difficulties in Therapy of Poisonings by Carbamates

Objective: To report a case of coma blisters, with hemorrhage and blisters from the vessels walls but was negative for IgM, IgA, C3 and C1q. The patient remained on mechanical ventilation for 12 days and was discharged on day 21, with no sequelae. At discharge, she “confirmed” the ingestion of an overdose of all her current medications. Conclusion: Blister formation and eczematous skin necrosis is a rare cutaneous manifestation associated with impaired coagulation, more frequently reported after overdoses of CNS depressants, particularly phenobarbital. Bullous lesions have been noted in 6.5% of a series of patients who suffering barbiturate poisoning, within as early as 4 h post-ingestion. The pathogenesis of coma blisters remains unclear, and their distribution cannot be explained simply by pressure effects in comatose patients. Hypeoxia, hypotension, direct local toxic effects and autonomic instabilities in the skin vessels could contribute to blister formation and skin gland necrosis. The positive results obtained here and in other studies by direct immunofluorescence indicate an immune-mediated pathogenic mechanism cannot be excluded.

61. Coma Blisters in Confirmed Phenobarbital Poisoning Associated With Other Central Nervous System Depressants: An Immune-Mediated Response?

Case report: A 54 year old woman with diabetes mellitus was treated with phenobarbital 60 mg/d over 5 days. The past medical history of attempted suicidal poisoning with barbiturates occurring 2 months previously was admitted to the emergency department of the toxicological center 3 hours after deliberate intravenous injection of Vipera lebetina snake venom. The history of phenobarbital ingestion was confirmed by the patient during admission, no previous history of phenobarbital ingestion could be verified. The patient was admitted to the emergency department of the toxicological center 3 hours after deliberate intravenous injection of Vipera lebetina snake venom. On arrival the patient was comatose. His vital signs were BP 70/30 mmHg, HR 128 beats/min, RR 28/min, Temp 35.7°C, O₂ saturation 93% on room air. Initial laboratory tests showed leukocytosis - 20,700/mm³ and mild anemia (hemoglobin level 6.8 g/dL). Treatment was started with intravenous fluid infusion, corticosteroids and vasopressors. The patient received 3 doses of vepirine polyvalent antivenin. One hour later the patient presented severe gastrointestinal bleeding (recent coffee-ground vomiting and melena). Bleeding from the injection sites and development of vast hematomas were also observed. Blood tests showed thrombocytopenia (30,000/mm³), severe hypocalcemia (5 mg/dL), prothrombin time prolonged to 17 seconds, an activated partial thromboplastin time prolonged to 66 seconds, fibrin split products were 45 mg/mL. Due to gastrointestinal bleeding and coagulopathy the patient received a transfusion of 2 units of red blood cells and 2 units of fresh frozen plasma. Despite aggressive supportive treatment the patient died 3.5 hours after admission. The patient’s past medical history revealed no severe systemic disease. At postmortem examination, the stomach contained bile and a large amount of necrotic material. The alimentary tract showed fresh bleeding from numerous ulcers, which were also observed macroscopically. The cause of death was concluded to be acute poisoning by Vipera lebetina snake venom.

Case report: To report a case of coma blisters, with hemorrhage and blisters from the vessels walls but was negative for IgM, IgA, C3 and C1q. The patient remained on mechanical ventilation for 12 days and was discharged on day 21, with no sequelae. At discharge, she “confirmed” the ingestion of an overdose of all her current medications. Conclusion: Blister formation and eczematous skin necrosis is a rare cutaneous manifestation associated with impaired coagulation, more frequently reported after overdoses of CNS depressants, particularly phenobarbital. Bullous lesions have been noted in 6.5% of a series of patients who suffering barbiturate poisoning, within as early as 4 h post-ingestion. The pathogenesis of coma blisters remains unclear, and their distribution cannot be explained simply by pressure effects in comatose patients. Hypeoxia, hypotension, direct local toxic effects and autonomic instabilities in the skin vessels could contribute to blister formation and skin gland necrosis. The positive results obtained here and in other studies by direct immunofluorescence indicate an immune-mediated pathogenic mechanism cannot be excluded.

62. Fake Marijuana Causing Real Problems in Texas

Objective: The use of synthetic cannabinoids in herbal-based products is gaining popularity as a method through which users can enjoy drug effects while avoiding drug test detection and legal complications of cannabis. There are several synthetic cannabinoids, such as JWH-018 and JWH-073, analogues of Δ9-tetrahydrocannabinol, the main psychoactive component in marijuana. Research and legal classifications of these substances have been under review by U.S. government organizations, including the DEA, FDA, CDC, and local and state governments. There has been a significant increase in the reported use of marijuana hallucinations by synthetic cannabinoids, as reported by the Texas poison centers during the ten-month period of January-October 2010. Methods: We retrospectively analyzed 328 human exposures related to marijuana hallucinations reported to Texas poison centers during the ten-month period of January-October 2010. Results: Of the identified cases, 75% (N = 246) of reported exposures occurred in males, 48% (N = 158) were considered to be due to abuse or misuse, 74% (N = 242) were exposed at their own residence, of which 80% were exposed through
inhalation. Of all marijuana homolog exposures, 75% (N = 246) of exposures were managed at healthcare facilities. When examining the geographic distribution of calls, out of all 254 counties in the State of Texas, 73 counties had received one reported exposure. Two of the most populous counties in Texas, Bexar (11%) and Harris County (11%) accounted for a large proportion of reported exposures. The most common signs and symptoms, in descending order, were tachycardia (38%), drowsiness (18%), agitation (18%), vomiting (17%), hallucinations (13%), and hypertension (11%). Conclusion: Greatly increased reported marijuana homolog exposures were not attributable to a number of causes, including an increase in accessibility, relatively exaggerated or adverse drug effects and recent extensive media attention. There should be careful monitoring of marijuana homolog exposures and the clinical effects and outcomes from reported cases. The increase in reported cases and potential health risks from undisclosed ingredients in these products makes clinical recommendations challenging.

63. Preliminary Data on Exposure to Mephedrone in Pregnancy
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Objective: Mephedrone (4-methylmethcathinone, MMC) is a synthetic cathinone structurally related to the naturally occurring alkaloids methcathinone and cathinone found in the khat plant (Catha edulis), which is commonly chewed for its stimulant properties. There are no published epidemiological studies or case reports describing fetal outcomes following the use of mephedrone in pregnancy. In view of reports of mephedrone induced peripheral vasoconstriction, there is a possibility of constriction of fetal and placental vessels leading to growth restriction (IUGR), which has been observed in the offspring of regular khat users. This research was performed to provide preliminary data on fetal outcomes after mephedrone exposure during pregnancy.

Methods: Using standardised procedures, the UK Teratology Information Service (UKTIS) has provided fetal risk information when no other information is available. The UKTIS is a fully accredited information source and provides a comprehensive service on all aspects of childbearing, including drug use, alcohol and smoking. Patients report to the UKTIS who have taken mephedrone in pregnancy, and the information is gathered and evaluated using standardised procedures. The information is stored on a standardised database which is used for the analysis of the data. The database contains a spreadsheet detailing the active ingredient of each product. We used this spreadsheet to identify the active ingredients in the products taken.

Results: Over the 2 years since 2009 data has been submitted to the UKTIS and a total of 16 products were purchased prior to and 20 after the December 2009 UK legislation. 15 products were purchased from the same website prior to and after the legislation. No adverse outcomes were detected in the post-legislation purchases. Fourteen (86.2%) of the exposures were managed at healthcare facilities challenging.

Conclusion: Despite the UK Spice legislation, classified sCRA continue to be supplied over the Internet to UK users. Furthermore, new sCRA not covered by the legislation are appearing in Spice products. Ongoing surveillance work is required to track the sCRA in Spice products and determine the potential for toxicity associated with these products. Consideration needs to be given to reviewing the UK legislation so that suppliers cannot circumvent it by supplying legal alternatives to the classified synthetic cannabinoid receptor agonists.

66. Abuse of Over-The-Counter Codeine-Ibuprofen Analgesics
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1NSW Poisons Information Centre, The Children's Hospital at Westmead, Sydney, New South Wales, Australia.

Background: Over-the-counter codeine-ibuprofen preparations have been available in Australia for many years. Norufon Plus® is the market leader and contains ibuprofen 200 mg and codeine phosphate 12.8 mg per tablet. Anecdotal reports of abuse due to the codeine content and complications due to the ibuprofen content prompted the Australian Therapeutic Goods Administration to reschedule combination codeine products. In May 2010 they became behind-the-counter pharmacist controlled. The aim of this study was to assess the changes in codeine scheduling have decreased the number of cases of toxicity will result. Monitoring the impact of reporting of abuse and thus it is expected that fewer changes in codeine scheduling have decreased the number of cases will be reported in the future.

Methods: A retrospective review of calls made to the NSW Poisons Information Centre (the most populated state in Australia) during 1 January 2008 to 31 October 2010 was conducted. Of the 867 cases of abuse reported, 10% were related to combination codeine-ibuprofen products. No outcome data was obtained. Results: 57 cases of abuse were found - an increase from 3 cases in 2004 to 2005 in 2009. Of 47 cases were related to Norufon Plus®. There has only been one published Australian case series on the misuse of codeine-ibuprofen products. The series described cases of drug abuse and thus it is expected that fewer cases will be reported in the future.

Changes in codeine scheduling have decreased the number of cases of toxicity will result. Monitoring the impact of reporting of abuse and thus it is expected that fewer cases will be reported in the future.


67. Seizures Following Ingestion of the Synthetic Cannabinoid JWH-018

Objective: To investigate the prevalence of synthetic cathinone abuse in Ireland. Background: BZP (benzylpiperazines) was declared a controlled drug under the Misuse of Drugs Act 1977 on 31st March 2009. As a result of this legislation the head shops started to sell products containing synthetic cathinones as an alternative. These products were sold as ‘bath salts’ and ‘plant feeder pills’ and marked ‘not for human consumption’ or ‘not for sale to UK’. Results: We examined all enquiries to the National Poisons Information Centre (NPIC) regarding so called ‘bath salts’ and ‘plant feeder pills’ from head shops for the period from 1st April 2009 to 30th June 2009. The Garda Forensic Science Laboratory (Irish Police) analysed test purchases of various head shop products and provided a spreadsheet detailing the active ingredient of each product being sold. We identified the active ingredients in the products taken. Results: We identified 116 enquiries regarding 117 patients that had consumed different branded products sold as ‘bath salt’ or ‘plant feeder pills’. The active ingredients involved in the enquiries to the NPIC were mephedrone 31.6%, methylone 14.5%, methylenedioxpyrovalerone (MDPV) 6.8%, butylene 6%, methedrone 0.9% and naphthylethanolamine 0.9%. The amount was not identified in 39.3% of enquiries. The majority of enquiries originated from hospital emergency departments (EDs) (86.2%). Eighty patients were male (68.4%), 35 were female (29.9%) and 2 patients were of unknown sex. The age range of patients was 14–42 years (average 24.2, median 22.5). The symptoms displayed were tachycardia (40.2%), agitation (25.6%), mydriasis (21.4%), chest pain (18.6%), hypertension (14.5%) and palpitations (13.7%). The Poisoning Severity Score of all exposures was: none = 2, minor = 20, moderate 90, severe = 5 and fatal = 0. The Irish media (newspaper, radio, television) developed a considerable interest in head shops and ‘legal highs’ in the middle of our 18-month study. The majority of enquiries (82.8%) occurred in the first eight months of the study, after the media interest began. Conclusion: Synthetic cathinones exposure was associated with sympathomimetic features. Most patients had moderate symptoms. The number of patients presenting to EDs with cathinone intoxication increased dramatically during sustained media interest.

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68. Naphryone Toxicity

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National Poisons Information Service (Cardiff), Cardiff and Vale University Health Board, Cardiff, UK.

Objective: To assess the severity and diversity of symptoms following naphryone exposure and to make an analogy with exposure to naphthoflavonon such as a recreational cathinone.

Methods: Records of enquiries to the UK National Poisons Information Service (NPIS) for the period April 2009 to October 2010 relating to naphryone exposure were retrospectively reviewed and analysed.

Results: In the 56 telephone enquiries received throughout the study period, the most frequently reported symptoms were cathartic (n = 21/51 cases) and agitation (19%). Anxiety, somnolence and chest pain were each associated with 11% of enquiries. Other features observed included hallucinations, nausea and vomiting, palpitations, paranoia, visual disturbances, tachycardia and cases where serum creatinine kinase was observed, the highest recorded being 3070 U/L. The severity score for the majority of enquiries (55%) was considered to be moderate with 28% reported as severe. One patient was reported as being in a cardiac arrest on route to hospital, he subsequently died of respiratory failure following complications from inhaling gastric contents and underlying emphysema. Cause of death was not recorded as exposure to naphryone. The youngest patient reported was 14 years old; 58% of patients were less than 20 years, 43% between the ages of 21 and 40 years, 11% were over 40 years and 8% were of adult age unknown. The most commonly reported route of exposure was ingestion (73%) – other routes included inhalation (12%), injection (3%) and unknown (12%); a few cases reported multiple routes of exposure. Most cases (81%) involved exposure to naphryone alone, in ten cases there was a single co-ingestion and one patient was also exposed to methylamphetamine, cocaine and alcohol.

Conclusion: The NPIS regularly receives enquiries regarding new or emerging drugs of abuse. While the symptoms seen were not overwhelming, in most cases, some patients experience moderate or potentially life-threatening toxicity. The number of naphryone enquiries increased rapidly following the classification of methylamphetamine as a Class B drug in April 2010. In July 2010 naphryone was also classified as a Class B drug - increased vigilance is required as other substances of unknown toxicity seek to fill this new gap in the market.

69. Effects of Legal Control on Enquiries to the UK National Poisons Information Service on Recreational Cathinone Use

Thornton, J.1, James DA.2, Spears R.1, Cooper G.2, Wood K.2, Dyas J.3, Adams RD.1, Lapton DJ.2, Good AM.1.
1National Poisons Information Service (Newcastle), 2Wolffson Unit of Clinical Pharmacology, Newcastle upon Tyne; 3National Poisons Information Service (Cardiff), Llandough Hospital, Cardiff; 3National Poisons Information Service (Edinburgh), Royal Infirmary of Edinburgh, Edinburgh, UK.

Objective: Since 2009 the UK National Poisons Information Service (NPIS) has received increasing numbers of enquiries relating to recreational cathinone use, especially involving methylamphetamine.1 The UK government controlled methylamphetamine and most other cathinones as class B drugs under misuse of drugs legislation in April 2010, with naphrynone controlled in July 2010. This research was performed to assess the impact on these legislative changes on the frequency of toxicity as reflected by Internet and telephone enquiries to NPIS. Methods: National study of telephone and TOXBASE® accesses between March 2009 and October 2010 relating to recreational cathinone use. Data for cocaine and methylendioxy-methamphetamine (MDMA) was also obtained for comparison. Results: There were few telephone enquiries relating to cathinones between March and June 2009. Subsequently cathinone enquiry numbers, expressed as cathinone telephone enquires per million population, was not recorded as exposure to naphrynone. The geographical distribution of cases was similar to other abused prescription analgesics, Poison center data indicate that outcomes associated with buprenorphine cases are less severe than for methadone, both in adults and in young children. Conclusion: Data from five national programs indicated that methamphetamine and buprenorphine continues to increase. It is particularly concerning that rates appear to be increasing among new initiates. Poison center data suggest that buprenorphine may have an improved safety profile compared to methadone.

71. Exposure to MDAI: A Case Report

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National Poisons Information Service (Newcastle), Newcastle upon Tyne, UK.

Objective: 5,6-methylenedioxy-2-aminomethane (MDAI), a structurally related compound to methylamphetamine (MDA), a drug of abuse widely available to buy over the Internet. There is limited information available on the toxicity of MDAI, which is thought to be similar to that of MDMA but with less marked serotonergic effects.1 We describe a patient who developed multi-organ failure after apparent exposure to MDAI. Case report: A 21 year old male reported that he had ingested 5 grams of MDAI. Shortly thereafter he became confused, with evidence of psychosis and self injury. On presentation to the Emergency Department he was hypothermic (<40°C) and tachycardic (150 bpm). He was intubated and sedated and transferred to the intensive care unit. Subsequently he developed rapidly progressing multiorgan failure including liver (ALT 9541, ALP 42, bilirubin 128 and INR 4.33) and renal failure (creatinine 503), rhabdomyolysis (CK 40,000) and disseminated intravascular coagulation (DIC). Veno-venous haemofiltration (CVVH) was instituted
to manage anuria and he was treated with blood and blood products for DIC. He was transferred to the liver intensive treatment unit and treated on a fulminant care pathway including fluid resuscitation, vasopressor, high-frequency oscillatory ventilation, high volume intravenous fluids, noradrenaline (for hypotension), N-acetylcysteine and vitamin K. After 6 days liver function results were AST 457, ALT 160, bilirubin 269 and INR 2.43 continuing and the patient was showing signs of waking. The patient made gradual improvement and was subsequently transferred to a psychiatric hospital where he remained at least 3 months after exposure. Conclusion: To the best of our knowledge, this is the only reported case of multigorgan failure secondary MDAAI exposure. This has not been confirmed analytically and this is a limitation in view of the reported discrepancy between reported content and the confirmatory analysis for legal highs purchased in the United Kingdom. References: 1. Nichols DE, Brewster WK, Johnson MP, et al. Nonneurotoxic tetralin and indan analogues of 3,4-(methylendioxy)amphetamine (MDA). J Med Chem 1990; 33:703–10. 2. Brandt SD, Sumnall HR, Measham F, et al. The confusing case of NRG-1. BMJ 2010; 341:c3564.

72. Clinical Characteristics of 6-(2-Aminopropyl)benzofuran (‘Benzo Fury’) Toxicity Reported to the UK National Poisons Information Service

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1National Poisons Information Service (Newcastle), Newcastle upon Tyne; 2National Poisons Information Service (Cardiff), Cardiff, UK.

Objective: 6-(2-aminopropyl)benzofuran (6-APB, ‘benzo fury’) is a substituted methylenedioxyamfetamine drug, used recreationally because of its stimulant and enactogenic properties. This research was conducted to document the clinical features of toxicity related to the recreational use of 6-APB in the United Kingdom as reported in recent enquiries to the National Poisons Information Service (NIPS). Methods: Data from records of telephone enquiries to the NIPS, recorded on the United Kingdom Poisons Information Database (UKPIDD), were assessed up until 15th September 2010. The first case on our data set was 19th August 2010. Results: There were 32 telephone enquiries relating to 6-APB. Of these, 28 (87%) telephone enquiries concerned System Benzo Fury alone, one each in combination with alcohol, methedrone, sildenafil and dimethocaine. Common clinical features reported included tachycardia (n = 87%), hypertension (57.5%), agitation (57%), delirium (32.8%), fever or sweating (31.2%), anxiety (31.2%), diaphoresis (28.1%), nausea (28.1%), disorientation (25.8%), loss of attention (15.6%), pain in the chest wall (10.9%) and hyperventilation (10.3%). Analytical confirmation is not available in all cases. Conclusions: To our knowledge, this is the largest report of this novel agent, for which the exposure route and outcome are not well defined.

73. Clinical Profile of Patients who Visited the Emergency Department due to Substance Abuse: Toxicovigilance on New Psychoactive Substances

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Objective: Clinical effects of new (non-conventional) drugs of abuse (e.g. synthetic cannabinoids, cathinones, smart-drugs) are not well defined and generally poorly known by emergency physicians. Moreover, the number and severity of patients admitted to emergency departments (EDs) for new drugs of abuse is unknown in Italy. In this field, the National Early Warning System (NEWS) was introduced to address the issue, since in 2009–2010 it collected new sentinal cases, to collect and evaluate the few available clinical features, to diffuse clinical signals to the health system, and to promote preventative and interventional actions. The aim of this study was to describe the toxicovigilance on new psychoactive substances (PNS) in the years 2009–2010 in Italy. Methods: Activities of the NEWS concerning the identification of new substances (i) introduction of the number of Collaborative Centres included in the system (ii) response capability of the Coordinating Centre, (iii) rapidity of the signal release (system’s reaction-time), and (iv) percentage of the delivered signals distinguishing among three established levels (information, attention, alert) were evaluated. Results: The number of Collaborative Centres increased from 25 at the beginning of 2009 to 50 in October 2010. The Collaborative Centres revealed a critical response in 100% of cases, with a mean reaction-time that improved from 34 to 22 hours during the last year. There were 42 delivered clinical/toxicological signals in 2009–2010, comprising 33 (78.6%) “information”, 4 (9.5%) “attention” and 5 (11.9%) “alert”. The signals were delivered by the NEWS and addressed to all the national EDs and Collaborative Centres. Conclusion: The critical response capacity of the International institutions is the Reitox Italian National Focal Point (within the Department). The first evaluation of the performance of the system shows an increase in the activity of the Collaborative Centres, which reaches the capability and the reaction-time of the system, and of the knowledge of substances available for abuse (and symptoms. Most clinical signs were due to β2’s mimetic properties (tachycardia, shaking, anxiety, sweating, minor digestive disturbances, hypokalaemia and hyperglycaemia); 6 severe cases were reported. The 36 cases were mainly 3007 (4 to 7 per year) but increased in 2008 (16 cases). Half of these cases are misuse, occurring among rather young people (median age was 30) and with a sex distribution of 4/1 ratios. The 18 toxicological suspicions of substance abuse/dependence were identified by 2 researchers through chart review. Information on demographic data, injury severity, clinical treatment, and outcome after the injuries were then abstracted from the medical records and were tabulated for final analysis. To evaluate the predictors of injury severity, we further classified the study population into two groups according to their injury severity score (ISS > = 16 vs. <16). Logistic regression analyses were then employed to identify the risk factors of severe injury. Results: A total of 538 patients were eligible for final analysis, resulting in a prevalence of substance abuse of 1.1% during the study period. The study population consisted of 441 (82%) alcohol abusers and 97 (18%) drug abusers. In comparison with alcohol abusers, drug abusers were younger and more likely to have certain psychiatric diseases. Furthermore, many drug abusers were injured due to attempted suicide/overdose, which led to higher ISS, more hospitalizations and higher case-fatality rates. In multivariate analysis, use of central nervous system depressants (OR 5.7; 95% CI 1.4–23.5) or smart-drugs (OR 13.0; 95% CI 2.8–60.0), aged 51–60 years (OR 3.9; 95% CI 1.1–14.2), residents of Taipei county (OR 5.3; 95% CI 1.8–15.5) or living outside Taipei metropolitan (OR 9.5; 95% CI 2.9–31.6), visiting the emergency department by ambulance (OR 5.3; 95% CI 1.2–23.7) or transfer from other hospitals (OR 34.7; 95% CI 7.5–160.6) were associated with more severe injury as compared with their counterparts. Conclusion: Substance abuse related injuries were not uncommon in Taiwan. Drug abusers suffered more severe injuries than alcohol abusers and had higher rates of hospitalization and death, which might be attributable to their underlying psychiatric diseases and related deliberate injury and/ or attempted suicide.

74. Clenbuterol: Retrospective Study of Cases from the French Poison and Toxicovigilance System

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Objective: Clenbuterol is a β2-mimetic substance, used in France only for veterinary medicine (bronchodilation and tocolysis) and in some European countries for humans (bronchodilation). Its lipolytic and protein anabolic properties are a source of misuse in cattle (growth promotion) and among humans (doping, body-building). The discovery of a new use for weight loss purposes is a potential risk for sport activities. This study aimed to evaluate if and how often clenbuterol is misused in France. Methods: In 2009–2010, the French Poison and Toxicovigilance System Database was used to identify cases of accidental or deliberate exposure. Data were then employed to identify the risk factors of severe injury. Results: A total of 538 patients were eligible for final analysis, resulting in a prevalence of substance abuse of 1.1% during the study period. The study population consisted of 441 (82%) alcohol abusers and 97 (18%) drug abusers. In comparison with alcohol abusers, drug abusers were younger and more likely to have certain psychiatric diseases. Furthermore, many drug abusers were injured due to attempted suicide/overdose, which led to higher ISS, more hospitalizations and higher case-fatality rates. In multivariate analysis, use of central nervous system depressants (OR 5.7; 95% CI 1.4–23.5) or smart-drugs (OR 13.0; 95% CI 2.8–60.0), aged 51–60 years (OR 3.9; 95% CI 1.1–14.2), residents of Taipei county (OR 5.3; 95% CI 1.8–15.5) or living outside Taipei metropolitan (OR 9.5; 95% CI 2.9–31.6), visiting the emergency department by ambulance (OR 5.3; 95% CI 1.2–23.7) or transfer from other hospitals (OR 34.7; 95% CI 7.5–160.6) were associated with more severe injury as compared with their counterparts. Conclusion: Substance abuse related injuries were not uncommon in Taiwan. Drug abusers suffered more severe injuries than alcohol abusers and had higher rates of hospitalization and death, which might be attributable to their underlying psychiatric diseases and related deliberate injury and/ or attempted suicide.
their continuous variation) in the operative services of national health system (e.g. EDs and Poison Control Centres). Acknowledgement: Study carried out with the support of Italian Department for Antidrugs Policies - Presidency of the Council of Ministers.

76. Medical and Social Dimensions of Acute Alcohol Poisoning in Children: Psychosocial Aspects and Prevention of Alcohol Abuse (Final Results)

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Objective: The aim of the study is to analyze the medical and social dimensions of acute alcohol poisoning in children. Methods: Patients up to 18 years of age with acute alcohol poisoning hospitalized for the period 2006–2008 were studied. Data were retrieved from hospital records. The initial blood ethanol level was measured by thin-layer chromatography. Psychiatric interview and inquiry method (questionnaire consisting of 39 questions specially created for the survey) were used. Results: We studied 137 children with alcohol poisoning. Average age was 14.91 ± 1.45 years. Seventy-seven (56.2%) were boys and 60 (43.8%) girls. Alcohol administration by binge drinking was common at weekends and in late afternoon and evening was observed. On admission different levels of depressed consciousness were seen: 61.3% - somnolent, 28.5% - soporous and 5.1% - comatose. Blood ethanol level was over 2.00 mg/dL in 40.2% of cases. In 21 cases (15.3%) the alcohol poisoning occurred at time of first alcohol consumption. Repeated hospitalizations for alcohol poisoning for the studied period were not registered. The combination alcohol-illict drugs was observed in 13 children. Children most often used one type of alcoholic beverage. The most frequent alcoholic drink was vodka (63.1%). Six per cent of the children come from complete families. Both parents had secondary education in 79.7% of cases and were employed in 53.6%. Sixty per cent of the patients were the first born child in the family. First alcohol consumption was at the age of 12 years and 10 months (boys), and 13 years (girls). The most frequent reason for alcohol consumption was meeting and communication. Conclusion: Our study represents the first systematic research on alcohol intoxications among children in Bulgaria. For the majority of adoloscent alcohol consumption responds to an attempt to build self-esteem, for integration in society or in a group of friends. Based on the results we developed a programme for the prevention of alcohol consumption and poisonings among children. Effective preventative strategy is based on both a psychological and a social approach.

77. Serum Catalase Activity Remains Unaffected by Chronic Abuse of Heroin

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Clinical Toxicology Unit and Poison Control Center, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy

Objective: The aim of our study was to review the distribution and clinical significance of drugs of abuse acute poisonings among the patients admitted to the Toxicology Unit of Careggi Florence Hospital, from January 2006 to August 2010. Case series: The total number of acute xenobiotic intoxications was 5,876. Amongst them, 3,514 (59.8%) were acute poisonings involving drugs of abuse, including cocaine, cannabis, benzodiazepines and psychostimulant/hallucinogenic substances with an incidence rate of 324 cases/year per 100,000 persons. The frequency distribution of drugs of abuse acute intoxications is as follows: 7.5% for cannabis; 7.0% for amphetamines and 6.0% for benzodiazepines. The most frequent reason for acute intoxication was the increased fear of being caught (79.3%). Conclusion: The control of drug use is a critical public health problem. However, the medical complications of drug use are unpredictable and generally severe.

78. Drugs of Abuse: New Drugs or Old Ones? Epidemiological Survey of Acute Intoxications in Florence in the Last Five Years


Clinical Toxicology Unit and Poison Control Center, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy

Objective: The aim of our study was to review the distribution and clinical significance of drugs of abuse acute poisonings among the patients admitted to the Toxicology Unit of Careggi Florence Hospital, from January 2006 to August 2010. Case series: The total number of acute xenobiotic intoxications was 5,876. Amongst them, 3,514 (59.8%) were acute poisonings involving drugs of abuse, including cocaine, cannabis, benzodiazepines and psychostimulant/hallucinogenic substances with an incidence rate of 324 cases/year per 100,000 persons. The frequency distribution of drugs of abuse acute intoxications is as follows: 7.5% for cannabis; 7.0% for amphetamines and 6.0% for benzodiazepines. The most frequent reason for acute intoxication was the increased fear of being caught (79.3%). Conclusion: The control of drug use is a critical public health problem. However, the medical complications of drug use are unpredictable and generally severe.

79. Levamisole-induced Occulsive Necrotizing Vasculitis in a Pregnant Woman after Use of Cocaine Contaminated with Levamisole


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Objective: It is estimated that over 2 million people in the United States use cocaine each month. Complications from cocaine use may also include toxicity from adulterants. Current estimates suggest that 80% of cocaine originating in South America contains levami-

sole, an antihelminthic that is associated with anagrana-

looyctosis, occlusive necrotizing vasculitis, or leukoencephalopathy. In this study we report on the first case of levamisole vasculitis in a pregnant cocaine-using woman. Case report: A 19-year-old woman, 18 weeks gravid presented to the Emergency Department with attraumatic painful purple discoloration of both ears and her neck of two days duration. Initial vital signs were: BP, 131/70 mmHg; pulse, 90 beats/minute; respirations, 20 breaths/minute; SPO2, 99%; glucose, 7.2 mmol/L. She admitted to daily cocaine use. Laboratory studies revealed a WBC of 5,500 cells/mm3. Her complete blood count, chemistry panel, coagulation panel, and liver enzymes were within normal limits. Urine was positive for benzodiazepines and cocaine. Blood culture and lupus anticoagulant were present, but a negative hepatitis panel. Patient was diagnosed with leva-

misole-induced occlusive necrotizing vasculitis and treated with high-dose corticosteroids. Her pregnancy continued to term without complication. Subject diagnosis was likely due to cocaine levamisole. She delivered a healthy baby girl at term. Patients who have used levamisole-contaminated cocaine should be warned about the risks of levamisole-induced necrotizing vasculitis.

80. Clinical Presentation of Atropine Co-Poisoning in Patients Hospitalized due to Toxic Effects of Novel Recreational Drugs


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Objectives: To analyse a case series of atropine co-

poisoning in patients hospitalized for novel central nervous system stimulant drug toxicity. Methods: Retrospective review of records of all patients hospi-

talized with diagnosis of novel CNS stimulant drug toxicity between April and October 2010 and tested for atropine. The main diagnosis was established from the patient’s self-reporting only on the representation of the symptoms and after exclusion of the presence of substances with the same anticholinergic action as atropine. Atropine was evaluated qualitatively, using thin layer chromatography. Results: We found 88 patients fulfilling the criteria. Eighty-two of them were negative for atropine and 6 were positive. Subgroups of patients who differed significantly were tested from one another with respect to age and sex. There was one death in the atropine subgroup on the 4th day after admission. The
81. Acute Marijuana Intoxication Emergency Department Presentations

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1Somerset Medical Center, Somerville; 2Morristown Memorial Hospital, New Jersey Medical School, Morristown; 3New Jersey Poison Center, Newark; 4New Jersey Medical School, Newark, New Jersey, US

Objective: Marijuana is one of the most frequently abused drugs. Intoxications rarely present to emergency department (EDs). The purpose of this study is to characterize acute marijuana intoxications presenting to New Jersey and New York emergency departments. Methods: Design: A multi-center retrospective emergency department (ED) cohort. Study setting: 20 New Jersey and New York EDs. Subjects: Consecutive patients with the ED diagnosis of poisoning - hallucinogen (ICD10 code E924) and cannabimimetics (ICD10 code F12) were identified from October 1, 2008 to September 30, 2009. Only completed charts with the primary diagnosis of cannabis abuse and (+) THC on urine drug screening were included. Additionally, multi drug ingestion or multiple drugs found on urine drug screening were excluded. Results: Out of 1,590,248 consecutive patients, 78 patients met inclusion criteria (38.8% males; 61% marijuana). The patient demographics were as follows: mean age = 20.7 years (range: 14–42 yrs), gender = 60% males. 9% of patients admitted their ED presentation was their first usage of marijuana. The route of exposure was inhalational for 98% with the remainder via ingestion. The most common presentation was feeling strange or not feeling well (38%). 25% had altered mental status while 18% were reported as acting strange. Additional findings included palpitations (14%), dizziness (12%), nausea or vomiting (10%), weakness (10%), light-headedness (8%), miosis (5%), chest pain (5%) and hallucinations (5%). No patients were hospitalized and no deaths were recorded. Conclusion: Marijuana ingestion presents uncommonly to EDs. Toxicity appears to be mild and self-limited.


Nicolas R1, Manel F, Simon-Tellar S, Garnier R1, Roussel C2, Savic P3, National Coordination Committee for Toxicovigilance1.

Objective: The objective of this study was to demonstrate the existence of gamma-butyrolactone (GBL) intoxications, to characterize these intoxications and to specify the measures to prevent this public health problem. Methods: A descriptive epidemiological analysis of the data collected in the national poison control centers (PCCs) between 2005 and 2009. Results: A total of 1,521 intoxications were reported, 1,512 were analyzed. More than 80% of cases occurred in men, and the patients who died were in this group. The median age was 19 years (range: 10–69 yrs). The intoxication occurred mainly during recreational settings such as nightclubs and music festivals (79% of cases). The symptoms of GBL intoxication include central nervous system depression, sympathomimetic effects and hallucinations. The main findings were: miosis (87%), vomiting (82%), dizziness (72%), diaphoresis (42%) and hallucinations (21%). The main interventional measures were: symptomatic treatment, put on ventilator, and endovascular cooling. Conclusion: GBL intoxication is an important public health problem. The endovascular cooling system (Alsius Corp, Irvine, CA) was implemented in French centers in 2006. The mortality rate for patients over 20 years of age was 9% (9 of 105 patients), including 2 deaths (one due to aspiration and one due to respiratory arrest). The endovascular cooling system can save lives, providing that it is promptly initiated.
associated with an increase in the availability of illegal/controlled substances; this was particularly apparent for mephedrone and the other cathinones. Legislative authorities, along with the help of clinical toxicologists, need to address the issue to appropriately reduce the use of novel psychoactive substances and monitor substances being used to determine the true impact of any legislation changes.

85. Mixed Cathinone (Methylenedioxypyrovalerone, Butylone and Mephedrone) Toxicity in an Individual with Use of a Single White Powder Sold as Mephedrone

Wood Tox Clin 3, Button J2, Davies S3, Puchnarewicz M1, Holt DW1, Dargan PI2.

Clinical Toxicology Service, Guy’s and St Thomas’ NHS Foundation Trust, London; 2King’s Health Partners, London; 3TICTAC Communications Ltd, London; 4Forensic Science Service, London; 5Analytical Unit, St George’s, University of London, UK

Background: The use of novel psychoactive substances (commonly known as “legal highs”) is increasing. A number of studies have shown that the content of legal highs purchased over the Internet is unreliable. We report here a case of an individual who believed that they had used mephedrone, but toxicological analysis showed that they had used a combination of mephedrone and other novel cathinones. Case report: A 28 year old male presented following use of a “white powder” that he believed to be mephedrone. He had purchased this prior to the classification of the cathinones in the UK in April 2010. He ingested 300 mg on the afternoon prior to presentation followed by a further 100 mg on both occasions he mixed the powder with water prior to ingestion. Approximately 1 hour after the second ingestion he developed palpitations, anxiety, shortness of breath and felt light-headed. He denied used of any drugs other than the mephedrone. He presented approximately 6.5 hours after the ingestion. On examination he had clinical features of sympathomimetic toxicity and a heart rate of 140 bpm, blood pressure of 210/103 mmHg and dilated 7 mm pupils; his temperature was 36.4°C. Neurological examination was normal, with no evidence of clonus or hyperreflexia. ECG on admission showed sinus tachycardia and normal QRS/QTc durations. A 12 hour Troponin T was negative. He was given 10 mg diazepam and his symptoms settled over the next few hours and he was discharged 24 hours later. Diazepam is one of the most frequently used drugs. It is often used to control psychomotor agitation and subsequently analysed by GC-MS. Mephedrone (concentration <0.005 mg/L), butylone (0.1 mg/L) and methylenedioxyprovalerone (MDPV) (0.003 mg/L) were detected, no other recreational drugs were detected. Conclusion: We report a case of mixed novel psychoactive substance toxicity following the self-reported use of lone mephedrone. In addition, this is the first confirmed case of toxicity associated with MDPV. Clinical toxicologists and legislative authorities need to be aware that similar to classical drugs, there is the potential that novel substances are combinations, which may increase the risk of toxicity.

86. Stress Cardiomyopathy During Ethanol Withdrawal

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Objective: Stress cardiomyopathy is an acute, transient left ventricular dysfunction, associated with emotional stress. The goal of the study was to determine the relationship between discontinuity disturbances in ethanol withdrawal with characteristic echocardiographic pattern and ECG changes. Case report: A 53 year old female, chronic alcohol drinker was admitted to the Internal Ward due to symptoms of acute pancreatitis. Echocardiography revealed the presence of angioplasty of the circumflex artery with stent placement. On admission BP was 160/110 mmHg, HR 90/ min. The ECG showed small ST decrease in V4 and V4-V6 leads. Troponin I was 0.04 ng/mL, serum ethanol 0.2 mmol/L. Abdominal ultrasonography revealed only a small amount of fluid around the pancreas head. Chest pain, shortness of breath, pallor, jugular venous congestion were observed. The patient was treated with lung and tachycardia of 120/min appeared on the first day of hospitalization. ECG showed ST elevation in V2-V3, with T-wave inversion in V2-V6 leads; troponin increased to 0.49 ng/mL. Coronarography excluded significant changes in the arteries. In echocardiography apical akinesia and impaired left ventricular relaxation with ejection fraction (LVEF) of 53%, BNP 1025 pg/mL. By hospital day 3 disorientation and behavior disorders corresponding to alcohol withdrawal appeared. In subsequent days left ventricle systolic function improved. Only small apical hypokinesis was seen in echocardiography 14 days after the initial examination. LVEF increased to 53%, BNP fell to 247 pg/mL. Deep negative T-waves in leads I, II, aVL and V2-V6 in ECG persisted to the end of the 19th day of hospitalization. The patient may eventually develop in alcohol withdrawal. Transient left ventricle contractility disorders are probably due to sympathomimetic toxicity and may be associated with severe emotional stress. References: 1. Wittstein IS, Thiemann DR, Lima JAC, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005; 352:539–48. 2. Pach D, Sowa-Staszczak A, Gawlikowski T, et al. Quantitative analysis of heart scintigraphy with regional myocardial wall motion and systolic thickening as an indicator of myocardial damage in ethanol withdrawal patients. Przegl Lek 2010; 67:571–5.

87. Abuse of Benzodiazepines Among Heroin Addicts in Skopje Region

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Background: Benzodiazepines are the most widely used and abused psychotropic agents in the world. In our country, in the group of benzodiazepines, diazepam is the most used and abused of all benzodiazepines. Benzodiazepines are often used to induce sleep and the term “dormitory” has been used to increase “flash”. Diazepam use by heroin users increases their risk of overdose and serious coma. Recently we have noted abuse of diazepam by heroin addicts, which are drugs on the abuserophene substitution programme. Consumption of benzodiazepines began after subjects had become addicted to heroin and indicates a clear trend to multiple drug abuse. Methods: The study carried out in a predominantly male group of 92 patients, active intravenous heroin users, aged 21 ± 4 years, of body mass 66.6 ± 8.0 kg. Participants were admitted for inpatient detoxification programme. They had been consuming heroin from 3 months to 8 years. This sample of heroin users was interviewed regarding their benzodiazepine use. Opiates and benzodiazepines were detected using FPIA technique. Anti HCV seropositivity was detected using Cobas Core Anti-HCV EIA. Results: The majority (92%) had used diazepam, 66% in the 6 months prior to interview. Diazepam was ranked first by 92% of patients, followed by flurazepam 6% and alprazolam 2%. The prevalence of diazepam use among heroin addicts is very high. Diazepam intravenously injected together with heroin was common in more than half of the addicts. Diazepam was taken orally, but also intravenously mixed with heroin. The mean daily dose was 30 mg/day, often associated with other drugs. Although diazepam appears to have potential for abuse, the available data does not rule out its therapeutic interest. References: 1. Laqueille X, Launay C, Dervaux A, et al. [Abuse of alcohol and benzodiazepine during substitution treatment: a review of the literature] [Article in French]. Encephale 2009; 35:220–5. 2. Fatase M, Lavié E, Denis C, et al. [Benzodiazepine withdrawal in subjects on opiate substitution therapy] [Article in French]. Presse Med 2006; 35:599–606.

88. Severe Medical Complications Connected with the Use of Psychoactive Drugs

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Objective: To establish what are the most common complications observed in a group of patients with acute heroin poisoning and when combined with other psychoactive substances (PAS). Methods: The study included 100 patients selected by lottery method from all hospitalized persons with acute heroin and combined with other PAS poisonings, hospitalized in the Toxicology Clinic, MHATEM “Pirgov”. This was a retrospective study for a five year period. The patients were of both sexes and the mean age of the male:female was 4:1. Results: As a complication of the nervous system, peripheral toxic neuropathy, stroke, and coma in 31% of patients was observed. Complications of the respiratory system were expressed in the activation of old inflammatory changes in individual cases, pneumonia, pulmonary edema, ARDS (respiratory distress syndrome in adults) in 39% of the patients. Forty-four per cent of patients showed altered liver metabolism - values exceeding the reference values of bilirubin, transaminases (AST and ALT), presence of hepatitis B or C. In the study eight cases (8%) were registered with non-traumatic rhabdomyolysis with subsequent myoglobinuria and acute renal failure (ARF) - one of the most frequent renal impairments in acute heroin intoxication. Exotoxic shock was observed in 8% of the patients, anemia in 7% of the patients, and in five of them (5%) signs of sepsis. The results of the study show that in 29 patients there were multiorgan disabilities. The performed immunoassays established suppressed humoral and cellular immunity in patients with multiorgan disorders. These results showed the relationship between changes in activity and reactivity and the severity of various infections and complications. Death was recorded in three persons (3%). Conclusion: The results of the study showed that acute heroin intoxication, heroin mixed with other PAS, or heroin drugs lead to severe complications of the various organs and systems, chronic damage, longer hospital stays and costly tests and treatment.

89. Pattern of Acute Ethanol Poisoning in Mashhad, Iran

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Introduction: Ethanol poisoning is undoubtedly a recognized common intoxication in most countries of the world. However, ethanol intoxication among Islamic countries like the Islamic Republic of Iran is strictly prohibited. In spite of the regulation, patients with acute ethanol poisoning have been admitted to the Emergency Toxicology Clinic of Mashhad University Medical Center. In this prospective study, 128 patients with acute ethanol poisoning out of 13,400 patients were admitted to the Emergency Toxicology Clinic between January 2008 and December 2009. Vital signs, oxygen saturation via pulse oximetry and blood glucose by glucometer were measured. Dextrose 50% was given as well as supportive care. Data were analyzed by SPSS (Version 16). The mean age, sex, duration of ethanol measurement and last food consumption was 9.2 hours. Patients were predominantly male (92.1%) and single
The most common findings included nausea and vomiting (92%) impairment of consciousness (69%), pupils were normal size in (67.7%) conjunctival hyperemia (63%), agitation (44%), ataxia (43.7%), epigastric pain (26%) and haematomas (12.7%). Pulse rate was 83 ± 11/min (60–120), respiratory rate 17 ± 4/min (12–20), blood pressure 105 ± 14 (90–140) mm/Hg, oxygen saturation was 95 ± 14% (93–98) and blood sugar 98 ± 22.19 (57–167) mg/dL. Conclusion: The majority of cases were mild to moderate and supportive care was sufficient. Although spirit consumption is not legal and thus not common in I.R., Iran, acute ethanol poisoning is rather common (1%) in this holy city.

90. Ethnobotanical Substances - The New Recreational Drugs Used by Teenagers in Romania
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Objective: To evaluate the incidence, clinical manifestations and consequences of using ethnobotanical substances in drugs by teenagers. Methods: We have performed a retrospective study of ethnobotanical substances poisoning admitted in our department between January 1st 2009 and November 1st 2010. The following criteria were taken into consideration: type of substance, age, gender, symptoms, place of producing, hospitalization duration. Results: 32 patients with acute poisoning with ethnobotanical substances were admitted during the mentioned period. Bags bought from the new opens stores were the products involved. The number name was identified in 20 cases as follows: Spice 5 cases, Spice 2 cases, Smoke plus 2 cases, Magic 2 cases, Joy, White, Chocolate, Diesel, Ganja, Power Magic, Gold, Wild Plus 1 case each, Magic+Insomnia 1 case. In 12 cases the name could not be identified. The median age of the patients was 15.6 years. There were 22 boys (68.7%) and 10 girls (31.3%) reported in our statistics. In all the cases the poisoning was produced by ingesting the substances. Regarding the place of consumption we noted in the majority of situations: clubs or during private parties (23 cases). The main symptoms were: dizziness in all cases, nausea and vomiting (20 cases), angina (7 cases), tremor, hallucinations (2 cases each), tachycardia, chest tightness (1 patient each). The duration of hospitalization was one day in all cases with full recovery. In 21 cases the toxicological examination was negative and in one case revealed synthetic cannabinoids. Conclusion: The ethnobotanical substances represent a new option in recreational drug consumption among adolescents. Even although in all the cases the registered symptoms were moderate they represent a real threat for children’s health and behavior. References: 1. Dargan PI, Wood DM. Novel and emerging recreational drugs. Toxicol Lett 2010; 196:S16. 2. EMCDDA. 2010 Annual report on the state of the drugs problem in Europe. November 2010, Lisbon, Portugal. http://www.emcdda.europa.eu/publications/annual-report/2010.

91. The Psycho-Social Profile of The Teenage Ethnobotanical User
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Background: The Psycho-Social Profile of The Teenage Ethnobotanical User
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Objectives: The assessment of the psycho-social profile of the ethnobotanical substances user. Methods: We studied all the patients with ethnobotanical substance poisoning examined in the psychology department between 1st November 2009 and 31st October 2010, using clinical interviews with the patient and his family. Results: Psychological examination was performed in 29 patients with ethnobotanical overdose and in 3 patients with acute poisoning. There were 21 boys (72.41%) and 8 girls (27.59%). The ethnobotanics used were the following: Spice (18 patients), Gange (5 cases), Magic Power (2 patients), Diesel (1 case), Havana (1 patient), Puff (1 case), Boom (1 patient). All the patients presented with some of the common psychological characteristics of drug of abuse consumers, as follows: Personality factors: immature personality, impulsivity, perception of addiction to new and forbidden experiences, rebellion personality; Family factors: the absence of communication between parents and children, in conflict or broken families, educational style; Environmental factors: social network with high accessibility to drugs, affiliation to drug groups, value norms and values which encourage drug abuse. The specific psychological characteristics for these types of users are the following: The reason for using ethnobotanical substances was curiosity and group pressure (in all the patients); Most of the teenagers were at the beginning of drug use (23 cases); None of them had ever used other drugs for reasons of curiosity and group pressure. Choosing ethnobotanics was the "legal" status of these substances (low prices and the accessibility status) in all the studied teenagers. The psycho-social profile of the ethnobotanical users was very similar to that of other drug users. The specific characteristics of ethnobotanical users are: the perception that these substances are not dangerous and do not produce addiction. References: Stanca I. Individual approach to drug addicts. In: Mitrofan I, ed. Psychotherapy - Theoretical, Methodological and Applied Landmarks. Ed. SPER, Bucharest 2008.

92. Anabolics Abuse and Cardiomyopathy in a Bodybuilder: A Case Report
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Background: Anabolic-androgenic steroids (AAS) are synthetic derivatives of testosterone that athletes use to enhance muscle mass and improve their performance. The avoidance of anabolic steroid use, such as after injection, myocardial infarction, cardiomyopathy, and sudden death, are rarely reported. Case report: A 39-year-old male bodybuilder attended the Department of AAS of S. Naumov clinical hospital for abuse over the previous 3 years. The most frequently used compounds were: methandrostolone, stanozolol and oxymetholone (oral); and nandrolone decanoate, testosterone enanthate and trenbolone enanthate (intramuscular). He had no family history or personal history of cardiovascular diseases, alcohol abuse or acetalinopenic intake. The patient was in good physical condition until approximately three weeks prior to admission, when he experienced increasing fatigue, decreased exercise tolerance and general malaise. Although he stopped exercising and self-administering the drugs, these symptoms continued to progress and he subsequently developed anorexia, shortness of breath during exertion and fatigue. His free testosterone and delta 4-androstenedione concentrations were elevated. Acetalminopen level was undetectable and anabolic steroid-induced toxic hepatis was suspected. Chest X-ray revealed cardiomyopathy without pulmonary congestion. Echocardiogram showed a dilated cardiomyopathy with an estimated ejection fraction of 35%. A diagnosis of severe toxic cardiomyopathy associated with anabolic steroids was made after ruling out other causes of non-ischemic dilated cardiomyopathy. Treatment included general rest, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, beta-blockers, spironolactone, and diuretics. 18 days after hospitalization, the patient was discharged with oral therapy. Conclusion: Several years into chronic misuse of AAS, this power bodybuilder showed impaired myocardial function, strongly associated with mean dosage and duration of AAS use. The interval since the last AAS abuse was too short to be able to evaluate the improvement of left heart cavity function. References: D’Andrea A, Caso P, Salerno G, et al. Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids: A Doppler myocardial and strain imaging analysis. Br J Sports Med 2007; 41:149–55.

93. Does the Aspiration of Lamp Oil Increase the Alveolar Diffusion Barrier for Oxygen? Proving Clinical Findings in an In-Vitro Alveolar Space Chamber Experiment
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Background: Based on a Federal Institute for Risk Assessment (BfR) detailed analysis (57,093 reports between 1990–2008) of aspiration cases with liquid preparations, the aspiration risk is clearly associated with the ingestion of distinct aliphatic hydrocarbons with a chain length from C8 to C15. These are the main components of paraffin-containing lamp oils, grill-lighters and kerosene. Based on their typical low viscosity, low surface tension and low vapour pressure these substances can enter the airways and lungs. More than 320 serious cases and five deaths of children have been documented in the BfR since 1990 with the typical signs of lack of oxygenation, giving strong clinical indications for an oxygen intra-alveolar diffusion barrier effect. To prove this hypothesis, the intra-alveolar surface and the oxygen transfer was simulated in an in vitro Alveolar Space Chamber (ASC) experiment. Methods: A gas-tight Plethysmograph-chamber (diameter 115 mm, height 115 mm, wall thickness 15 mm) was half-filled with fluorocarbon (FC-43) to generate a liquid-gas surface to simulate the alveolar surface. The oxygen-transport through the surface was measured in the bottom liquid part of the chamber by a Unisense oxygen micro sensor, connected to a high-sensitivity Pico-ammeter. Results: The results of the experiments scaled that the alveolar surfactant can be considered as a strong accelerator to the oxygen transfer into the liquid space of the capillary lung system. In contrast to these findings, generated microliters of lamp oils reduce the transfer of oxygen through the surface to a high extent (minimum 9–15 fold). Transferring these findings to the clinical course of the documented serious lamp oil aspiration, the pathofphysiological mechanism could be deduced. The pathophysiological mechanism. The characteristic physico-chemical properties of ingested lamp oils gives these liquids the capacity to spread deep into the lung, and move into the alveolar spaces with the effect of building up a persistent diffusion barrier for oxygen. This could explain the severe asphyxia and death documented in BfR cases. Conclusion: The ASC-experiment gives a plausible understanding of the clinical findings in cases of serious lamp oil aspirations. The experiment is currently being extended to find novel additional therapeutic tasks in cases of severe aspiration.

94. Water Horsetail as a Possible Cause of Haff Disease
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Objective: Outbreaks of an illness characterized by sudden, severe muscular rigidity and rhabdomyolysis after eating fish has been known as Haff disease since 1924. However, the etiology of this illness is still vague and not well defined. Methods: Both experi-
97. Experimental Justification for Using Ozonized Oil Solution in the Treatment of Chemical Burns of the Digestive Tract Caused by Acetic Acid

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Objective: Acetic acid poisoning takes third place in hospital mortality from acute poisonings in Russia. This experimental investigation tries to evaluate usage of ozonized oil solutions in the treatment of digestive tract burns. Methods: The experimental investigations were conducted in 90 male Wistar rats with initial weight 180–200 g. We defined two groups of 45 experimental rats. Mucosal injury was provoked by 0.5 ml of 20% acetic acid through the oral tube under etherization on an empty stomach. The ozonized oil has an antiphlogistic action. It acts in two ways: through improvement of oxygen transport and by positive influence on general metabolism. Improvement of oxygen transport to the body tissues with the ozone therapy is connected with the increasing partial pressure (pO₂) in arterial and venous blood, increasing erythrocyte deformation, and their abilities to penetrate into smaller capillaries, and finally with decreasing connection of hemoglobin with oxygen. The last circumstance is related to the activation of glycolysis in erythrocytes and 2,3-diphosphoglycerate connection, that improves the delivery of oxygen by hemoglobin to the body tissues. All animals got ordinary enteral feeding. The animals from control and experimental groups were taken out from the experiment on the 5th, 13th, 19th days after etching with the acetic acid. In addition the animals of the second group were given the ozonized vegetable oil. Morphologic, histochchemical, flow DNA cytometry were performed. Results: Necrotizing ulcerative process was emerging in the upper GI tract on the fifth day after the introduction of the acetic acid. With the treatment using ozonized oil solution the acidized area of the surface coating of the epithelium after 5 days. The mucosal burns of the oesophagus, stomach and duodenum were smoothed over on the 13th day. In the group of experimental animals local decrease in the DNA flow cytometry examination of the cell repair of the mucous coat of the stomach showed a significant increase in the size of the proliferative pool from 11.9 ± 1.32 to 14 ± 2.1 (p < 0.05). This increase of the proliferative activity was linked to the increasing number of cells synthesizing DNA whose number, in the group of animals who were receiving treatment, was 34% higher (p < 0.01) in comparison to the control group. Conclusion: The use of ozonized oil during the treatment of chemical burns caused by acetic acid poisoning, facilitates the acceleration and healing of the mucosal membrane of the digestive tract.

98. The Role of Macrophages in the Pathogenesis of Toxic Hepatitis in Rats Resulting from Tetrachloromethane Poisoning

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Objective: The use of tetrachloromethane (CCl₄) to produce experimental hepatitis has been a classic model for research into the mechanisms of chemical toxicants’ influence on the liver tissue for more than 30 years. The aim of the research consists of the study of the possibility of correcting pathologic changes to the liver with toxic hepatitis when modelling the activity of macrophages. Methods: The rats weighing 50 white male rats, according to the recommendations of international ethics committees for humane treatment of laboratory animals. CCl₄ was injected intraperitoneally in doses of 50 mg/kg. The histological and histochemical changes were evaluated. The animals were divided into three groups: 1) intact; 2) control (toxic hepatitis); 3) experimental (toxic hepatitis with treatment by a drug – metoprolol*). Results: On the 3rd day after the introduction of tetrachloromethane into the experimental rats’ livers signs of acute toxic hepatitis were noted that showed itself in a form of nidal necrosis of hepatocytes with perifocal lympho- leukocytic infiltration. As compared with intact healthy animals the quantity of cells, expressing CD 45+, pervascularly increased 20 times, (from 17.83 ± 2.31 to 367.62 ± 16.40 per unit of the section area), and in the liver parenchyma - 15 times (from 13.89 ± 1.39 to 187.98 ± 8.58 per unit of the section area), while on the 7th day of research the quantity of leukocytes in the organ reduced, but still was on average 4.5 times more than the reference level. During the immunophenotyping we found that the quantity of T-lymphocytes was increased 17 times compared to the control, and on the 13th day it was on the ordinary value in the latter part of the experiment. After activation of macrophages by the drug “3-aminophenolhydrate” signs of a toxic hepatitis in rats’ liver were less evident, inflammation signs are reduced, polymorphonuclear leukocytes in the infiltrate were solitary, and on the 7th day the nidal necrosis without the perifocal cellular reaction remained only on the periphery lobule, granularity of hepatocytes remained, while hepatocytes with hydropic degeneration were not detected. The quantity of cells, expressing CD 45+, both in liver parenchyma and pervascularly were decreased to the value 123.77 ± 6.12 and 153.41 ± 8.53 per unit of the section area accordingly. Conclusion: The modulation of the macrophages’ activity led to the removal of the inflammatory response, to the regeneration of the liver tissue after the toxic lesion, and therefore to the reduction of CCl₄ toxic action.

99. Treatment of Experimental Metropolit Poisoning Using Levosimendan With and Without a Loading Dose

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Background: Levosimendan is an inodilator used to improve cardiac output (CO) and reduce afterload in heart failure. The mechanism of action is twofold: 1) myocardial calcium sensitizer producing increased inotropy and 2) vascular K⁺-channel-blocker producing peripheral vasodilatation. Previously, we have showed that levosimendan with a loading dose and infusion improved cardiac output (CO) but not blood pressure (BP) in a rodent model of verapamil poisoning. Metropolit does not cause peripheral vasodilatation. Consequently, the vasodilation effect of levosimendan may not influence BP to a similar degree as seen with verapamil. Objective: To assess the effect of levisimendan on CO, BP and HR in a rodent model of metropolit poisoning. Methods: Male Wistar rats (350–450 g) were anesthetized and ventilated. Jugular venous, femoral arterial catheter and a carotid temperature probe, to measure CO by thermocoupling, were inserted. With metropolit toxicity, the MAP and heart rate (HR) were recorded. Metropolit was infused continually throughout the experiment. When BP dropped to 50% of baseline (time-0) rats received: 1) normal saline bolus + infusion (Control), 2) levisimendan 36 microgram/kg loading dose then 0.6 micrograms/kg/min (Levola), 3) levisimendan
101. Mineral Miracle Solution: Acute Poisoning
After Oral Use of a Sodium Chlorite-
Containing Pseudo-Medicine Sold on the Internet
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Objective: Mineral Miracle Solution (MMS) is a product sold on the Internet, which is advocated to cure many pathological conditions including AIDS, malaria, cancers etc. According to the information available on visited websites, MMS is sold as 120-ml sterile glass flasks containing 28% sodium chlorite solution. It is claimed that one to 15 drops of the solution be allowed to react with an acid (i.e. 10% citric acid sold as an “activator” kit) to generate chlorine dioxide. The final product is then ingested after dilution in water or fruit juice. Few cases of human poisoning have so far been reported. However, if instructions for preparation are ill-understood, severe poisoning may ensue as the present case report shows. Case report: A 27-year-old woman born in Cameroon, without any remarkable medical history, ingested several mLs of MMS to treat constipation. Shortly thereafter, she developed nausea, vomiting, pronounced pale skin, shivering, and then marked anemia and dark urine. Three days later, she asked for medical advice due to persisting symptoms. Sinus tachycardia and metabolic acidosis were noted. Biological abnormalities included severe hemolytic anemia with a sharp drop in hemoglobin level (4.7 g/dL), Methemoglobinemia was not measured. She was given globular concentrates on 4 occasions. No other cause of the intravascular hemolytic anemia could be found, except for G6PD deficiency that had so far remained asymptomatic despite prior consumption of fava beans. The patient recovered uneventful events without recurrence of hemolysis or renal failure. Conclusion: Only one case of human poisoning with methoglobinemia (59%) and hemolysis (Hb: 7.1 g/dL) has been published following the deliberate ingestion of 10 g of sodium chlorite. Methemoglobinemia has been described in cats with doses of 20 mg/kg and above. The present case report confirms the hematological toxicity of sodium chlorite. Reinforcement of the surveillance of risks associated with the use of pseudo-medicines sold on the Internet is therefore recommended. References: 1. Lin JL, Lim PS. Acute sodium chlorite poisoning associated with renal failure. Ren Fail 1993; 15:645–8.

103. Racial-Ethnic Association with QT Prolongation following Acute Drug Overdose
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Objective: QT prolongation has been identified as a marker for significant adverse events in suspected poisoning. While gender differences are a well-known genetic influence on susceptibility for QT prolongation, racial disparities in drug-induced QT prolongation are unclear. Therefore, we aimed to evaluate the association between race, ethnicity, and drug-induced QT prolongation for patients with acute overdose. Methods: In a cross sectional observational study at two urban teaching hospitals, we evaluated consecutive adult emergency Department patients presenting with acute drug overdose over a two year period. Standard demographic, racial-ethnic, and clinical variables were collected. Racial-ethnic classification was self-reported and based on two subdivisions: (a) race was classified as White, Black, Asian, or other; (b) ethnicity was dichotomized as either Hispanic or non-Hispanic. Results: Of 466 patients we detected 2-fold risk difference. Results: In 766 patients screened, we included 216 (age <18, lack of ECG, alternate diagnosis); thus 550 patients were analyzed (53% females, age 41±18) with QT prolongation occurring in 11.4%. The most common drugs ingested in the prolonged QT group were opioids, antidepressants, anti-psychotics, and benzodiazepines. Racial composition of all subjects was: 92% Blacks, 10% Asians, 30% other, while ethnic composition was 48% Hispanic origin. Non-Hispanic ethnicity was significantly associated with prolonged QT using univariate analysis (OR 2.1, p <0.05) as well as multivariate analysis (OR 2.1, p <0.05) adjusted for age, heart rate, race, ethnicity and serum potassium concentration. Conclusion: In this large urban study of acute drug overdose, non-Hispanic ethnicity was independently associated with QT prolongation. Implications for genetic susceptibility to drug-induced QT prolongation require future study. References: 1. Manini AF, Nelson LS, Skolnick AH, et al. Electrocardiographic predictors of adverse cardiovascular events in suspected poisoning. J Med Toxicol 2010; 6:106–15.

Destaillats F 1, Cruz-Hernandez C 1, Guiffria F 1, Dionis F 1, Mostin M 1, Verstegen G 1.
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Objective: Pine nuts are traditionally consumed in Europe, but local production is not enough to meet the current demand. Therefore, pine nuts are primarily imported from Asian countries such as China, Korea or Pakistan. Over the last 10 years complaints were increasingly reported from consumers experiencing taste disturbances following consumption of pine nuts. Problems were reported with imported pine nuts. The exact geographical origin or botanical identities of the products were not reported. Methods: Authors previously proposed a method based on the analysis of sodium acid pyrolysis (SAP) of pine nuts to confirm the botanical origin of pine nuts. This method has been used to confirm that some of the pine nuts found in commercial products originate from species such as *Pinus armandii* instead of or in mixture with currently traded pine nuts. Results: Sixteen suspected pine nuts samples were analyzed. The fatty acid composition of the samples was determined and diagnostic index values were compared with the reference data for the botanical origin of pine nuts. This method has been used to confirm that some of the pine nuts found in commercial products originate from species such as *Pinus armandii* instead of or in mixture with currently traded pine nuts. *Pinus armandii* nuts were identified in all the samples, pure (n = 12) or in mixture with *P. koreensis* nuts (n = 4). Conclusion: All the samples, excepted nuts from *P. armandii* in mixture or not with *P. koreensis* nuts, confirmed that consumption of *P. armandii* nuts may lead to dysgeusia. The nature of the compound(s) responsible for the dysgeusia associated with *P. armandii* nuts is not reported in the Food and Agriculture Organization. Based on the present study and previous work, we advise companies to trade pine nuts from traditionally recognized species. Additionally we think that the food regulatory authorities should introduce a positive list of edible pine nuts in the legislation. References: 1. Munk MD. “Pine mouth” syndrome: cacaosia foliaceaa poisoning from pine nuts (genus: pinus). An emerging problem? J Med Toxicol 2010; 6:158–9. 2. Destaillats F, Cruz-Hernandez C, Guiffria F, et al. Identification of the botanical origin of pine nuts found in gas-liquid chromatography analysis of fatty acid profile. J Agric Food Chem 2010; 58:2082–7. 3. Seeds, fruits and cones. In: Non-wood forest products from conifers, edited by the Food and Agriculture Organization (OR 2004). Retrieved Online 1995. [http://www.fao.org/docrep/X00453E/X00453e12.htm. Accessed on 7 November 2010.](http://www.fao.org/docrep/X00453E/X00453e12.htm)
105. Novel Synthetic Cannabinoids, CRA13, JWH-015, JWH-081 and JWH-210 - Detected in a Case Series
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**Objective:** Inquiries to the Swedish PC concerning 'Spice'-type products, have increased rapidly and dramatically during 2010. These are plant materials abused by smoking and known to be deliberately spiked with synthetic cannabinoids (e.g. CP 47 497, HU-210, JWH-018). Methods: For two months in the period 2007 until the end of October 2010 concerning 'Spice' products, including product name, co-ingestants, inquirer, geographical location, age, sex and clinical features were collected. All cases with sufficient information were scrutinised and graded according to the poisoning severity score (PSS), and, when obtainable, compared to analytical data. Confiscated materials of 'Spice'-products were analysed by the Laboratory of Forensic Science and the Customs Laboratory and serum samples from poisoning cases were analysed by Karolinska University Laboratory. Results: A total of 214 cases were found, 42% were under 20 years old and 96% were 25 years or younger, with males being over-represented (78%). One hundred and forty-five cases were graded: 74% were mild (PSS 1); and 26% were moderate (PSS 2) poisonings. No severe or lethal (PSS 3 and 4) cases were registered. Most common clinical symptoms were tachycardia (51%), drowsiness (36%), mydriasis (28%), muscular symptoms (26%), hypotension (13%) and vomiting (12%). In 56 of these cases, 26 unique Spice-products were identified. Three new synthetic cannabinoids CRA13, JWH-081, JWH-210 were detected, and JWH-081 and JWH-250 occurred most frequently. In 22 cases, serum samples were available. Fourteen of these were positive for one or two cannabinoids; JWH-018 (2 cases), JWH-081 (11 cases), JWH-250 (2 cases) and another new cannabinoi JWH-015 (3 cases). Most of these patients experienced typical symptoms but a few also presented atypical symptoms, e.g. unconsciousness and loss of eyesight and speech. **Conclusion:** In the literature a few cases regarding Spice have been published. In our study four new synthetic cannabinoids were identified, and JWH-015, JWH-081 and JWH-210. Recently three of these became controlled substances in Sweden. Clinical features in this case series were mild or moderate.

106. Effects of BQ-788, an Endothelin B Receptor Antagonist, on Amitriptyline-Induced Cardiovascular Toxicity in Rats
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**Objective:** Sodium channel blockade in the heart and the decreased synthesis of NO by NO synthase in the main mechanisms of amitriptyline-induced hypotension. Although endothelin releases blood pressure via endothelin A (ETA) receptors by causing vasoconstriction, it can cause vasodilation by stimulating AT1 receptors and finishing the amitriptyline infusion, 5% dextrose (n = 8) and BQ-788 (n = 6) were given to control and experimental groups, respectively. **Results:** Amitriptyline-induced hypotension in MAP (48.7 ± 1.1% and 50.3 ± 1.8%), prolongation in QRS (183.4 ± 6.3% and 166.7 ± 8.6%) and decrease in HRs (73.3 ± 4.5% and 69.5 ± 8.8% for control and BQ-788 groups, respectively). BQ-788 improved MAP at 5, 10 and 15 minutes (61.2 ± 5.4%, 22.6 ± 4.1% at 5 min; 70.5 ± 9.1%, 23.6 ± 5.3% at 10 min; 69.6 ± 10.2% p < 0.01 and p < 0.05, respectively). BQ-788 also shortened the prolonged QRS at 5 and 10 minutes (150 ± 11.4%, 254 ± 25.2% at 5 min; 144.4 ± 7.0%, 225.0 ± 25% at 10 minutes in BQ-788 treated HRs at 5, 10 and 15 minutes (72.3 ± 9.9%, 31.4 ± 6.7% at 5 min, 74.6 ± 7.5%, 35.8 ± 12.8% at 10 min and 83.9 ± 3.8%, 40.4 ± 9.6% at 15 min, p < 0.05, respectively).References: 1. Kalkan S, Haco˘glu N, Arici AA, et al. Effects of adenosine receptor antagonists on survival in amitriptyline-poisoned mice. Drug Chem Toxicol 2010; 33:253–27. 2. He G, Liu M, Yang Q, et al. Role of endothelin-1 receptor antagonists in vasoconstriction mediated by endothelin and other vasoconstrictors in human internal mammary artery. Ann Thorac Surg 2007; 84:1522–7.

107. Epidemiology of Acute Intoxication in Croatia
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Department for Intensive Care Medicine, University Hospital Internal Clinic, Rebro, Zagreb, Croatia.

**Objective:** Epidemiology of acute intoxications and the rate of complications in Croatia were studied. The data of the last year were divided into two main groups: patients from our country and patients from other countries. Methods: All patients with acute intoxications admitted to the ICU during last year were included. Glasgow coma score (GCS), APACHE II score were measured on admission and after 24 hours (GCS1). Toxi-lab and gas-chromatography were performed. Level of consciousness, blood pressure, pulse, oxygen saturation, gas exchange and other laboratory findings were measured on a daily basis. X-rays were performed on admission, later if patients developed febrile complications and on discharge from ICU. Results: 34 patients were admitted in ICU during last year. Mean age 48.1 ± 17.1 (range 20–79). The majority of the patients (23), were intoxicated with pharmaceutica (71%), 7 patients were addicts intoxicated with drugs alone or with combination (18%); 4 patients had mushroom intoxications (Amanita phalloides). GCS0 8.5 ± 4.3 GCS1 13.3 ± 3.2, APACHE II 9.9 ± 4.6, APACHE III 13.2 ± 3.2. All patients needed additional oxygen supply, 5 patients needed mechanical artificial ventilation, all patients needed volume substitution, 3 needed vasoactive support. Two patients died, one from myocardium intoxication in multiple organ failure (MOF) and one by MOF caused by drug overdose. **Conclusion:** The total incidence of acute intoxications admitted to ICU in our country is stable. The most common intoxications were psychopharmaceuticals, as published in other countries.

108. The Public Health Role of Poisons Centres - Signals from Human Cases. Examples of Collaboration with Poisonous Centres and Public Health Authorities
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**Background:** With the Chemicals Act (ChemG), legislation in the Federal Republic of Germany has provided a basis to protect humans and the environment from harmful effects of active substances and preparations, particularly to make them recognizable, to avert and to prevent the development of such effects. Data on human toxicology that are obtained from the evaluation of cases of poisoning in humans are especially important for a realistic assessment of risks for human health. A physician who is consulted for treatment or evaluation of sequelae of diseases caused by chemical substances or products is obliged to submit essential data on poisonings to the ‘Centre for Documentation and Assessment of Poisonings’ at the Federal Institute for Risk Assessment (BfR). Additionally, in different European countries the contributors of products are obliged to notify formulations of chemical products (1990), cosmetics (1997), biocidal preparations (2002) and dietary supplements (2009) to the BfR for risk assessment and to provide the German Poison Centres (PCs) with formulations for emergency advice. The PCs assist the BfR by submission of data on health hazards resulting from their work. So in cooperation between BfR Committee: “Assessment of Poisonings” which has members of the German PCs, Industry, Universities, Consumer Councils and Ministries and based on two joint research projects with the German PCs, the BfR has implemented an effective toxicological network. **Results:** Since 1990 the BfR has received more than 78,000 reports. Additionally, the German PCs were provided with more than 280,000 product records. The “classic” distribution of cases in PCs is different to the BfR reports: The greatest part (90%) was due to accidents, 6% were hazards during normal use and only 2% of the cases were due to attempted suicides. More than 90% of the cases happened in adults, most of them at the work place. Only 7% happened in children. Collaboration between the national and the federal German PCs and the BfR have been developed in the Länder (German federal states) according to the American model. Renowned experts were appointed to the Committee who supported the German poison information centres’ consultation and treatment of accidents. The Committee, on which more than 190 experts have collaborated up to now, provides input for the European network. For the development of the Committee BfR proposed the EU-wide restriction of the sale of paraffin-containing, coloured and perfumed lamp oils which led to a marked drop in poisonings. Also the EU standard on “Child-resistant closures” the restrictions on methanol in consumer preparations and changes in formulations and warnings on mechanical dishwashing products are shown. The Committee has shown that there must be better orientation on the labels and packages to identify the real trade-name with these oils. Also the EU standard on “Child-resistant closures”, the restrictions on methanol in consumer preparations and changes in formulations and warnings on mechanical dishwashing products are shown. The Committee has shown that there must be better orientation on the labels and packages to identify the real trade-name with these oils. The Committee concluded that it is necessary to have a number of intoxication accidents with these oils.
The success of RAS-CHEM is intrinsically important to enable EU Member States to protect their citizens from these hazards; RAS-CHEM has the potential to provide this service throughout the EU.

110. Clinical Effect Profiles for Chemical Agents of Concern - Role of Syndromic Surveillance and Rare Symptoms


Objective: The aim of the ASHTII project is to develop a Rapid Alert System for Chemical Health Threats (RAS-CHEM), to facilitate the rapid exchange of information on relevant events, which have the potential to become public health threats, and to improve national response strategies to real or potential chemical incidents, including deliberate and accidental releases, for the benefit of all EU Member States.

Introduction: As part of the ASHTII project, RAS-CHEM has been further developed and extended to allow different levels of access to the alerting system by the creation of the risk assessment (formerly termed EUPC Forum) and risk management tiers to RAS-CHEM. For RAS-CHEM to operate successfully in an interdisciplinary multi-language environment it is important to adopt standardised terminologies to describe clinical effects associated with exposure to chemical agents and standardised classification and nomenclature for the agents. To effectively identify a comprehensive range of clinical effects and development of non-formal reporting system for chemical health threats. RAS-CHEM will identify sentinel exposure events allowing efficient communication of risk, assessment and intervention in a coordinated manner, from the local level up through national structures to the other EU Member States. In addition RAS-CHEM will operate in the context of the new EU-wide chemical monitoring system (ChemAlert) and the German harmonized categories. Conclusions: Signals from human cases, analysed on a national monitoring level, are of great importance for initiating preventative measures. The documentation of signals from human cases is mainly based on the excellent collaboration between PCs and Public Health Authorities. RAS-CHEM provides a mechanism for facilitating the rapid communication of chemical health threats, ranging from reports on unusual cases to potential mass poisoning incidents. RAS-CHEM also provides toxicological profiles for toxic chemicals that can be used to identify potential agents of intoxication. RAS-CHEM has been extensively tested and the results from these evaluations have been fed into the iterative design of the system. The informatics application allows a real time exchange of information among two different sectors of users in the 27 EU Member States: the risk assessment sector and the risk management one, with precise rules and standard operational procedures for operating and accessing the system; the second sector encompasses a specific user, the Member State and the integration of the system into current health threat reporting structures from the local or regional level (poisons centres) through the National level (national public health officials or health ministers) to the International forum (Commission, EU Member States and WHO); 3: successful integration of the RAS-CHEM into Member States' rapid assessment and management of chemical health threats is essential to enable EU Member States to protect their citizens from these hazards; RAS-CHEM has the potential to provide this service throughout the EU.
oped by IPCS/EAPCCT was used, where appropriate. From the 118 chemical agents included in the literature review, over 1000 clinical effects were collated. This list was then cross-checked for missing terms needed to describe any features of symptoms of poisoning that may have been missed during the initial literature review. An additional 200 terms not previously identified during the literature review were added to the list.

Conclusion: The ASHTII project team has further developed the concept of the RAS-CHEM to provide DG. SANCO with a central alerting tool enabling Member States to warn each other and to share information regarding chemical accidents or threats that may have cross border implications. It is important to the overall success of the ASHTII project that RAS-CHEM can capture the whole range of symptoms associated with exposure to a given chemical rather than being limited to non-specific broad clinical terms. CEPs are intended to be used as ‘agent-related model cases’ in the database. RAS-CHEM users with no knowledge of toxicology will be able to search for chemical agents and easily find selected or all potential symptoms caused by this agent. Another way of using the data from the CEPs is to search for all agents that cause the symptoms selected by the user, including all real cases and all model cases stored in the database. The so-called ‘syndrome surveillance’ may be a key in the search for the cause of the increased frequency of unusual symptoms of unknown origin in the database or in the poison centres in one or several countries of Europe.


Objective: The aim of this study was 1) to assess a variety of factors related to cyanide/nitrile poisoning, 2) to describe the clinical spectrum of cyanide/nitrile poisoning, 3) to identify potential treatment approaches for cyanide/nitrile poisoning, and 4) to identify potential treatment approaches for cyanide/nitrile poisoning. Materials and Methods: A retrospective study of all patients with cyanide/nitrile poisoning admitted to the emergency department of the University Hospital of Zürich, Switzerland, from January 1, 2005, to December 31, 2009, was performed. Results: A total of 147 patients with cyanide/nitrile poisoning were included in the study. The most common cause of cyanide/nitrile poisoning was industrial exposure (n = 87; 59.3%), followed by suicide attempts (n = 35; 23.9%), accidental exposure (n = 17; 11.6%), and environmental exposure (n = 8; 5.4%). The most common symptoms were respiratory (n = 140; 95.4%), cardiovascular (n = 109; 74.5%), and neurological (n = 96; 65.5%). The most common treatment was oxygen therapy (n = 147; 100%), followed by hydroxocobalamin (n = 37; 25%), thiosulfate (n = 30; 20%), and activated charcoal (n = 16; 11%). Conclusion: Cyanide/nitrile poisoning is a severe and relatively uncommon condition. The availability of antidotes is crucial for the management of cyanide/nitrile poisoning. Further studies are needed to improve the treatment of cyanide/nitrile poisoning.
Objective: Prognostic factors of cyanide poisoning remain unknown. We attempted to assess determinants of the Poison Severity Score (PSS) in cyanide poisonings. Methods: Published and two unpublished cases with individual data included by poison experts, except FJB. Analysis was made by an independent expert (PL) using Stepwise General Linear Model to predict PSS from the variables. All cases were analysed including those with missing data handled by maximum likelihood optimization. Results: In 283 cyanide poisonings, high concordance of PSS was found between the two raters (Kendall τ = 0.94). Mild, moderate, severe, and lethal PSS were 33, 19, 29, and 19% respectively. Five determinants predicted severity (R² = 0.377, p < 0.001): 1) the dose with Incremental Effect IE = 1.07Log(dose), 95%CI [0.85,1.29], 2) the delay in presentation with 7-fold and 10-fold increase in PSS 3 and 4 when delay was more or less than 2 hours, respectively 3) age: greatest severity was observed in young and old patients; 4) women: more vulnerable than men. 5) gaseous HCN with greatest severity IE = +0.74 [0.53,0.94] compared with salts and cyanogen. Conclusion: The most potent predictors of PSS were the dose and the delay in presentation and cyanide type were secondary potent predictors. The delay in presentation, including recognition of cyanide poisoning and prompt treatment were factors that may be improved by preparedness.

114. Systematic Review of Efficacy and Adverse Effect of Methemoglobin Forming Antigens in Cyanide Poisoning. Preliminary Results

Objective: Acute cyanide poisoning is an extremely serious event due to the potentially fatal outcome. A study was undertaken by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECE-TOC) to evaluate the efficacy and adverse effect of methemoglobin forming antigens using all available sources. Methods: Evaluation was performed of all case reports of cyanide intoxications which were treated by Met-Hb-forming agents ever published and of non-published cases from European PCCs. All cases (n = 336) were classified according to source of intoxication, severity determined by an adapted PSS (excluding PSS 6) and the outcome. Two hundred and sixty-four (78.5%) were treated with the US antidote kit (amyl nitrite, sodium nitrite, and sodium thiosulfate). Forty-one patients (12%) received pyridine, 31 patients (9%) were given 4-DMAP and thiosulfate. One hundred and thirty-five persons (40%) were poisoned by HCN/cyanide salts, 155 (46%) by nitrites, 34 (10%) by cyanide, 41 carried dimethylaminophenol, 35 thiosulfate and 10 hydroxocobalamin. Administration was reported in one case only. Four hundred and thirty-two fire related fatalities were registered in Germany in 2009, in 238 of these cases smoke intoxication was stated as cause of death. Ten fatalities caused by hydrogen cyanide or cyanide salts were officially notified. Conclusion: Severe fire smoke intoxication is much more frequent than (pure) cyanide intoxication. At least 16% of smoke fatalities (39/238) died out-of-hospital despite intensive medical care. Cyanide antidotes are usually available for emergency physicians in the preclinical setting in Germany, the use in smoke intoxication exposures is rare. Recently started analytical studies, one of these in the authors’ hospital, will provide further evidence on the role of cyanide and thus the potential role of cyanide antidote application in several fire smoke intoxications. References: 1. Zilker T, Seefrin G, Scherer B, et al. Intoxication through Smoke Exposure: A Toxicological Challenge. In: Deter, W. (Ed.). Der Notarzt 2010; 26: 95–102. 2. www.google.de, accessed 2009-01-01 to 2010-09-30. 3. Gesundheitsberichterstattung des Bundes, www.gbe.de, accessed 2010-11-15.

115. Potential for Effective Preclinical Use of Cyanide Antidotes after Fire Smoke Exposures
Kaiser G, Deusinger F. GIZ/Noral Poisons Centre, University Medical Center, Göttingen, Germany

Objective: Recently, hydroxocobalamin has become available for antidotal use in Germany and leading medical experts recommended its use for severe smoke intoxication immediately after. To evaluate the potential of smoke intoxication the incidence and mortality of smoke intoxications and the actual patient treatment were investigated for the year 2009. Methods: All media reports about presumptively severe fire smoke exposures in Germany listed in Google News Deutschland in 2009 were analysed. In cases with Emergency Medical Service (EMS) treatment, additional information was requested from the local services by questionnaire within a 12 month period. For comparison, national statistics on mortality due to fire smoke exposures were evaluated. Results: 141 cases of severe smoke intoxication treated by EMS were available for analysis. 91 patients survival was provided, failing in 39 cases. An additional 19 patients died after admission to hospital. Cyanide antidotes were available for their treatment: 41 carried dimethylaminophenol, 35 thiosulfate and 10 hydroxocobalamin. Administration was reported in one case only. Forty, and three two fire related fatalities were registered in Germany in 2009, in 238 of these cases smoke intoxication was stated as cause of death. Ten fatalities caused by hydrogen cyanide or cyanide salts were officially notified. Conclusion: Severe fire smoke intoxication is much more frequent than (pure) cyanide intoxication. At least 16% of smoke fatalities (39/238) died out-of-hospital despite intensive medical care. Cyanide antidotes are usually available for emergency physicians in the preclinical setting in Germany, the use in smoke intoxication exposures is rare. Recently started analytical studies, one of these in the authors’ hospital, will provide further evidence on the role of cyanide and thus the potential role of cyanide antidote application in several fire smoke intoxications. References: 1. van der Schans GP, Scheffer AG, Mars-Groenendijk RH, et al. Immunochromatographic detection of adducts of sulfur mustard to DNA of calf thymus and human white blood cells. Chem Res Toxicol 1994; 7:408–13. 2. Smith, WJ. Vascular patients and antivesicant medical countermeasures: clinical toxicology and psychological implications. Mill Psycho 2002; 11:145–57.

117. Analyzing the Diagnostic Value of Amanita-ELISA in Mushroom Poisoning
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Objective: Poisons containing amatoxins are a common feature in autumn and provide a challenge for clinical toxicologists, poison centres and analytical facilities as well. Whereas symptoms are quite characteristic, the diagnostic potential of these analytes remains under discussion. To evaluate this, clinical data of intoxicated patients were matched to analytical results. Methods: The Poison Information Centre Berlin processed 412 calls concerning human mushroom exposures between January 2000 and October 2010. Comparing the last seven years, the number of contacts peaked in the year 2010 with a total of 493 calls which was due to an exceptional occurrence of mushrooms. In 79 cases of these the diagnosis of amatoxin-poisoning was assumed or confirmed. In parallel, 52 urine samples were analyzed for amanitines using an ELISA method, (Fa. Buehllmann, Switzerland). Results: In ten patients amanitines were detected in a concentration higher than 10 ng/mL judged as positive. Nine of these intoxications were related accidentally self-harm was assumed. The median latency between the ingestion and start of symptoms was 14.5 hours. All patients were hospitalized 29.4h at median after the ingestion of mushroom. The median concentration of amanitine in urine was 63.4 ng/mL (15.3–125.1 ng/mL). In four of ten cases amanitines were detected later than 48 hours after exposure (median 57.9 hours). All patients tested positive had the typical symptoms of amatoxin-intoxication - nausea, vomiting, abdominal pain, diarrhea, elevation of liver enzymes and coagulopathy. The maximal ALT-value was 3907 U/L, the maximal AST-value was 3242 U/L and lowest median prothrombin time was 53%. Nine patients were treated with activated charcoal and laxative. All patients received sildinib intravenously. Three patients were additionally treated with penicillin. Six patients got N-acetylcysteine intravenously. All ten patients survived without liver transplant treatment. The immunoassay is specific and sensitive enough to detect amatoxin intoxications. A positive correlation between amatoxin urine concentrations and maximum liver enzymes was observed. This study has to be focused on the risk of false negative test results in early samples (<8 hours). References: 1. Butera R, Locatelli C, Coccini T, et al. Diagnostic accuracy of ELISA for detection of mushroom poisoning: a pilot study. J Toxicol Clin Toxicol 2004; 42:901–12.
Table 1. Plant cases with fatal outcome reported to the Swiss Toxicological Information Centre 1995–2009

<table>
<thead>
<tr>
<th>Age</th>
<th>Plant</th>
<th>Symptoms</th>
<th>Therapy</th>
<th>Causality</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>Taxus baccata</td>
<td>Tachycardia, bradycardia, AV-Block Grade 3, asystolia</td>
<td>activated charcoal, atropine, magnesium, diazepam, pacemaker, defibrillation</td>
<td>probably confirmed</td>
</tr>
<tr>
<td>3</td>
<td>Colchicum autumnale</td>
<td>Bradycardia, cerebral edema, vomiting, seizures, respiratory and hepatic failure</td>
<td>supportive therapy</td>
<td>analytically confirmed</td>
</tr>
<tr>
<td>57</td>
<td>Colchicum autumnale</td>
<td>Pulmonary edema, arrhythmia, coagulopathy, renal failure</td>
<td>Multiple dose activated charcoal, supportive therapy</td>
<td>analytically confirmed</td>
</tr>
<tr>
<td>62</td>
<td>Colchicum autumnale</td>
<td>Renal failure, myoglobinuria, necrosis, coagulopathy</td>
<td>Multiple dose activated charcoal, supportive therapy</td>
<td>analytically confirmed</td>
</tr>
</tbody>
</table>

118. Acute Severe and Fatal Plant Poisoning: Analysis of Clinical Features and Circumstances of Exposure

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Objective: Human contact with potentially toxic plants, which may occur in abuse or in an accidental or suicidal setting, is frequent and sometimes results in clinically significant toxicity. The aim of the present study was to identify which plants may lead to severe poisoning and to define the clinical relevance of plant toxicity for humans in Central Europe. Methods: By means of a retrospective case-study design, we analysed 42,193 cases of human plant exposure and 255 acute moderate, severe and lethal poisonings, which were reported to the Swiss Toxicological Information Centre between January 1995 and December 2009. We present here the severe and fatal cases. Results: We found 45 severe and 4 lethal poisonings. Fifteen plants were responsible for these cases, foremost among them the abuse of Datura spp by ingestion, although no fatalities resulted from its ingestion. Other frequently involved plants were Atropa belladonna, Aconitum napellus and Euphorbia spp. The 4 fatal cases: one suicide with Taxus baccata; and 3 accidental ingestions of Colchicum autumnale mistaken for Allium ursinum are reported in cases 1. In all but one of the severe cases, a complete recovery was documented (one case of permanent visual impairment after ocular contact with corrosive Euphorbia plant sap). Conclusion: Plant contact was rarely responsible for serious poisoning. Fatal intoxications were extremely rare and were caused by plants with cardiotoxic (Taxus baccata) or misoec inhibiting (Colchicum autumnale) properties. A complete recovery can usually be expected even in severe cases.

119. Epidemic of Physalis physalis Stings on the French Atlantic Coast During Summer 2010

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Introduction: Man-of-war (Physalis physalis) is a marine animal which is the cause of severe envenomation in tropical seas. In Europe stings induced by this pelagic species are rare. During the summer of 2008, 40 cases were reported by the Bordeaux poison centre. This first man-of-war epidemic case series was considered as an exceptional event but during the summer of 2010, such a phenomenon was observed again on the French Atlantic Coast. Methods: In order to evaluate the health impact of the second Aquitaine region man-of-war bloom, the Bordeaux Poison Centre performed a survey concerning the summer medical activity of 577 coastal practitioners and 57 first-aid stations on the beach. Case series: 124 observations were collected in 3 departments, "Landes" (79%), "Pyrénées Atlantiques" (16%), "Gironde" (2.5%) unknown location (2.5%). Patients were mainly men (OR = 1.6) with an average age of 19.4 years ± 14, with 58% of children less than 15 years. Surprisingly patients were mainly standing on the upper limb (66%) and in contact for less than 1 minute. Of the species involved, P. transvaalicus was scientifically identified for 37% of the cases and highly suspected thanks to the patients’ descriptions for 63%. Transient pain, paresthesia, or tingling were constant symptoms (100% of the patients describing burning, electric shock sensations, 36% of them with complete limb pain). Local skin burns were observed for all patients, and systemic symptoms were reported in 46% of them (26% myalgia, 25% abdominal pain, 21% malaise, 14% nausea, 13% respiratory distress). All patients were managed by the first-aid beach system with referral to practitioners (11%) and to hospital (6%). All patients managed with symptomatic treatment in the hospital recovered in about 24 hours. Conclusion: The second epidemic case series of man-of-war stings observed in 3 years in the Aquitaine region is much more important than the first one (124 patients compared to 40). After the description of two collective episodes of man-of-war envenomations on the French Atlantic Coast, the local health structures must be prepared in order to be able to manage new blooms and more envenomed patients in future summers. References: 1. Labadie M, Lombrot AL, Cavalli M, et al. Collective envenomation by Physalis physalis on the French Atlantic Coast. Clin Toxicol 2010; 48:309.

120. Parabuthus granulatus Identified as the Most Venomous Scorpion in South Africa: Motivation for Development of a New Antivenom

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Objective: The efficacy of the currently available scorpion antivenom in South Africa is questionable. At best, a moderate therapeutic effect is seen 4–6 hours post administration. This antivenom is manufactured from the venom of Parabuthus transvaalicus. In view of the above, a study was undertaken to assess and identify the scorpion species responsible for cases of severe scorpionism in South Africa in order to facilitate the development of a more effective and rapid-acting antivenom. Methods: A retrospective study of all cases of scorpionism (scorpion sting associated with systemic toxicity) dealt with by the Tygerberg Poison Information Centre over a period of 10 years was undertaken. The geographical locations of all the cases as well as the identification of species involved were recorded. Results: Of the 148 cases studied, 95% occurred in the Western and Northern Cape provinces. In 38 of the 148 cases, the scorpion was available for identification. All of them were identified as Parabuthus granulatus.

Conclusion: The medically important scorpions in southern Africa belong to the Parabuthus genus. In addition to the highly toxic species, Parabuthus scorpion stings may cause a life threatening toxic syndrome. Respiratory failure, which may develop within one to two hours post envenomation, is usually the primary cause of death. The finding that P. granulatus was the only scorpion species involved in scorpionism was unexpected. It is important to note that P. transvaalicus (the venom of which is used in the production of the current antivenom) does not occur in the Western and Northern Cape, areas known for a high incidence of scorpionism. The most probable reason, therefore, for the sub-optimal efficacy of the antivenom is that the venom of the wrong scorpion is used in its production. In light of this, a strong case exists for the development of a specific P. granulatus antivenom, or the inclusion of both P. granulatus and P. transvaalicus venom in the production of a polyvalent antivenom.

121. A Randomised Controlled Trial of Two Infusion Rates to Decrease Reactions to Antivenom

Ibister GK1,2, Shahry S2, Makarin MM2, Fahim MF1, Abouille CG1,2, Karunatilake H1, 1Department of Clinical Toxicology and Poison Control, Calvary Hospital and School of Medical Practice, University of Newcastle, New South Wales, Australia; 2South Asian Clinical Toxicology Research Collaboration; 3Faculty of Medicine, University of Peradeniya, Peradeniya; 3General Hospital, Chilaw; 3Department of Clinical Medicine, University of Colombo, Colombo, Sri Lanka

Objective: Snake envenoming is a major clinical problem in Sri Lanka, with an estimated 40,000 bites annually. Antivenom is only available from India and there is a high rate of hypersensitivity reactions. This study aimed to investigate whether the rate of infusion of antivenom reduced the frequency of severe hypersensitivity reactions. Methods: This was a randomized comparison trial of two infusion rates of antivenom for the treatment of non-pregnant adult patients (>14y) with snake envenoming in Sri Lanka. Snake identification was by patient or hospital examination of dead snakes when available and confirmed by enzyme-immunoassay for Russell’s viper vepining. Patients were blindly allocated in a 1:1 randomisation schedule to receive antivenom either as a 20 minute infusion (rapid) or a two hour infusion (slow). Results: Of 811 patients presenting with suspected snakebites, 225 patients received antivenom. Twenty-five patients were excluded or not recruited leaving 103 patients allocated to the rapid antivenom infusion and 97 to the slow antivenom infusion. The median duration of antivenom infusion in the rapid group was 20 minutes (Interquartile range [IQR]: 20–25 minutes) versus 120 minutes (IQR: 70–120 minutes) in the slow group. Severe systemic allergic reactions (anaphylaxis) occurred in 26 patients (25%) receiving the rapid infusion compared to 28 patients (29%) receiving the slow infusion which was not statistically significantly different (4%; 95% CI: [–0.6%, 4.1%]). The frequency of mild/moderate reactions was also similar between groups. Similar numbers of patients in each arm received further doses of antivenom (71 of 103 versus 92 of 97 to the slow antivenom infusion. The median frequency of mild/moderate reactions for the rapid group was 20 minutes (Interquartile range [IQR]: 20–25 minutes) versus 120 minutes (IQR: 70–120 minutes) in the slow group. Severe systemic allergic reactions (anaphylaxis) occurred in 26 patients (25%) receiving the rapid infusion compared to 28 patients (29%) receiving the slow infusion which was not statistically significantly different (4%; 95% CI: [–0.6%, 4.1%]).
122. Poisoning by Topical Medications
Nelson LS, New York City Poison Control Center, New York, NY.

Objective: To review the pharmacology and toxicology of transdermal drug delivery, including the functional barrier role of the skin, relevant physicochemical properties of transdermal agents, clinical considerations, and drug delivery misadventures. Discussion: Drug may be applied directly to the skin or may be applied in the form of a transdermal delivery system, or a patch. Medication may be delivered by the concentration gradient between the stratum corneum and the patch. Many medications are available in transdermal formulations, including buprenorphine, clonidine, diolcetan, estrogens, lidocaine, methytrexatin, scopine, and testosterone. In order to access the circulation a chemical must pass through the stratum corneum, which is impervious to hydrophilic compounds, and subsequently dissolve in the aqueous subcutaneous tissue. A compound therefore must be sufficiently soluble in both lipid and water, or a carrier substance can be used to enhance permeation. Although there are clinical benefits of transdermal delivery (e.g. long term, continuous delivery, convenience) and the number of transdermal products is increasing, this route of absorption is subject to substantial inter and intra-individual variability that may prove consequential. Among the dermat variables that can predictably alter delivery are the thickness of the stratum corneum, amount of subcutaneous tissue, integrative dermae, and hydration status. There are a number of patch technologies available, including matrix patches, reservoir type, membrane matrix hybrid type, drug-in-adhesive patches and micro reservoir patches. The reservoir patch holds liquid medication in bulk in contact with the skin across a semipermeable, rate controlling membrane. Medication in a matrix patch is dispersed within a polymer that is in contact with the skin. Regardless of the technology, patches typically contain a large amount of drug that can cause problems both to those intending to abuse (such as with fentanyl) and to children (such as with clonidine). Among the transdermal medications currently available, the fentanyl patch is associated with the greatest toxicologic importance. This patch formulation is indicated for the treatment of chronic pain in opioid tolerant individuals, and not indicated for the control of acute pain, intermittent pain, or postoperative pain, and should not be used for opioid-naive patients. The drug is absorbed from a depot in the upper skin layers, and the drug slowly diffuses through the remainder of the skin and is uptaken systemically. Plasma fentanyl concentrations are barely detectable for about 2 hours after patch placement, and the time for maximum plasma concentrations can range from 12 to 48 hours. When the fentanyl patch is removed, fentanyl continues to be absorbed into the systemic circulation from the depot. Fentanyl concentrations in plasma and urine remain elevated for about 17 (range 13–22) hours. Fentanyl absorption may increase slightly with fever or substantially with the amount of external heat (e.g. heating pad, hot tub). Concern over patch leak due to a manufacturing defect with subsequent leaking led to a recall of certain patches. The affected patches were immediately removed from the market. Fentanyl in the reservoir patch may be extracted with a hypodermic needle and self-administered. This practice may lead to clinical toxicity, the abuse potential of fentanyl. Fentanyl Pharmacokinet 2000; 38:59–89. 2. Marquardt KA, Tarratt RS, Musallam NA. Fentanyl remaining in a transdermal system following three days of application. Ann Pharmacother 1999; 33:2996–71. 3. Anderson DT, Muto JJ. Duragesic B® transdermal patch: postmortem tissue distribution of fentanyl in 25 cases. J Anal Toxicol 2000; 24:627–34. 4. Nelson L, Schwaner R. Transdermal fentanyl: pharmacology and toxicology. J Med Toxicology 2009; 5:230–41.

123. Notification and Reporting Health Threats Caused by Chemicals and Radiological and Nuclear Agents (RAS-CHEM): The Informatics Tool, Networking for Risk Assessment and for Risk Management
Guglielmo P, Busters B, ASHTIL, CARRA-NET, CARMEC, CIE-Toolkit and EU Exercises working groups, SANCO C3, Health Threats Unit, European Commission; SANCO AM, Informatics Systems, European Commission, Luxembourg.

Introduction: Risk assessment and management of chemical health threats (as well as of other health threats of biological, radiological and nuclear origin) with cross border impact need to be coordinated to ensure the safety and security at EU level. Under the current Treaty the European Commission coordinates the response to cross border health threats, including those of chemical origin. A number of actions and initiatives are supported through funding targeted to strengthening the preparedness and response to such health threats under the Health Program 2008–2013. The existing mechanisms of coordination through the EU Health Security Committee (HSC) allow additional support in order to ensure coordination and alignment of public health measures between national authorities, the European Commission and the relevant EU agencies. Among the priorities identified both in the HSC work plan and in the public health program initiatives are targeted to develop mechanisms for information exchange, consultation and coordination for the handling of health-related issues linked to acts of terror in which biological and chemical agents might be used or have been used. The current public health work programme seeks to address gaps in the effective assessment and management of chemical health risks at the local, national and EU level. Understanding and agreeing on how the deliverables from these actions and projects can be integrated into the public health measures of Member States is essential for the successful coordination of the response to cross border chemical health threats within the EU. Methods: To bridge gaps in the operational repertoire in order to respond more effectively to cross border events caused by chemical incidents a number of innovative actions and projects have been funded under the Health Program 2008–2013: 1. The IT platform CARRA-NET (Rapid Alert System for Chemical Health Threats Project [2007210]) aims to identify sentinel exposure events, detected at the poison centre level, allowing agencies to implement a national crisis management plan; and 2. The CIE-Toolkit (The Public Health Response to Chemical Incidents and Emergencies Toolkit [2007205]) aims to establish a network of risk assessors) will improve the safety and security of EU citizens and will increase the ability to answer questions about the safety and security of EU citizens and improve the ability to answer questions about the safety and security of EU citizens.

124. European Poison Center Reporting Database - Building on the US Experience
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Objective: To summarize the National Poison Data System (NPDS) development experience and applicability to EU manufacturers and distributors. The American Association of Poison Control Centers (AAPCC) operates the NPDS. The original system became operational in 1983 with call data originally recorded on paper卡片. The current system is center centric. The PCs have access to their own data and US national aggregate data as well as many pharmaceutical and chemical manufacturers for product surveillance and regulatory compliance. Geographic identifiers allow for graphical representation of case data. NPDS is hosted in a protected facility and available via a secure website to PC staff at the 60 PCs. Each PC submits data in a standardized format from information and exposure cases collected during the course of providing telephonic patient tailored exposure management. Most enter data contemporaneously during the call obviating the need for paper charts. Over 50 data fields are submitted to NPDS. These include a variety of demographic items such as sex, race, age, and state of residence. The database is continually updated and provides information that is typically difficult to obtain for smaller centers. Geographic identifiers allow for graphical representation of case data. NPDS is hosted in a protected facility and available via a secure website to PC staff at the 60 PCs. Each PC selects a regional organization administrator who assigns users roles for that PC. PC data are secured. Geographic identifiers allow for graphical representation of case data. NPDS is hosted in a protected facility and available via a secure website to PC staff at the 60 PCs. Each PC selects a regional organization administrator who assigns users roles for that PC. PC data are secured. Geographic identifiers allow for graphical representation of case data. NPDS is hosted in a protected facility and available via a secure website to PC staff at the 60 PCs. Each PC selects a regional organization administrator who assigns users roles for that PC. PC data are secured.

Abstracts 227
and any of the more than 150 case based surveillance definitions (including syndromic surveillance) definitions that regional PCs and national users such as CDC have created to detect and track public health events. In addition, because all case types are recorded and in real time, surveillance tools are invaluable when assessing the size that both manufacturers and consumers understand health and environmental risk of product use. PCs and NPDS data tools play a vital role in this effort. PCs have developed data definitions and surveillance tools such as RODS (Real-time Outbreak and Disease Surveillance). Data can also be accessed by enterprise reports and customized queries for both PC study and manufacturers. PCs attempt to specifically identify the products involved in each exposure. The PCs and NPDS rely on the products database (Micromedx Healthcare Series [Internet database]. Greenwood Village, CO, US: Thomson Reuters [Healthcare] Inc.). The database includes US and international products. The products database contains over 360,000 pharmaceutical and chemical products and is continuously updated. Products are assigned unique numeric codes in 7 major categories. Currently, NPDS uses a standard list of 131 clinical effects that have been developed over the past 27 years. Case management outcomes are categorized into one of 11 medical outcomes. Results: The cumulative AAPCC database now contains over 51 million human exposure case records. A total of 13,010,466 information calls have been logged by NPDS since the year 2000. The median time for data upload in 2009 was 19.9 minutes [9.7, 58.7] (median [25%, 75%]). Over 154 case based definitions and 223 volume definitions run daily. Case data is shared with CDC National Center for Environmental Health - Health Studies Branch at the Centers for Disease Control and Prevention (CDC). NPDS has 518 active users who have executed thousands of enterprise reports and surveillance queries. Manufacturers request data about their products. Numerous product recalls from selenium to peanut butter have been tracked by NPDS. Several State Health departments access NPDS data via the web services in a federated approach. NPDS data can monitor single or multiple exposure outbreaks providing information on exposure patterns. The feature of the NPDS that can assist manufacturers and government in tracking usage trends and events of public health significance. Rapid identification of unexpected adverse effects can prevent or minimize risk and liability. Agencies can track the results of governmental rule changes and post marketing surveillance mandated efforts. Recent analyses have shown that deployment of these systems can result in savings of development costs and can help minimize risk and liability. Although identification of the index case is the holy grail of computer surveillance systems, these systems are most valuable in showing evolving exposure patterns. With the advent of near - real time mapping (GIS), geographical visualizations can aid outbreak analysis. Lastly, outbreaks can be the source of new hypotheses. The unique share data between NPDS and other systems like RAS-CHEM is imperative. Maximizing the ability to share data especially during an outbreak is vital. Although data collection may be different, a common import export such as use of MedDRA clinical effect terms is essential. Conclusion: NPDS contains 27 years of US poison information and exposure data. National aggregate data is freely accessed by the 60 US PCs and affiliated organizations. The Rapid Alert System for Chemical Threats (RAS-CHEM) shares features of NPDS and can provide similar EU reporting capabilities. The advantage of both systems under the federated manner is imperative. References: 1. Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2008 Annual Report of the American Association of Poison Control Centers’ Poison Incidents (AAPCC). 2. NPDS: 26th Annual Report. Clin Toxicol (Phila) 2009; 47:911–1084. 228 2009; 47:911–1084.

127. Taxines are not Effectively Removed by Hemodialysis

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Introduction: Yew plants are highly toxic, with reported fatalities in humans and animals. Taxine A and B, the toxic alkaloids of Taxus baccata, block sodium- and calcium-channels mainly in cardiomyocytes, inducing conduction abnormalities up to cardiac arrest. We present a severe T. baccata poisoning case, after an unexpected intentional consumption of parts of a yew plant, in a patient treated with hemodialysis. This allowed us to test the hypothesis - based on the physicochemical properties of taxines (molecular weight > 500 Da, relatively water-insoluble) - that they have similar distribution (60 L/m2) of the related chemotherapeutic drug paclitaxel - that taxines are not effectively removed by hemodialysis. Case report: A 17-year-old patient was admitted to the Emergency Department the ECG showed a premature ventricular tachycardia with an irregularly variable QRS-axis (torsade-like). Magnesium (2 g) and amiodarone (300 mg) were administered i.v. and electrical cardioversion was performed. The dysrhythmia disappeared into pulseless electrical activity, followed by asystole. He was intubated and advanced cardiac life support was initiated (duration: 30 minutes). He regained a bradycardic broad-complex rhythm, but required repetitive intermittent cardiopulmonary resuscitation because of recurrent episodes of hemodynamically unstable sustained ventricular tachycardia. A temporary transvenous pacemaker was inserted and catecholamines were administered. Hemodialysis was initiated due to progressive metabolic acidosis unresponsive to sodium bicarbonate. The patient gradually improved after 36 hours with restoration of sinus rhythm. He recovered without sequelae. He admitted having ingested T. baccata with suicidal intention. The toxicological-screening was negative for benzodiazepines. Quantification of serum and dialysate concentrations of taxine B was performed by liquid chromatography-tandem mass spectrometry (LC/MS/MS). Serum taxine B concentration at 6 hours was 126 ng/mL (+100%), 90.7 ng/mL (72%), and 83.2 ng/mL (66%), respectively. Dialysate taxine B

Acute Cocaine Toxicity

Heard KJ, Toxicology and Poison Center, Denver, Colorado, US

Long-term administration of antipsychotic medications alters the distribution of several neurotransmitter receptors in animal models. Several of these neurotransmitter receptors are relevant to cocaine poisoning, but the effect of altering the distribution of these receptors on cocaine poisoning is unknown. Many patients who abuse cocaine use antipsychotic medications, increased sensitivity to cocaine would have significant health implications. Methods: It was our hypothesis that administration of common antipsychotic medications for 21 days will decrease the LD50 of cocaine in a mouse model. Methods: This was a placebo-controlled, IACUC approved study using male CF-1 mice weighing between 25 and 40 g at baseline. Study drug doses were determined in preliminary experiments to produce therapeutic concentrations with oral dosing in drinking water. Study drugs were dissolved in 5% dextrose to deliver the following doses: haloperidol 3.3 mg/kg, olanzapine 10 mg/kg, ziprasidone 20 mg/kg. Placebo was delivered. After 21 days of treatment, mice were tested for cocaine toxicity. Results: Seven mice were tested for each drug and one mouse was killed for each mouse that died over the course of the study. There were no significant differences between the groups. Conclusion: Antipsychotic medications increase sensitivity to cocaine poisoning, but the small changes in sensitivity suggested by our work are not likely to translate into a substantially increased risk of cocaine poisoning for humans taking antipsychotic medications.

125. Effect of 21 Days of Antipsychotic Medication Administration on the Sensitive to Mice to Acute Cocaine Toxicity

Acute Cocaine Toxicity

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Clinical Toxicology vol. 49 no. 3 2011

Abstracts

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Heard KJ, Toxicology and Poison Center, Denver, Colorado, US

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129. Disulfiram like Syndrome after Consumption of Chopped Edible Mushrooms (Echinodermata aspera) with Ethanol - a Case report

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Objective: Disulfiram-like acetahedydrome is well known after consumption of the coprine containing Cephalotaxus austrasominus in combination with ethanol. Here we report two events involving three patients who experienced similar symptoms after a meal of the mushroom Echinodermata aspera (formerly Lepiota aspera) with rice and wine collected at a museum of saffron (Mund, Switzerland). She collected the stamens of a flower resembling Crocus sativus. The similarity in this case is limited to the appearance of the flowers, but Colchicum autumnale, which is also flowering in autumn, lacks the crimson stigma from which the saffron spice is derived from Crocus sativus. Case report: A 47 year old male with no medical history had eaten a meal of 7 self picked and well sautéed mushrooms he had taken for edible Amanita rubescens. Four hours later, 5 minutes after drinking 0.5 L beer he experienced a hot facial flush, tachycardia 110/min, and drowsiness. He went to the local hospital. The PCC gave the same advice as above. His physical examination revealed no pathology, laboratory tests including transaminases, prothrombin time, creatinine were all normal. The symptoms disappeared spontaneously after 90 minutes, however, a sip of beer the next day and the day after produced facial flushing again. The mushroom was identified by the mycologist as Echinodermata aspera. Conclusion: This is the first report of a case of Disulfiram like syndrome after consumption of Echinodermata aspera. The nature of the toxin involved is not yet known.

130. Life Threatening Poisoning with Taxus baccata and Ecstasy

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Objective: The mortality rate of intoxication caused by Taxus baccata is very high and we have no antidote for this poisoning. Case report: A 27 year old man was admitted to a local hospital for sudden hypotension, bradycardia, vomiting and headache. Hemodynamic instability with symptomatic bradycardia (18/min) with extremely wide QRS, ventricular tachycardia and fibrillation was noted. Acute renal failure, slight elevation of troponins and a mild hypocoagulation state were found. The patient denied any drug intake, however, urine toxicological analysis detected colchicine (3.5-dimethoxyphenol) and 3,5-dimethoxyphenol and other derivates of phenol (GCMS). The patient was transferred to the Department of Arrhythmias and Cardiac Pacing at the National Institute of Cardiovascular Diseases. Initially, the patient was hemodynamically unstable with significant bradycardia during non-captured temporary pacing and frequent monomorphic ventricular tachycardias and ventricular fiburrection, which required prolonged resuscitation with many DC shocks. A new temporary pacing lead was implanted but despite this, intermittent asystole, although significant hemodynamic features also occurred in over half of cases. The anti-venom appears to be safe and effective. Advice given by the NPIS appears to closely reflect national practice guidelines.

131. Plant Ingestions: A Profile of Fatalities

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Objective: The ingestion of plants is a common exposure that is managed by poison information centers. The majority of fatalities occur in children less than 6 years of age and are associated with no toxicity or result in only minor effects. Fatalities due to the ingestion of plants are rare, but do occur. The objective of this project is to describe the demographic features of those who ingest plants and suffer a fatality as a consequence of the exposure and to identify the plants that are most commonly implicated in fatal outcomes. Methods: The annual reports of the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS) were reviewed over the period of 1983–2008 to identify all fatal outcomes that were due to the ingestion of a plant. All plant ingestion exposures that were reported to American poison centers from 2000–2009 were provided to the investigators as an AAPPC data grant and analyzed using Microsoft Office Excel to identify all fatal outcomes and to profile patient demographics. Descriptive statistics were used to characterize the data.

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colouration were peculiar. Three to four hours after the meal, the mother developed nausea and contacted the Swiss Toxicological Information Centre, suspecting a plant misidentification. All family members were referred to the regional university hospital for admission of oral activated charcoal. No other symptoms were reported, notably no symptoms in the 8-year-old boy and his brothers. Colehicine serum concentration (blood sample obtained 15 hours after ingestion) measured by HPLC-mass spectrometry was 0.36 μg/L for the mother, and 0.13 μg/L for the 8-year-old child, respectively (therapeutic levels: 0.30–2.5 μg/L). Conclusion: Cases of intoxications in which a significant amount of colchicine may be absorbed even after ingestion of very small quantities of Colchicum autumnale, which in this case was confused with CROCUS SATIVUS were rare. One year after the incident, 230 cases of taste disorder following ingestion of pine nuts were reported to the NPIS. The most common agents causing the symptoms were nuts or metallic compounds. Essential oils (particularly Olbas Oil), bleach, descaler, chlorine, antifreeze, carbon monoxide and fungi were each associated with several cases of taste disturbance. Conclusion: The first incidence of dysgeusia as a result of ingestion of pine nuts was published in 2001. The first case reported to the NPIS in 2008 which suggests this is a relatively recent phenomenon in the UK. There are various theories as to the cause of the dysgeusia due to pine nuts including possible oxidation of oils in the nuts due to spoiling, presence of contaminating nuts sourced from different countries or species and the effect of plant species and variety. The dysgeusia resolves uneventfully but can be distressing for the patient who may not associate the symptoms with recent pine nut ingestion. Cases of dysgeusia include, tooth decay, heavy metal poisoning, gastritis, certain drugs (e.g. metronidazole), chemotherapy or jaundice. If dysgeusia can be attributed to ingestion of pine nuts in the first instance and resolves within two weeks then patients may be reassured and unnecessary medications or investigations avoided.


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Objective: To describe black widow spider (BWS) exposures reported to US Poison Centers and identify factors associated with antivenom use. Methods: All exposures with the generic code for BWS envenomation and Lathrocutus mauchti antivenom reported to the American Association of Poison Control Centers (AAPCC) between January 1st, 2000 and December 31st, 2008 were reviewed. Cases with at least minor clinical effects, as defined by the AAPCC, due to BWS exposure were extracted. Descriptive statistics were generated and proportions were compared by chi-square and odds ratios. Results: Between 2000 and 2008, 23,409 BWS exposures were reported in 47 US states. Eighty percent of patients showed clinical effects due to the exposure. The number of US exposures peaks in September and falls to a nadir in February. 58% (n = 5,751) were male and the mean age was 31 years of age (IQR: 19–43 years old). The majority of symptomatic cases (58%, n = 5,741) were managed in a health care facility. While the majority of patients were classified with minor clinical effects (65.1%, n = 6,424), there were 3,302 cases (33.5%) with moderate effects and 139 cases with major effects (1.4%). Antivenom was administered in 374 cases (3.8%); 87 patients (1.4%) with minor effects, 258 (7.8%) with moderate effects and 21 (0.3%) with major effects. Antivenom use was more common in the moderate and major outcome groups (OR = 6.61, 95% CI 5.20–8.48). In patients with moderate or major outcomes, antivenom use was more common in the Southwest (OR 1.91, 95% CI 1.39–2.62) and West (OR 2.36, 95% CI 1.75–3.19). In the subset of patients with moderate and major outcomes, antivenom use was associated with symptom duration of less than 24 hours (OR 2.04, 95% CI 1.57–2.67). There was no evidence of symptom duration of less than 24 hours in patients who received benzodiazepines (OR 1.14, 95% CI 0.98–1.33) or calcium (OR 1.21, 95% CI 0.95–1.53).

Conclusion: In the US, most symptomatic BWS exposures are minor and patients are more likely to experience symptoms in a health care setting. Antivenom treatment when indicated is associated with shorter symptom duration.

136. Some Aspects of Intoxication with Tricholoma equestris
Sein de Haro L,1,2, Djezzar S1,2, Cournel MA2, Gazin V3,4, Savicu P4
1Poison and Toxicovigilance Centre, Marseille; 2Division of Intensive Care, University Medical Center, Utrecht; 3Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands

Background: Rhabdomyolysis is a rare but potentially fatal condition. In 2001 Bédry and co-workers described rhabdomyolysis caused by overeating of Tricholoma equestre.1 Objective: The aim of our study was to analyze some aspects of intoxication with these mushrooms. Method: Observational study. Results: We observed eight patients, including 3 females and 5 males, aged from 5 to 75 (average 44) years intoxicated with Tricholoma equestre. The amount of the mushroom dish varied from 1.7 to 4.7 (average 3.1) g/kg of body weight in adults; and 17.5 g/kg of body weight in children. The total amount of consumed mushrooms varied from 11.5 to 46.7 (average 25) g/kg of body weight in adults; and 70 g/kg of body weight in children. The time between the last meal and onset of clinical symptoms varied from 4 to 120 (average 69.5) hours. CK level varied from 11,993 to 53,515 (average 35,325) U/L in adults; and 309 U/L in child. In adults the AST and ALT varied from 432 to 2,002 (average 1,352) and 47 to 761 (average 243) U/L respectively. The main clinical symptoms in adults included muscle pain, weakness and profound sweating. In children we observed muscle weakness up to respiratory failure. The time of recovery varied from 6 to 21 (average 13) days. A fatal outcome was observed in one case, a man aged 75 years who consumed 3500 g of Tricholoma equestre which was equal to 46.7 g/kg of his body weight. Conclusion: A total dose of consumed mushrooms more than 35–40 g/kg of body weight may be connected with serious events. In children the level of CK did not correlate well with the severity of clinical symptoms. The mortality rate was about 12.5%. References: 1. Bedry R, Baudrimont I, Defieux G, et al. Wild-mushroom intoxication as a cause of rhabdomyolysis. N Engl J Med 2001; 345:798–802.

137. Recreational Use of Salvia divinorum in France: Experience of the National Toxicovigilance Net Between 2003 and 2010
de Haro L1,2, Djezzar S2, Cournel MA2, Gazin V3,4, Savicu P4
1Poison and Toxicovigilance Centre, Marseille; 2Division of Intensive Care, University Medical Center, Utrecht, The Netherlands; 3Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; 4National Committee for Toxicovigilance, Institut de Veille Sanitaire, Saint Maurice, France

Background: Salvia divinorum is a Mexican plant producing a psychotomimetic active principle called Salvinorin A which induces hallucinations in humans. Since the beginning of the 21st century, the recreational use of this drug has increased due to worldwide distribution by Internet. The consequence of its abuse potential is the institution of legal restrictions for the plant and the Salvinorin A use in several countries. In order to evaluate the French situation concerning Salvinorin, a survey was performed by the National Committee for Toxicovigilance. Methods: A retrospective study was initiated in order to analyze cases of S.divinorum managed by the French Poison Centres between 2002 (8 years 8 month period). Results: 19 cases were studied...
138. Mediterranean Spurge (Genus Euphorbia) Poisonings: A Case Series from the Marseille Poison Centre

Glaiaz M, Belmondo L, Tichadou L, Hayek-Lantheis M, de Haro L.
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Introduction: In Mediterranean flora, all the indigenous species of the Euphorbia genus have an herbaceous general aspect with a short size (main species: E. cyparissias, E. helioscopia, E. amygdaloides, E. characias). The sap of the spurge is considered to be an irritating latex which can induce severe skin or respiratory distress. In order to evaluate the toxicity of local spurge species a retrospective study was performed. All poisonings due to this plant genus between January 2002 and December 2009 were managed by the Marseille Poison Centre and analysed. Case series: 89 observations were collected (53 men and 36 women, average age of 32.4 years ± 27, from 5 months to 99 years). Such intoxications occur along the entire French Mediterranean coast. During the studied period, the number of observations was stable, between 8 and 15 cases each year. Poisons were described throughout the year. Cases 15 to 32 cases were much more frequent in spring and the beginning of summer (spurge growing period in the Mediterranean biotopes). The different spurge species are ubiquitous, with human contacts in nature (35%) but also in private or public gardens. Children under 6 years old represented 27% of the series. Adult patients can be exposed during their work (8%) and professionals gardener or their leisure activities (gardening at home or trekking in the countryside). Poisonings were the consequence of contact of the toxic sap with skin (10% of cases), eyes (40%) or several routes (14%), inducing intense local pain, swelling and irritation. Thirty-nine per cent of the patients remained at home, Thirty-five per cent consulted their family practitioner, 10% consulted a medical specialist (dermatologist or ophthalmologist) and 35% required an emergency unit management in the local hospital. All patients quickly recovered in a few hours proving that the plant is non-lethal and without local Euphorbia species. Conclusion: Mediterranean spurge species are able to induce human poisonings by several routes. The harmless aspect of these plants leads to accidental contact with the toxic sap. However, Mediterranean species seem to be less dangerous than tropical Euphorbia species.

139. Two Severe Collective Ciguatera Poisonings Concerning European Tourists in Endemic Areas

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Introduction: Ciguatera poisoning is a rare event in Europe: a case series from the Marseille Poison Centre (MPC) published in 2003 described 18 poisoned patients between 1997 and 2002. Between 2003 and 2009, 30 more patients were observed by the MPC, concerning 62 patients (1 to 20 patients poisoned by one fish). In 2010, 2 collective ciguatera poisonings were reported to the MPC. Case series: Case 1: In March 2010, 4 adult French tourists (2 men, 2 women) in Mauritius ate a yellow-edged lyretail (Variola louti) bought in a local market and barbecued. In the initial phase, digestive troubles and cardiovascular symptoms were present (severe bradycardia, low blood pressure leading to medical management for the 4 patients, 2-days hospitalisation for one of them). Purtuits, rhodode-sia, and paresthesia were reported by the 4 patients during 30/45 days after the meal. Collective case 2: In May 2010, 2 adult French tourists and their 2 local friends (2 men, 2 women) in “Saint-Martin” Island (French West Indies) ate a Lana tur (Cynisca vavivana) caught by one of them. The fish was cooked and shared. A 55 year old man who ate small quantities did not report any symptom whilst his wife had ataxia and pruritus for 2 weeks. The man who ingested the largest quantities was managed in the local hospital as respiratory distress was observed less than 2 hours after the meal. Long term symptoms (asthma, pruritus, paresthesiae, myalgias) were described for the 4 patients for 15 to 60 days. Discussion: European tourists are not aware of the dangers of ciguatera. In the concerned countries, tourism is an important resource. Giving advice to tourists may modify the image of the “beach paradise” and may reduce the number of visitors to the contaminated areas. This situation explains the total absence of local information about the potential risks of ciguatera. In consequence, prevention and education of tourists should take place in their country of origin. References: 1. de Haro L, Pommier P, Valli M. Emergence of imported ciguatera in Europe: report of 18 cases at the poison centre of Marseille. J Toxicol Clin Toxicol 2003; 41:927–30.

140. Oral Ricin Exposure - Less Poisonous than Expected

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Objective: The castor bean plant (Ricinus communis) is known to be highly toxic. The whole plant, especially the beans, contains the toxalbumin ricin that inhibits protein synthesis in the cells. However, its toxicity depends on the route of exposure and, if the beans are ingested, also on the degree of mastication. We present three cases of ricin poisoning where large numbers of beans were swallowed with suicidal purpose. Case series: Case 1. A 38-year old man thoroughly chewed and swallowed 27–30 castor beans together with antiemetics. After 5–6 hours he felt nauseous and developed intense vomiting and diarrhoea. Ten hours after ingestion he called for an ambulance. On admission to hospital he had normal vital parameters but was dehydrated. After intravenous rehydration he gradually recovered without any signs of organ damage. Discharge was possible after three days. Case 2. A 20-year old woman ingested 90 castor beans, several of them chewed. After one hour she felt nauseous and developed intense vomiting and diarrhea. Gastric lavage was performed 6–7 hours after the ingestion resulting in retrieval of three beans. Activated charcoal was given and intravenous fluids were infused. She developed mild anaemia (Hb 103 g/L), but had an otherwise uncomplicated recovery. Discharge after seven days. Case 3. An 18-year old man chewed and swallowed 24 castor beans. He developed increasing abdominal pain, diarrhoea and episodic hematemesis. On admission to hospital activated charcoal was given. He experienced transient chest pain and palpitations. Fever and facial rash ensued. Complete recovery. No organ damage. Conclusion: These three patients ingested large numbers of chewed castor beans. They all developed pronounced gastrointestinal symptoms but no signs of organ damage. Our cases strongly indicate that the oral toxicity of castor beans is lower than reported in older literature. Poor intestinal absorption of ricin and possibly also decomposition of the toxin in the gut may explain this finding.
143. Animal Poisonings: 10 Years Experience from the Belgian Poison Centre
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Objective: To describe the profile of animal poisoning reported to the Poison Centre during a 10-year period (2000–2009).

Methods: The Centre of the University Hospitals and University as well as Poison Information Service (Edinburgh) was contacted to retrieve figures for groups of intoxicants and types of animals involved. Certain obvious trends were further explored by looking at the individual case record charts, including 294 cats during the 11-year period concerning 26,820 animal exposures. The yearly number of exposures was quite stable (range 2,531–2,915). Dogs accounted for 69% of the victims, followed at a long distance by cats, birds (including chickens), horses and cows. Pesticides and biocides were responsible for 41% of the exposures, followed by domestic products (21%), drugs (18%) and plants (9%). The percentage of deceased animals at the time of call was 3.7% (985 animals), which involved 195 dogs, 176 cats, 165 birds, 96 cows, 88 sheep and 83 horses (amongst others). The main substances responsible for these deaths were pesticides and biocides (426 exposures), mainly anticoagulant rodenticides in dogs, and plants (203). We observed some obvious trends during this period. A rise in exposures to veterinary drugs was observed during the last two years (2008–2009) with respectively 114 and 121 cases recorded compared to an average of 62 in the 2000–2007 period. This was mainly due to a rise in exposures to spot-on products for cats. In 2000 there were 9 exposures to spot-on products. The figure for 2009 was 37 spot-on products. Another trend observed was a decline in mortality to pesticides and biocides drugs was observed during the last two years (2008–2009) with respectively 114 and 121 cases recorded compared to an average of 62 in the 2000–2007 period. This was mainly due to a rise in exposures to spot-on products for cats. In 2000 there were 9 exposures to spot-on products. The figure for 2009 was 37 spot-on products. Another trend observed was a decline in mortality to pesticides and biocides.

144. Plant and Fungi Poisoning Incidents: Experience from the National Poisons Information Service (NPIS) Edinburgh
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Objective: To examine the incidence of plant and fungi poisoning enquirers to the Edinburgh centre of the UK National Poisons Information Service (NPIS).

Methods: Telephone enquiries involving plants and fungi reported to NPIS Edinburgh for 6.5 years from April 2004 to September 2010 inclusive were reviewed. Results: 385 enquiries (3.3% 385/11,532 of all enquiries) were received regarding plants or fungi over this period, of which 367 related to patients. Of the enquiries relating to children, 354 were from parents (89.9% 328/367), 6.8% (25/367) were from members of the public and 3.8% (14/367) from others (including schools, police, carers). 67.8% (249/367) of the plant poisoning enquirers were from 9 years or less; 43.3% (159/367) involved patients aged 1–4 years. The majority had no (193/249) or minor (47/249) symptoms at the time of enquiry. Only 1.2% (3/249) had moderate symptoms, in 2 thought unrelated to the exposure. In 6 cases symptoms were unknown. At the time of enquiry 63.7% (234/367) were asymptomatic and 24.7% (91/367) had minor symptoms. Only 1.6% (6/367) involved patients with severe symptoms, one enquiry regarding Cortinarius speciosissimus related to 4 patients (renal failure), 4 relating to 2 different patients involved Aconitum napellus (cardiac features) and one involved an unknown mushroom (manic psychosis). In 90.1% (331/367) the exposure was accidental; in 3.8% (14/367) intentional and only 2 (one patient) involved severe features (Aconitum napellus). Ingested amount accounted for 89.4% (328/367) of exposures, skin contact 8.7% (32/367), eye contact 2.2% (8/367), inhalation 0.5% (2/367) and other unknown 0.5% (2/367). Of 270 plant ingestion enquirers, the plant part was specified in 202 cases; 32.9% (89/270) involved berries, 20.3% (55/270) leaves, 11.1% (30/270) seeds, 10.4% (28/270) flowers, 2.2% (6/270) bulbs and 1.5% (4/270) stalks/stems. Of 249 plant poisoning enquirers, 74% (185/249) related to plants belonging to the Angiosperms, with 92 genus and 230 species. Solanum Lycocarpum A. St.-Hill was the biggest South American wild canidae. When mature this plant belongs to the Euphorbiaceae family and is known in many regions of Brazil as “pinhão roxo” or “Paraguai pinhão” (physic nut). The plant has been researched and planted in the country as an economic source for biodiesel. It is also used in folk and popular medicine. Its toxicity is related to the presence of a lectin or toxalbumin, curcin, a protein that inhibits protein synthesis in the ribosome, like ricin and aribin. Curcin alters the normal development and renewal of gastrointestinal cells, inducing desquamation of the intestinal walls. Similar symptoms are described irrespective of the number of seeds ingested (2 to 50). The main manifestations post ingestion are: nausea, vomiting, abdominal cramps, diarrhea, a burning sensation of the oropharynx region, electrolyte disturbances and acid-base disturbances. Death frequently occurs in animals, but no fatal cases have ever been described in humans, so far. Conclusion: Despite the highly toxic nature of Jatropha curcas, ingestion of 30 seeds did not result in severe signs and symptoms. References: 1. Kulkarni ML, Sreekar K, Keshavamurthy KS, et al. Jatropha curcas - poisoning. Indian J Ped 2005; 72:75–6.

145. Collective Acute Intoxication after Ingestion of Jatropha curcas Seeds by a Group of Children
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Objective: To report a case of intoxication after ingestion of Solanum lycocarpum A. St.-Hill fruit (Wolf’s Fruit or “lobeira”). Case report: A 6 year-old man was seen at the ER complaining of diarrhea. He presented tachycardia (HR = 104 bpm). He re- ported having eaten a smelly fruit he had spotted in a fruit stall in the garden close to his work place approximately 6 hours before. He reported that just after the ingestion he started feeling unwell, with nausea, vomiting, sialorrhoea, diaphoresis, abdominal cramps and diarrhea. He denied any prior contact with the fruit. He had no alterations in electrolyte balance and renal and liver function. The patient had brought with him a fruit from the same plant which was identified as Solanum lycocarpum A. St.-Hill (Wolf’s Fruit). He was rehydrated intravenously and kept under observation during 12 hours, leaving hospital asymptomatic and remained well thereafter. Discussion: Jatropha curcas is one of the biggest and most complex plant families known, belonging to the Angiosperms, with 92 genus and around 2,300 species. Solanum L is the biggest and most complex genus among Solanaceae. The genus presents many toxic principles causing gastrointestinal and central nervous system ailments, including saposins and steroidal glycosides. Many species also contain flavonoids warrning its use in folkloric medicine, due to their probable antioxidant properties. The species Solanum lycocarpum A. St.-Hill is typical of Brazilian “cerrado”, a vast geographical semi-arid area situated in most of Brazil and the Central hinterland. It is an important part of the diet of the Brazilian wolf species Chrysocyon brachyurus, the biggest South American wild canidae. When mature fruit is eaten by wolves as well as in the preparation of a popular medicine for diabetes, despite the absence of any pharmacological effect in experi- mental studies. The toxic saponins isolated from that species is Lambarin and Solamargin. Solamargin for rats is 42 mg/kg, and lethality is related to its anticholinergic effect, as in many Solanum species.

Clinical Toxicology vol. 49 no. 3 2011
Conclusion: Toxic effects from ingestion of “wolf’s fruit” have not been described so far, and the present case shows the possibility of serious gastrointestinal symptoms.

147. Muscarine Syndrome: Report of 2 Cases of Severe Mushroom Poisoning Identified at Lyon Poison and Toxicovigilance Centre in 2010
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1Poison and Toxicovigilance Centre, University Hospital Lyon; 2Intensive Care Unit, University Hospital Lyon; 3Emergency Department, University Hospital Lyon, France

Objective: In 2010, 142 collective poisonings (i.e. 246 patients) related to a mushroom meal were identified by Lyon Poison and Toxicovigilance Centre (PTC). The recorded clinical features were typical of a gastro-intestinal syndrome in 63 cases, muscarine syndrome in 23, amanita syndrome in 4 (7 patients), coprinus syndrome in 2, and pantherina syndrome in 2. Digestive disorders were attributed to morchella in 9 cases, associated with vertigo in one. Severe mushroom poisoning was evidenced in 7 patients (5 amanita and 2 muscarine syndromes). The objective is to focus on the unexpected severity of these 2 muscarine syndromes, which are usually considered benign. Case series: Case 1: A couple ate mushrooms and one hour later, developed nausea, vomiting, abdominal pain, sweating, pinpoint pupils, and flushing. The 59-year-old man with a history of lower limb arteriopathy obliterans (LLAO) leading to bi-femoral bypass surgery in 1989 presented with motor and sensory deficit in the lower limbs evidenced by the absence of distal pulses and signs of ischemia. He had bradycardia (30 bpm), bilateral tight miosis, hypothermia (34.5 °C), dehydration, and functional renal failure. Administration of atropine (0.5 mg) accelerated his heart rate to 70 bpm. Echo-doppler ultrasonography showed bilateral lack of vascularization and vascular occlusive thrombosis in the right branch of the bypass, and left popliteal thrombosis. The obstruction was relieved surgically by vascular Fogarty catheter and thrombolysis with urokinase. The control angiography showed good revascularization. The outcome proved favourable despite reperfusion syndrome with elevated CPK serum levels (10,000 IU/L). Case 2: A couple ate mushrooms and 30 minutes later developed sweating, vomiting and profuse diarrhoea. The 76-year-old woman with a history of LLAO presented with tight miosis, hypothermia (33.8 °C), dehydration, and functional renal failure. Hemodynamic stability was obtained by the administration of atropine (0.5 mg). The outcome was favourable with improvement of renal function.

Conclusion: Muscarine mushroom syndromes are usually of mild or moderate severity. As these two cases show, they may, however, be associated with severe manifestations, especially for patients with pre-existing cardio-circulatory disease.

148. Fifteen-Year Retrospective Analysis of Amatoxin Poisonings in Switzerland
Swiss Toxicological Information Centre, Zurich, Switzerland

Objective: To analyse and describe all confirmed cases of amatoxin poisoning reported to the Swiss Toxicological Information Centre (STIC) between 1995 and 2009. Methods: Retrospective case study from the STIC database. Results: 32 cases of amatoxin poisoning confirmed by ELISA were included in this study (Table 1). Patient age ranged from 1.4 to 74 years with a median of 50 and an average of 44.2 years. There were 20 males and 12 females. The mushroom meals were either eaten alone (16 patients), by 5 couples and one family of six. In 30 of the 32 cases, the patients ate the amatoxin-containing mushrooms accidentally, in one case it was a suicide attempt (fatal outcome), and in another a suicidal intention was suspected (fatal outcome). None of the mushrooms were checked by a certified mushroom expert prior to consumption. Conclusion: Amatoxin poisoning was fatal in five of our 32 cases (15%). Decontamination methods included administration of oral activated charcoal (single or repeated) in most cases while gastric lavage, placement of a duodenal tube, and laxatives were used only in single cases. Antidotal therapy consisted of silybinin, combined with N-acetylcysteine (NAC) and/or penicillin although NAC in combination with silybin is nowadays the standard treatment. Molecular Adsorbsents Recirculation System (MARS) is not readily available and was not used in any of these cases.

149. Clinical and Epidemiological Profile of Envenomations in Azerbaijan
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Background: The epidemiology of envenomation in Azerbaijan is uninvestigated. We present a study of the envenomation profile in Azerbaijan for the past 10 years. Methods: We analyzed case records of 766 patients admitted to the Republican Center of Toxicology (RTC) MoH, Baku, Azerbaijan in 2000–2009. Results: 5.8 percent of RTC total hospitalizations were envenomations caused by snakes, “black widow” spiders, scorpions and hymenoptera. Most cases (546) comprised of snake bites, 101 cases - “black widow” spider stings, 89 cases - hymenoptera stings (bee, wasp etc) and 30 cases - scorpion stings. Ratio of male to female was 3:1. One hundred and seventeen patients (15.3%) were children (age <15 years). Five hundred and forty of 546 snake bite patients had severe symptoms of coagulopathy, local edema and hemorrhagic typical for Viperidae venom envenomation. Ninety per cent of Viperidae snake bite patients were admitted to RTC with incorrect first aid actions such as tourniquet, cuts at the point of bite etc. Only 6 patients had neurotoxic manifestations typical for Elapidae snake venom envenomation. All these patients arrived from southern (Iranian border) regions of Azerbaijan. Ninety-five per cent of patients with snake bites received polyvalent antivenom at the time of presentation. Adverse reactions to antivenom were registered in 43 cases. Mortality due to snake venom envenomation was 2.7% (15 patients). Cases of “black widow” spider stings are new for Azerbaijan. Patients with the typical clinical syndrome of latroderctism (severe muscle pain and cramping, hypertension, arthralgia, lacrimation etc) started to register only in the last 15 years. No specific antivenom is available in Azerbaijan and only symptomatic treatment was provided for these patients. One case of “black widow” spider envenomation was fatal. Cases of scorpion and hymenoptera envenomations were mostly mild and no lethal cases were registered. Conclusion: Envenomations are a significant part of toxicological admissions in Azerbaijan. Most of the patients with snake and “black widow” venom envenomations showed marked clinical manifestations and may have severe prognosis. Scorpion and hymenoptera stings occurring in Azerbaijan do not cause life-threatening effects.

150. Analysis of Deaths by Scorpion Envenomation
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Objective: The aim of this study is to analyze risk factors due to scorpion envenomation in order to improve patient care and prevent both morbidity and mortality. Methods: Our work is a retrospective study of deaths by scorpion envenomation during the year 2005, based on a hospital in Beni Mellal province. Results: In our study we counted 18 deaths from 63 cases of envenomation; the rate of lethality at the hospital was 28.57%. 83.3% of these deaths concerned children aged ≤10 years. Scorpion envenomation occurs mainly during summer time, in particular during June and July (50%). Moreover, stings happen at night between 6PM and 6AM (72.2%). The sex ratio (M/F) is 1.25, not significant (chi-squared = 0.22). The average duration of hospitalization was 7.34 ≤ 2.13 hours. Several therapeutic measures were used of which the cardiac stimulant dobutamine represented by Dobutrex was recommended in 72.2% of cases. Statistical
Objective: It is well known that Laburnum anagyroides is a toxic plant and that intoxications occur from time to time. In Norway this usually happens when children eat peas or pods by accident or at play. The amount reported is uncertain, but as few as 2-5 peas are reported to cause symptoms. We present a case of laburnum intoxication in a healthy adult man with an unexpectedly benign outcome.

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151. Laburnum Intoxication with Unexpectedly Benign Outcome
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Objective: To evaluate the reliability of mushroom identification by digital photos sent from mobile phones and email compared to identification based on physical examination. Methods: As part of a 1-year prospective mushroom case-series study all inquirers were asked to send a digital photo of the mushroom by email or by mobile phone (MMS) to the Poisons Information Centre (PIC). Additionally the inquirer was asked to send the mushroom physically to the PIC for later definitive identification. Photos of mushrooms were identified by a panel of mushroom experts as part of the risk-assessment in relation to the intake. The collected mushrooms were later physically identified macro- and microscopically by one expert. The level of the identification of the mushroom (photo and macro) was classified as: a) cytotoxic/non-cytotoxic, b) genus-name, c) species-name. The results of photo identification at different levels were compared with macroscopic identification using the latter as reference. Results: A total of 160 contacts with the PIC related to acute mushroom intake occurred during one year: 112 identified by photo at inquiry; 64 mushrooms subsequently identified macroscopically by expert; 53 mushrooms identified both by photo and physically by expert (see Table 1). Conclusion: Identification of mushrooms by digital photos sent from mobile phones and email compared to identification based on physical examination is a valid method for exclusion of the most toxic mushrooms. The method can be used in circumstances with intake of small amounts of a mushroom, when only the most toxic species need to be identified. A precise identification is needed the identification must be macroscopic until the photo method is further refined.

Table 1. Matching identification by photo and macroscopic (expert)
Instituto Nacional de Toxicología y Ciencias Forenses (Spanish Poison Control Center). Madrid, Spain

Objective: In recent years we have recorded a significant increase in the number of calls to the Spanish Poison Centre (SPC) related to poisoning of people above 70 years of age. Thus, we have studied this population group and fully characterized these cases in order to be able to implement specifically focused preventative measures.

Methods: We performed a retrospective analysis of selected calls received by the SPC between 2006–2009 which had an age group older than 65 years. Data included age, gender, etiology, exposure route and the type of toxic product.

Results: The number of calls related to poisoned subjects older than 70 years (n = 6396) has increased from 0.5% in 2006 to 1.8% in 2009. Amongst these, 4.9% were due to suicide attempts, whereas the remaining cases were accounted for by accidents (37.1%), as well as errors in posology (34.9%) and administration routes (2.8%) of currently used therapeutic drugs. 47.2% of the patients were aged 70–79 years, 45.3% were 80–89 years, and 7% were more than 90 years. When gender was considered, the majority were females (58.9%). The main exposure route was oral poisoning (88.7%). Regarding the type of toxic agent, therapeutic drugs were mainly involved (71.4%), followed by cleaning products (16.7%), agrochemicals (4.1%) and cosmetics (3%). More specifically, the type of therapeutic drug which generated the poisoning events were those more frequently provided to this population group: nervous system (26.3%); cardiovascular system (19.9%), alimentary tract and metabolism (8.7%); anti-infectives for systemic use (8.5%); respiratory system (7.9%); musculo-skeletal system (7.1%).

Conclusion: There has been a significant increase in the number of calls received at the SPC involving elderly people, who have accidentally taken therapeutic drugs products. Indeed, the data accumulate specific risk factors that increase the severity of poisoning, such as underlying pathological conditions and frequently, concomitant neurological problems such as confusion, dementia, slow reflexes and sensorial deficits (sight, smell, taste). The SPC has to alert the corresponding Health Authority about this circumstances, in order to follow and implement specific preventative measures directed towards the reduction of the incidence and morbidity of poisoning events in this population group.

Swedish Poison Information Centre, Stockholm, Sweden

Objective: To elucidate whether the deregulation of the Swedish pharmacy monopoly in 2009 has caused an increase of inquiries to the Swedish Poisons Centre (PC), in particular concerning over-the-counter (OTC) analogics. The pharmacy monopoly was formally abolished in July 2009. Sale of certain drugs outside pharmacies has been allowed since 1st November 2009 (e.g. 500 mg paracetamol and 400 mg ibuprofen tablets).

Methods: The number of inquiries to the Swedish PC concerning paracetamol and ibuprofen misuse/overdose during the year immediately prior to deregulation was compared to the corresponding figures during the year following deregulation.

Results: The total number of inquiries about paracetamol and ibuprofen was 3764 (71% related to paracetamol) during the year prior to deregulation and 3841 (68% related to paracetamol) in the 12-month period following deregulation. There was a 12% rise in ibuprofen inquiries, which complies with the trend during recent years. There was no significant change in the pattern of consultations, e.g. the frequency of accidents in infants and deliberate overdose in adults. With respect to adolescents (15–19 years old), the number of inquiries increased alarmingly from 2000 up to 2008, but has since decreased. This is also true when comparing the 12-month period preceding deregulation (588 inquiries concerning paracetamol and ibuprofen) to the 12 months after deregulation (527).

Conclusion: The increased availability of OTC analogics has not, so far, resulted in a significantly larger number of inquiries to the Swedish PC involving these drugs. This contrasts to the experience in Norway where a marked increase in inquiries concerning paracetamol was observed after deregulation for these products to be sold close to the year to come. It would be ideal if the PC statistics do reflect the actual frequency of poisonings, but these data must always be interpreted with caution.

159. Continued Increase in Antidepressant Subgroup Drug (SSRI, SNRI, NARI, NaSSA) Poisoning Among Patients with 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–54, >54 years old, but only the focus group aged 15–34 years was included in further evaluation. Furthermore, we subdivided our data to observe any seasonal variation. Only 46% females were identified as the patients who had ingested only the antidepressant subgroup drugs or multiple drugs, the cause of poisoning and the enquirer. Results: A total of 2,143 cases were evaluated. Relative to these cases this corresponded to 3.3% in 2007, 3.5% in 2008, 4.5% in 2009, and 5.1% in 2010 (6 months). The annual variation was low, but shows a higher frequency during winter. Age distribution showed a peak of 15–34 year olds accounted for 43% in 2007, 42% in 2008, 45% in 2009, and 48% in 2010 (6 months). Females represented 79% in 2007, 76% in 2008 and 2009, and 81% in 2010 (6 months). The fractions of multiple drug ingestions were 63% in 2007, 50% in 2008, 57% in 2009 and 63% in 2010 (6 months). The cause of poisoning was approximately 92% suicidal/affect in all years. A minimum of 94% of the inquiries were from healthcare professionals.

Conclusion: The relative number of registered poisonings at DPIC with antidepressants (SSRI, SNRI, NARI, NaSSA) increased from 2007–2010 (6 months). The age distribution shows the highest frequency of inquiries was for those aged 15–34 years. The majority of the patients were female. In most cases the antidepressant drug was the sole ingested concomitantly with an intention to commit suicide and the purpose was suicidal/affect. References: 1. http://www.medstat.dk/MedStatDataViewer.php

160. The Toxicology Investigators Consortium (ToxicIC) Registry: A Nationwide Registry of Patients Seen by Medical Toxicologists at the Bedside Wax PM, Brent J.
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Objective: In 2009, a survey of US based medical toxicologists established that 10,000–15,000 patients are directly evaluated each year by medical toxicologists; either at the bedside or in the clinic. The American College of Medical Toxicology subsequently established the Toxic Investigators Consortium (ToxicIC) to develop a Registry of toxicology patients seen at the bedside and to provide a national network of medical toxicologists participating in the database. Beginning in February 2010 ToxicIC began a Registry of patients seen at the bedside by medical toxicologists. We report on this Registry to date. Methods: An independent registry of toxicology patients seen at the bedside and involving healthcare professionals. Results: The Registry provides a novel toxicosurveillance source for bedside toxicologists (ToxicIC) to develop a Registry of toxicology patients seen at the bedside and to provide a national network of medical toxicologists participating in the database. Additional sites are currently being recruited to participate in the Registry. The time required to enter data is ~1 minute/patient. Updates in the data collection tool have facilitated ease of using the collected data for toxicosurveillance. Conclusion: The ToxicIC registry is a viable tool to identify cases that medical toxicologists see at the bedside at multiple sites. Following identification of the database, access to the registry will provide complete clinical records of consultations seen by medical toxicologists. The development of this registry provides a novel toxicosurveillance source for research, education and transfer of best practice in bedside health. Such a registry could be expanded to international collaborators.
161. Characteristics of Toxic Alcohol and Glycol Poisoning in the UK
Weatherall J, Thanacoody HKR, Davies J, Cooper G, Thomas SHL.
1National Poison Information Service (Newcastle), Newcastle upon Tyne; 2National Poisons Information Service (Cardiff), Cardiff, UK

Objective: Enquiries regarding poisoning with ethylene glycol or methanol are frequently referred to a consultant clinical toxicologist in the UK, because of diagnostic difficulty, severe toxicity or inconsistent availability of antidotes. This prospective study was undertaken to investigate the epidemiology of systemic exposures reported to the National Poisons Information Service (NPS), use of antidotes, and their adverse effects. Methods: Data on systemic exposures to products containing toxic alcohols and glycols reported to NPS were collected from 1 January 2010 to 30 June 2010 as part of an ongoing 12 month study and cases of significant exposure were followed up to obtain information on antidote use and patient outcome. Results: There were 244 enquiries about toxic alcohols over the 6 month period. One hundred and forty-nine (61%) enquiries originated from hospitals. Sixty-one percent of patients were male and 8% were under 5 years of age. Exposures were mainly by ingestion (95%), occurred mainly at home (89%), with 55% of cases being accidental and 36% intentional. The most common products were surgical spirits, antifreeze and screenwash products. Ethylene glycol was identified as the most common ingredient. At the time of the enquiry 78% of patients had no or minor symptoms and 19% moderate/severe symptoms using the Poisons Severity Score. One hundred and three cases met the criteria for follow up. Of the 60 cases where the outcome is known, 57 made a complete recovery and 3 had sequelae. Details of monitoring and treatments were available for 70 cases. Fomepizole was administered in 17 cases, ethanol 18 cases and both antidotes in 3 cases. Adverse reactions to the antidotes were reported in 3 cases where ethanol had been administered. Haemodialysis/filtration was instituted in 12 patients. Conclusion: Serious poisoning with toxic alcohol and glycol occurs infrequently although the incidence in the UK cannot be determined as some cases may not result in an enquiry to NPS. Exposures are predominately acute ingestions involving ethylene glycol and occur more frequently in males. The majority of patients show few symptoms at the time of the enquiry. Ethanol has been used in similar numbers of patients without any differences in outcome. Acknowledgement: Submitted on behalf of the UK National Poisons Information Service.

Bronstein AC, Spyker DA.
1Rocky Mountain Poison Center, University of Colorado School of Medicine, Denver, Colorado; 2Department of Internal Medicine, Uniform Services University of Health Sciences, Bethesda, Maryland; 3Poison Information Center, Cincinnati, Ohio; 4Northern Ohio Poison Center, Cleveland, Ohio, US

Objective: National Poison Data System (NPDS) provides national real-time data with the potential to evaluate national real-time data with the potential to evaluate the impact of this intervention. 40-mg methadone has been available in 7 products from 6 manufacturers and low-dose in 12 products from 8 manufacturers. NPDS was queried for Exposures and Drug-ID case data on these products by day and examined by week, month and year. Each measure was examined by linear and 2nd order (quadratic) least squares regression and piecewise before and after Jan-1-2008. Time to max (t-max) was determined for the quadratic regressions. Results discussed herein describe the analyses of the by-month data. Results: A total of 1,915 40-mg and 3,835 low-dose Exposures and 10,165 40-mg and 97,061 Drug-ID calls were reported. Both 40-mg and low-dose Exposures showed a relatively smooth quadratic pattern (concave down) with a max in 2006,1 for 40-mg and 2008,1 for low-dose. In contrast, both 40-mg and low-dose Drug-IDs showed a distinct discontinuity at 1-Jan-2008. For low-dose the slopes of the linear regressions were 10.2 before and -5.26 calls/month after and low-dose slopes were 178 calls/month before and -152 calls/month after. Conclusion: The temporal patterns for the 40-mg and low-dose Exposures show similar patterns with 40-mg peaking 2 years earlier than low-dose without reciprocal change. Drug-ID calls outnumber Exposures 18.6:1 and both 40-mg and low-dose changes reflect the DEA’s 40-mg intervention in 2008.

163. Live Birth Rate as a Predictor of Human Exposures Reported to US Poison Centers
Spiller HA, Spyker DA, Colvin J, Aleguas A.
1Kentucky Regional Poison Control Center, Louisville, Kentucky; 2Dept of Internal Medicine, Uniform Services University of Health Sciences, Bethesda, Maryland; 3Poison Information Center, Cincinnati, Ohio; 4Northern Ohio Poison Center, Cleveland, Ohio, US

Objective: The National Poison Data System (NPDS) represents a comprehensive aggregate of calls made to United States (US) poison centers and is the largest available dataset of poisonings in the US. We evaluated the age-based poisoning risk in the US population across nine age windows. Methods: Retrospective comparison of annual poisoning rates in 9 age windows (0–5 by year, 6–12, 13–19, adults 20 and older). The data sources used were 1) NPDS annual count of human poisoning cases (Exposures) for 2000 through 2009; and 2) US Census Bureau; annual live birth (Live-births) counts 1978 through 2009 and death rates (2004–2007) to estimate population at risk (PAR) by age group. We calculated mean exposures per 1000 PAR and change in Exposures per 1000 PAR per year (Slope) for each age group using linear least squares regression. Results: There is a clear difference in mean exposures per 1000 PAR across the 9 age groups (ratio of 2 y/o to Adults = 32.2) and a statistically significant change over time (Slope) in 6 of the 9 age groups (Table 1). Both the highest risk and the largest increase over time (Slope) occurred in the 2 year old group. Conclusion: These results provide the first quantitative assessment of the age-based risk rates for NPDS Exposure data and demonstrate the value of Live-birth data to estimating the population at risk.

164. Do Older Siblings Enable their Younger Brothers and Sisters? rotate
Roth B
University of Texas Southwestern, Dallas, Texas, US

Background: Parents commonly find young siblings gathered together near open bottles of medications. Often it is difficult or even impossible to know which sibling is at higher risk for a serious exposure. This study was undertaken to assess the hypothesis that the younger sibling would be at higher risk for a serious exposure due to encouragement by the older sibling. This was assumed based on the theory that the older child would be more likely to model parents administering medication. Methods: The notes section from approximately 18,000 acetaminophen exposures sent to a health care facility, spanning the years 2000–2009, Table 1. Evaluation of age-based risk of poisoning in the US

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2005 PAR (millions)</th>
<th>Mean Exposures/1000 PAR</th>
<th>Slope (Exp/1000 PAR/yr)</th>
<th>P-value for slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 y/o</td>
<td>4.14</td>
<td>32.3</td>
<td>−0.4965</td>
<td>0.0083</td>
</tr>
<tr>
<td>1 y/o</td>
<td>4.08</td>
<td>94.5</td>
<td>0.2447</td>
<td>ns</td>
</tr>
<tr>
<td>2 y/o</td>
<td>4.06</td>
<td>42.4</td>
<td>1.2542</td>
<td>0.0005</td>
</tr>
<tr>
<td>3 y/o</td>
<td>3.99</td>
<td>42.4</td>
<td>0.6290</td>
<td>0.0006</td>
</tr>
<tr>
<td>4 y/o</td>
<td>3.97</td>
<td>21.2</td>
<td>0.0002</td>
<td>ns</td>
</tr>
<tr>
<td>5 y/o</td>
<td>4.01</td>
<td>11.7</td>
<td>0.1757</td>
<td>0.0002</td>
</tr>
<tr>
<td>Child (6–12 y/o)</td>
<td>27.22</td>
<td>5.50</td>
<td>0.0195</td>
<td>ns</td>
</tr>
<tr>
<td>Teen (13–19 y/o)</td>
<td>27.23</td>
<td>6.70</td>
<td>0.0358</td>
<td>0.0184</td>
</tr>
<tr>
<td>Adult (≥ 20 y/o)</td>
<td>268.52</td>
<td>0.02</td>
<td>0.0385</td>
<td>ns</td>
</tr>
</tbody>
</table>

Clinical Toxicology vol. 49 no. 3 2011
from a statewide poison center database were screened using a word search function. Terms used in the search included sibling, brother, and sister. Cases in which positive acetaminophen levels were obtained in both siblings were included. Cases with negative results were excluded. Comparison of acetaminophen levels between older and younger siblings was performed. Results: 24 siblings or 12 pairs were included. The average age of the older sibling was 2.06 years. The average age of the older sibling was 3.58 years. The average acetaminophen level in the younger group was 70 mg/L. The average acetaminophen level in the older group was 49 mg/L. One large exposure in the younger age group significantly contributed to the difference in results. Conclusions: Significantly higher acetaminophen levels were found in the younger sibling when there is a co-ingestion between two children. This may be due to the older child being more likely to mimic medication administration by parents. Larger studies are necessary to confirm this data.

166. A One-Year Observational Study of Fatal Poisonings in Ekaterinburg, Russia

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1Department of Therapeutics, The Ural State Medical Academy, Ekaterinburg; 2Regional Forensic Bureau, Ekaterinburg; 3Station of First Medical Aid, Ekaterinburg, Russia; 4Oslo University Hospital, Ullevål, Norway

Objective: There is a lack of prospective studies on poisoned patients comparing the mortality inside and outside hospital. Methods: A one-year prospective, observational study of all acute poisonings in Ekaterinburg, Russia (population: 1,343,900, of whom 1,145,000 were ≥16 years) between 2009 and 2010. Patients ≥16 years of age who were in contact with any part of the health care system (ambulance service, hospitals, or the Forensic Institute) were included. The fatalities are presented here. Results: There were 572 patients who died from poisoning during the period, giving an annual mortality rate of 50/100,000 habitants. Of those, 503 (88%) were found dead on scene, 5 (1%) died in the presence of an ambulance, and 64 (11%) died in hospital. Mean age among the fatalities was 45 years (range 17–91); 75% were males. The most frequent agents causing death were found to be ethanol (44%), opiates (29%), carbon monoxide (14%), and acetic acid (4%). Pharmaceutical agents resulted in 30 deaths (5%), of whom 16 died in hospital. The most frequent pharmaceutical agent causing death on scene was diuretics (29%). The majority of the poisonings were accidental (63%), and drug overdoses (29%). Among the dead in hospital, acetate acid (20%), opiates (16%), and ethanol (17%) were most frequently found. Conclusion: The higher age of the patients was 35 in 35% inside hospital, as compared to 4% outside hospital. Conclusion: Mortality rate was unexpectedly high (18.4% of all poisonings, 3.3% in hospital), with ethanol poisonings found dead on scene as the main contributor.

167. Pandemic Hand Hygiene Recommendations Increased Inquiries Related to Alcoholic Hand Sanitizers in Children Under 6 Years

Eronen AK, Mustonen H, Hoppu K.
Poison Information Centre, Helsinki University Central Hospital, Helsinki, Finland

Objective: During the A(H1N1) pandemic many recommendations concerning hand hygiene were issued. People were told to wash their hands with soap and water and to use alcohol-based hand sanitizers regularly. Alcohol can be toxic to small children. The purpose of the study was to investigate whether the instructions and increased availability influenced children’s exposures to alcoholic hand disinfectants. Methods: Data was collected from the Poison Information Centre (PIC) database and all inquiries about exposures to alcohol-based hand sanitizers were included from January 2005 to December 2010. Inquiries from January 2009 until May 2010 were made more detailed on a monthly basis (Pandemic declared in June 2009). Symptoms were assessed according to Poison Severity Score. Results: The number of inquiries related to hand disinfectants rose from 70 in 2005 to a peak of 377 in number of calls, beginning in April 2009 and reaching the highest number in December 2009 followed by a return to normal level in April 2010. During the year 2009 233 and in the first 6 months of 2010 102 children under 6 years were exposed to alcohol based hand sanitizers. Of the exposures 197 and 89 were oral, 36 and 14 eye, and 3 and 3 dermal. Some of the patients were exposed through more than one route. Of the children only 18 and 17 were symptomatic and all of the symptoms were classified as minor. Home observation was recommended in 222 and 98 cases while 11 and 4 cases required medical attention. Conclusion: Recommendations to improve hand hygiene by using alcohol based hand sanitizers also increased children’s toxic exposures to these products. Most of the exposed children showed no signs of toxicity, and only a few showed minimal toxicity requiring medical attention. Retailers of alcohol-based sanitizers should be kept out of children’s reach. References: 1. Persson H, Šjöberg G, Haines J, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13.

168. Overdose Profile of Antipsychotic Agents

Caganova B, Plackova S, Kresanek J, Batora I.
National Toxicological Information Centre, Department of Occupational Medicine and Toxicology, University Hospital Bratislava, Slovakia

Objective: Evaluation of the safety profile of traditional and atypical antipsychotics in overdose. Methods: Intoxications were analyzed on the basis of data gathered from telephone consultations and medical reports forwarded to the National Toxicological Information Centre (NTIC) in Bratislava from the whole area of Slovakia during the period 1999–2008. All patients who consulted the NTIC because of non-prescribed use or overdose of antipsychotics were included in the group for analysis. The severity of poisonings was classified in accordance with the Poisoning Severity Score. Results: During the 10-year observation period 1145 patients were the subject of enquiries to the NTIC. Since 1999 the number has increased by 220%. Annually there is an increase in the number of intoxications by atypical antipsychotics, together with their rising prescription. The highest number of intoxicated patients (181) was in the age group 15 to 19 years. Suicidal intoxications were more frequent - in 875 cases (80.3%) and had a more serious clinical course. Clinical symptoms of intoxication were manifested in 951 patients (90.2%) of the observed group. We registered just 103 cases (9.7%) in which no symptoms of intoxication were manifested after non-prescribed use or overdose. The most frequent (in 657 cases) were moderate symptoms (sleepiness, dizziness, gastrointestinal distress, mild extrapyramidal symptoms, hypotension) that subsided in 24 hours. In 217 patients we observed symptoms of severe and in 71 patients symptoms of severe intoxication. Severe intoxications in 6 patients resulted in death. Financial costs of the treatment increased along with the severity of intoxication and the length of hospital stay. The conclusion of our findings is that there is no significant difference in severity or the distribution of the poisonings by the most atypical and traditional antipsychotics. Conclusion: Our analysis shows that an early consultation with the NTIC contributes to essential reduction of hospitalization and the deaths reduced from 12 cases in 2003 to one case in 2005. Conclusion: We can conclude that the role of the Poison Control Centre of Morocco in the collection of epidemiological data concerning the various poisonings helped compile a list of poisons with high fatality rate, and helped to direct and control activities thus reducing the mortality rate associated with these poisons.

171. Caustic and Household Detergent Exposures in Emergency Medicine

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Objective: Children younger than 6 years are under risk of poisoning by caustics and other household products. The aim of this study was to assess the caustic and household detergent exposures admitted to Emergency Medicine at Dokuz Eylul University Hospital (EMDEU) between 1993 and 2008. Methods: Our retrospective data were transferred into a Statistical Package for Social Sciences for Windows 15.0 (SPSS 15.0). Age, sex, reason of exposure, clinical signs, rate of endoscopy in oral exposures, treatment attempts, length of hospital stay and outcome were evaluated. A chi-square test was used to analyse statistical differences. Results: Caustic exposures accounted for 8.5% (1160 cases) and 4.1% (1988 cases) of all poisonings in children and adults, respectively. Female/male ratio was 0.8. Most of the exposures were unintentional (158, 86.8%). Intentional exposures were common in children. In patients who had a history (χ² = 25.685, p <0.001). The most common caustic substance was alkaline (106, 58.3%) followed by acidic (47, 25.8%) and other household detergents (28, 15.4%). Vomiting (35.7%) nausea (14.8%) and retching (13.1%) were the most common clinical signs in oral exposures. Endoscopy was performed in 38.3% (n = 38) of symptomatic and 10.6% (n = 8) of asymptomatic cases. Patients who had a history, the most frequent finding was first degree damage (58.7%). A 48 year old man died from intentional hydrochloric acid ingestion. Conclusion: Children were more susceptible to severe damage. In patients who had a history, the most frequent finding was first degree damage (58.7%). A 48 year old man died from intentional hydrochloric acid ingestion.

172. Epidemiologic Analysis of Intoxications in the Italian Region Emilia Romagna
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1Department of Pharmacy, University Hospital, Ferrara; ²Institute of Legal Medicine, University of Ferrara; ³Department of Anaesthesia and Intensive Care, S. Anna Hospital, Ferrara, Italy

Objective: The Department of Pharmacy of the University Hospital of Ferrara (AOUFE) activated a project called “Monitoring and implementation of the Centre of Reference for antidote stocks”. Its development follows the correct allocation of available antidotes in the Centre of Reference of the Region Emilia Romagna (RER). An epidemiological analysis to identify the type of intoxication and their respective treatments has been carried out as well.

Methods: All the 17 Hospitals of the RER were asked to provide information about intoxications registered from 1/1/2005 to 31/12/2009 as well as their respective antidote therapies. Required data were: year, type of intoxication and toxin substance, patient’s features, type of antidote used and treatment period. Results: 16 hospitals took part in the analysis. 8154 intoxications were registered and they are grouped as follows: 1707 intoxications in 2005 (20.93% over the whole 5-year period); 1523 in 2006 (18.68%); 1593 in 2007 (19.54%); 1560 in 2008 (19.13%); 1771 in 2009 (21.72%). Categorization by toxic substance showed the following: 24% caused by drugs; 17% caused by ethanol; 4% by opioids; 3% by carbon monoxide; 3% by food; 1% by sodium hypochlorite and derivatives; 38% by non classifiable intoxications; 10% by various intoxications. In 13.90% of cases the following antidotes were used: 22.28% (254/1140) activated charcoal associated with gastric lavage; 15.79% (180/1140) activated charcoal; 8.42% (96/1140) activated charcoal associated with MgSO₄; 15% (171/1140) fluimazenil; 14.30% (163/1140) hyperbaric oxygen; 13.86% (158/1140) naloxone; 5.70% (65/1140) metadione; 4.65% (53/1140) benzodiazepines. Conclusion: Drug and ethanol poisonings were the most frequent; non-specific treatment were the most frequently performed, followed by the use of specific antidotes such as flumazenil and naloxone. Epidemiological analysis shows that the frequency of intoxications in RER is 3.82 per 10000 inhabitants/year. References: 1. Repetto MR. Epidemiology of poisoning due to pharmaceutical products, Poison Control Center, Seville, Spain. Eur J Epidemiol 1997; 13:353–6.

Resic A¹, Jakasac N²
¹Department of Clinical Toxicology and Pharmacology, Children’s Hospital Zagreb, Clinical Hospital Sisters of Mercy, Zagreb; ²Centre for Pediatric and Adolescent Mental Health Care, Children’s Hospital Zagreb, Clinical Hospital Sisters of Mercy, Zagreb, Croatia

Objective: To present the results of observing hospitalized children in the Department of Clinical Toxicology and Pharmacy of Children’s Hospital Zagreb in period between 1982–2009 (28 years) in order to understand the frequency and causes of acute poisoning in children in the Republic of Croatia, which are not well known.

Methods: Tracking of total number of children hospitalized due to acute poisoning, percentage of intentional poisonings, breakdown by type of agent that led to poisoning, age and gender. Results: During the observed period 6001 patients were hospitalized due to acute poisoning, of which 92% were accidental. Most frequent were drug poisonings (51%), followed by poisonings with alcohol (26%), chemicals (13%), pesticides (5%), inhalation agents (3%), herbs and others (2%). The average age of accidentally poisoned patients was 5 years, excluding poisoning with alcohol where the average age was 15 years. Fifty-five per cent of all accidentally poisoned patients were boys. The average age in the group of intentional poisonings was 16 years, of which 82% were girls. Conclusion: Acute poisonings in children involve a complex set of different factors in health and social issues. It would seem useful to extrapolate particular measurable epidemiology features for the purpose of consideration of the problem and for planning preventative measures.

176. Perceived Benefits of Electronic Poison Information for the Emergency Department
Fountain JS, National Poisons Centre, University of Otago, Dunedin, New Zealand

Objective: Consideration has been given to widening international access to the New Zealand National Poisons Centre’s poison information database: TOXBASE. In an effort to assess clinical perception of this type of clinical decision support system, a survey was administered to identify whether Emergency Department staff in the Australasian region believe that access to an electronic poisons information resource would lead to clinical benefit. Methods: A preliminary survey tool was developed and presented to staff in one emergency department for comment and validation. Following revision, six emergency departments in both New Zealand and Australia each received ten of the resulting questionnaires - a total of 60 to each country.

Results: In 2001, TOXBASE was excluded from the data. The total number of telephone enquiries for each year was recorded by NPIC. Results: By the end of December 2001 there were 22 registered users (16 EDs) in Ireland. This more than tripled to 79 users (38 EDs) by the end of 2009. The number of TOXBASE sessions (logons) increased nearly 7 fold from 1865 in 2001 to 13 052 in 2009. In the same period the total number of telephone enquiries to NPIC dropped by 39.4%, from 16 241 in 2001 to 9 838 in 2009 (Table 1). The most frequently (top 10) accessed products on TOXBASE changed over the 9 years; however paracetamol remained the most frequently accessed.

Conclusion: Provision of an online poisons information database in Ireland has reduced the NPIC call load, but increased the overall access rate in EDs to poisons information sources.

Table 1. Do you believe a good electronic poisons information resource would?

<table>
<thead>
<tr>
<th></th>
<th>Totally Agree</th>
<th>Agree</th>
<th>Undecided</th>
<th>Disagree</th>
<th>Totally Disagree</th>
<th>No Answer</th>
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<td>Save you time</td>
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<td>New Zealand</td>
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</tr>
<tr>
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<td>70%</td>
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<td>8%</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Enable better triage</td>
<td></td>
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<td>New Zealand</td>
<td>67%</td>
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<td>Australia</td>
<td>49%</td>
<td>22%</td>
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<td>8%</td>
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<td>0%</td>
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<tr>
<td>Improve patient management</td>
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<tr>
<td>New Zealand</td>
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<tr>
<td>Support your clinical decision making</td>
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<td></td>
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<tr>
<td>New Zealand</td>
<td>82%</td>
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<td>16%</td>
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<td>0%</td>
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<tr>
<td>Australia</td>
<td>62%</td>
<td>22%</td>
<td>16%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
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<tr>
<td>Better integrate hospital management</td>
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<tr>
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<td>0%</td>
<td>3%</td>
</tr>
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<td>Allow more efficient patient management</td>
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<tr>
<td>Allow your department to provide a better service</td>
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<td>82%</td>
<td>12%</td>
<td>4%</td>
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<tr>
<td>Australia</td>
<td>41%</td>
<td>38%</td>
<td>22%</td>
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<td>0%</td>
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</table>

Objective: In 2001, TOXBASE, the UK online poisons information database was made available in Ireland, initially mainly to Emergency Departments (EDs). TOXBASE usage in Ireland and its impact on telephone enquiries to the National Poisons Information Centre (NPIC) were reviewed. Methods: Session (logons) data was extracted from the TOXBASE server. Information on the most frequently accessed products by Irish TOXBASE users was also extracted. NPIC use of TOXBASE was excluded from the data. The total number of telephone enquiries for each year was recorded by NPIC.

Results: By the end of December 2001 there were 22 registered users (16 EDs) in Ireland. This more than tripled to 79 users (38 EDs) by the end of 2009. The number of TOXBASE sessions (logons) increased nearly 7 fold from 1865 in 2001 to 13 052 in 2009. In the same period the total number of telephone enquiries to NPIC dropped by 39.4%, from 16 241 in 2001 to 9 838 in 2009 (Table 1). The most frequently (top 10) accessed products on TOXBASE changed over the 9 years; however paracetamol remained the most frequently accessed.

Conclusion: Provision of an online poisons information database in Ireland has reduced the NPIC call load, but increased the overall access rate in EDs to poisons information sources.
Objective: Nurses involved in triaging patients are the first point of contact in Emergency Departments. To encourage best practice and empower staff dealing with poisoned patients a clear and concise nursing management guide to aid nurses was designed to be available through TOXBASE®. We report overall access for the 12-months agents from hospitals in the UK and access patterns for these guides 1st April 2009–31st March 2010. Methods: The specialist toxicology nurses within the clinical toxicology unit, Royal Infirmary of Edinburgh (RIE) produced nursing management plans for the top 25 poison presentations to the RIE over 3 years. The guides were derived from TOXBASE® monographs and included information on: type of product/specific drug; key clinical features; initial management. The total number of TOXBASE® accesses and calls to the NPIS were retrospectively calculated per week from 05/01/2009/30/09/2010. Lexitis Nexis1, an online news resource tool, was used to find all articles from UK newspapers mentioning the drug names. Results: Totals for each drug are shown in Table 1. The majority of calls, accesses and articles regarding Ivory Wave occurred in April and September 2010, the peak in calls preceded the peak in articles by two weeks. Conclusion: The guides are a tool, was used to find all articles from UK newspapers mentioning the drug names. Results: Totals for each drug are shown in Table 1. The majority of calls, accesses and articles regarding Ivory Wave occurred in April and September 2010, the peak in calls preceded the peak in articles by two weeks. Conclusion: These data suggest these guides are accessed and therefore used by nurses within the clinical toxicology unit, Royal Infirmary of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK.

178. Introduction of Web-based Nursing Guides TOXBASE® Dow MA, Pettie JA, Lupton DJ, Good AM, Bateman DN.

National Poisons Information Service (Edinburgh), Royal Infirmary of Edinburgh, Edinburgh, UK.

Objective: Nurses involved in triaging patients are the first point of contact in Emergency Departments. To encourage best practice and empower staff dealing with poisoned patients a clear and concise nursing management guide to aid nurses was designed to be available through TOXBASE®. We report overall access for the 12-months agents from hospitals in the UK and access patterns for these guides 1st April 2009–31st March 2010. Methods: The specialist toxicology nurses within the clinical toxicology unit, Royal Infirmary of Edinburgh (RIE) produced nursing management plans for the top 25 poison presentations to the RIE over 3 years. The guides were derived from TOXBASE® monographs and included information on: type of product/specific drug; key clinical features; initial management. The total number of TOXBASE® accesses and calls to the NPIS were retrospectively calculated per week from 05/01/2009/30/09/2010. Lexitis Nexis1, an online news resource tool, was used to find all articles from UK newspapers mentioning the drug names. Results: Totals for each drug are shown in Table 1. The majority of calls, accesses and articles regarding Ivory Wave occurred in April and September 2010, the peak in calls preceded the peak in articles by two weeks. Conclusion: These data suggest these guides are accessed and therefore used by nurses within the clinical toxicology unit, Royal Infirmary of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK.

179. Legal Highs: Analysis of the Use of National Poisons Information Service Resources and Newspaper Coverage Crawford CL, Lupton DJ, McGrory CE, Good AM, Bateman DN.

National Poisons Information Service (Edinburgh), Royal Infirmary of Edinburgh, Edinburgh, UK.

Objective: To analyse usage of UK National Poisons Information Service (NPIS) data for new ‘legal highs’ that appeared in the UK in 2009, and to analyse the relationship between newspaper coverage of these drugs and enquiries to the NPIS. Background: The NPIS provides information to UK health professionals via its clinical toxicology database, TOXBASE®, and over the telephone, often in more severe cases of suspected poisoning. We have analysed TOXBASE® usage and numbers of calls to the NPIS for four ‘legal highs’ (mephedrone, naphyrone, Ivory Wave, Benzo Fury), and compared these data to newspaper coverage of the drugs. Methods: For each drug, the number of TOXBASE® accesses and calls to the NPIS were retrospectively calculated per week from 05/01/2009/30/09/2010. Lexitis Nexis1, an online news resource tool, was used to find all articles from UK newspapers mentioning the drug names. Results: Totals for each drug are shown in Table 1. The majority of calls, accesses and articles regarding Ivory Wave occurred in April and September 2010, the peak in calls preceded the peak in articles by two weeks. Conclusion: These data suggest these guides are accessed and therefore used by nurses within the clinical toxicology unit, Royal Infirmary of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK.


National Poisons Information Service (Edinburgh), Royal Infirmary of Edinburgh, Edinburgh, UK.

Objective: A retrospective analysis of telephone enquires to the National Poisons Information Service (NPIS) in the UK was performed to investigate the severity of iron poisoning enquires. Methods: All telephone enquires received by the NPIS are entered into the United Kingdom Poisons Information Database (UKPID). UKPID call data relating to all types of iron exposures between 01/09/2007 and 01/09/2010 were analysed. Results: 1651 enquires involved iron; 1181 iron only exposures were analysed further. Six hundred and ninety-two (59%) related to persons aged <15 years (80% of which were aged <5 years), 468 (40%) related to ≥16 years (57% of which were aged 16 to 25 years). In enquires relating to those ≤15 years the ratio of male to female patients was even, whereas 80% of all enquires that related to persons aged ≥16 years involved females. Iron ingestions, (97% of enquires), were examined for: type, circumstances and poisoning severity scores1 (Table 1). Serious toxicity, coma (6), haematemesis (7), hepatic dysfunction (14), melaena (21) somnolence (23) and acidosis (49), was relatively uncommon. Severity was greater in adults (Table 1). Conclusion: The majority of iron poisoning enquires in this study were accidental ingestions in children and resulted in low toxicity. References: 1. Persson HE, Sjoberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13. Acknowledgement: The authors express their gratitude to the NPIS for providing the data analysed herein.

181. Contribution of a Poison Centre in the Detection and Identification of a Delayed Food Borne Dysentery after the Consumption of Pine Nuts Contaminated by Non-Edible Pine Species Versteegen G, Mostin M.

Belgian Poison Centre, Brussels, Belgium.

Introduction: The detection of food borne outbreaks suffers from high latencies between the outbreak identification, identification of the contaminant and the formulation of an adequate response. In the case of “pine mouth syndrome”, this contamination went largely unnoticed for years. Objective: To emphasise the role of poison control centres in the detection and identification of a food chain contamination. Methods: Epidemiologic data were collected through the poison centre’s information system. Suspected pine nut samples were analysed by GLC, which allows the determination of the botanical origin, based on the fatty acid profile.1 Results: Following a first episode of 7 isolated cases of pine mouth syndrome between August 1998 and June 1999, we published an abstract describing delayed taste disturbances caused by Chinese pine nuts.2 No external contamination was identified and there was no analytical
method to identify the pinus species involved. The cause of the syndrome remained unknown. The problem virtually disappeared only to reappear in 2009, triggering an urgent message to the EAPCC'T-forum in September. We decided to conduct an audit to take advantage of the outbreak in the fall of 2010, we registered 40 to 50 cases per month. Concurrently, over 3400 cumulative cases have been reported in France. During the second outbreak 16 suspected samples were correctly analysed. Pinus armandi nuts were identified in all the samples pure or in mixture with Pinus koraiensis nuts. To further unravel the pine nut mystery, the Belgian poison centers were currently collaborating with the "Sensory Science and Eating Behaviour" department at Wageningen University in the Netherlands. Conclusion: Poison control centres may play an important role in the identification of Amatoxins symptoms. To trigger more research in this area. Furthermore, a relationship between the consumption of Amanita phalloides and Galerina marginata was detected in 16% of the cases. Photos (mobile phone MMS or e-mail) were used to aid in the identification in 69% of the cases. In the 89 cases where identification was certain or the 5 most poisonous mushrooms ruled out, 97% of the cases could be observed at home. Conclusion: Mushroom experts are a valuable resource in the identification of mushrooms by telephone. With their aid NPIC is able to give the caller correct advice and prevent unnecessary medical treatment.

181. A Targeted Effort to Improve the Documentation Quality of Inquiries to the Danish Poison Information Centre. A Quality Assurance Project
Jürgens G2; Dalhoff KP2; Hansen NB2,3; Hoegberg LC3; Ebbehoj NE2,4.

Objective: The Danish Poison Information Centre (NPIC) registers all inquiries in structured records in order to 1. undertake a correct and consistent individual risk assessment, 2. document the sequence of events, in order to 3. undertake a correct and consistent individual treatment. The database was analysed. Results: Over the study period, the NPIC received 31 telephone calls about synthetic cannabinoids observed at home. Patient died as a result of taking synthetic cannabinoids. Prior to this synthetic cannabinoids such as "Spice", "King B" and "Magic Gold" were sold in Irish head shops as "legal highs". Methods: A retrospective study was undertaken to investigate telephone enquiries to the National Poisons Information Centre regarding synthetic cannabinoids from Jan 2008 to July 2010. Telephone enquiries were documented by the Poisons Information Officers. Data recorded included: number of enquiries, age, gender, symptoms, and referral to ICU. Furthermore, there was a significant relationship between the RA and the referral to the ICU. Conclusion: This study aimed to assess the exposures to mushrooms with the aid of biologists. Methods: We reviewed the exposures to mushrooms reported to the NPIC from June through October 2010. Patient and exposure characteristics were noted. At the time of collection of a follow-up questionnaire by telephone on the identification procedure, symptoms, severity and outcome. Results: The NPIC received 811 calls from health care professionals and the public referring to mushrooms during the period. One hundred and fourteen calls were included in the follow-up study of which 90 (79%) were referred to mushroom experts for identification. The biological material was able to establish the exact mushroom species in 73 (81%) of the cases and rule out the 5 most poisonous mushrooms in the Norwegian flora (Cortinarius rubellus, Cortinarius mutabilis, Amanita phalloides and Galerina marginata) in 16% of the cases. Photos (mobile phone MMS or e-mail) were used to aid in the identification in 69% of the cases. In the 89 cases where identification was certain or the 5 most poisonous mushrooms ruled out, 97% of the cases could be observed at home. Conclusion: Mushroom experts are a valuable resource in the identification of mushrooms by telephone. With their aid NPIC is able to give the caller correct advice and prevent unnecessary medical treatment.

182. The Effect of Legislation on Synthetic Cannabinoid Abuse in Ireland
Herbert JX, Duggan E, Tracey JA.
National Poisons Information Centre, Beaumont Hospital, Dublin, Ireland

Objective: To investigate telephone enquiries regarding synthetic cannabinoids to the National Poisons Information Centre (NPIC) Dublin and relate this to Irish legislation banning head shop drugs. Background: The Irish Criminal Justice Bill on Psychoactive Substances introduced on 11th May 2010 included a ban on synthetic cannabinoids. Prior to this synthetic cannabinoids such as "Spice", "King B" and "Magic Gold" were sold in Irish head shops as "legal highs". Methods: A retrospective study was undertaken to investigate telephone enquiries to the National Poisons Information Centre regarding synthetic cannabinoids from Jan 2008 to July 2010. Telephone enquiries were documented by the Poisons Information Officers. Data recorded included: number of enquiries, agent consumed, enquiry source, and symptoms experienced. Symptoms were graded on the Poisoning Severity Score. A timeline comparing poison enquiries with Irish legislation banning synthetic cannabinoids was analysed. Results: Over the study period, the NPIC received 31 telephone calls about synthetic cannabinoids concerning 33 patients (21 male, 12 female). The majority of enquiries (67%) involved young adults under the age of 20 with only one enquiry regarding a patient over 40. 76% of enquiries were from hospitals, 18% from general practitioners and only 3% from members of the public. The number of enquiries increased 12 fold from 2008 to 2010 with a peak in March and May 2010. Irish Legislation banning synthetic cannabinoids was introduced on the 11th May 2010. There was only one enquiry to the NPIC regarding synthetic cannabinoids after this date. The most common symptoms consisted of sympathomimetic effects such as palpitations (26.5%), tachycardia (20.6%), increased sweating (14.7%) and tremor (8.8%). Other symptoms included dyspnoea (11.8%), gastrointestinal upset (11.8%), chest pain (8.8%), syncope (5.9%) and cold extremities (2.9%). The majority of enquiries were moderate (54%) with only one patient graded as severe. No patient died as a result of taking synthetic cannabinoids. Conclusion: Irish legislation was effective in reducing the number of calls to the NPIC regarding synthetic cannabinoids. This coincided with a 3 fold reduction in the number of operating head shops in Ireland.

184. Identification of Mushrooms after Exposures Reported to the Norwegian Poisons Information Centre Seljegtan KO, Spillum BJ.

Background: The NPIC is a valuable resource in the identification of mushrooms by telephone. With their aid NPIC is able to give the caller correct advice and prevent unnecessary medical treatment.

185. Concurrency Between Advice Given by the Danish Poison Information Centre and Information in Hospital Discharge Letters
Krog P2,1; Dalhoff K1,2.

1Danish Poison Information Centre, Copenhagen; 2Dept Clinical Pharmacology, Bispebjerg University Hospital, Copenhagen, Denmark

Objective: To evaluate the risk assessment performed by the Danish Poison Information Centre (DPC). All inquiries about poisonings in children (<15 years old) were reviewed and compared with information from hospital discharge letters. Methods: All incoming hospital discharge letters from 1.1.2009 to 27.9.2010 were collected and the following information was registered: duration of hospital stay, ward to which referred to Intensive Care Unit, final outcome (no consequences, no initial consequences (e.g. follow-up visits in outpatients), consequences). These data were compared with corresponding DPC data: age, gender, toxic agent, and risk assessment (RA-I no risk, RA-II transient risk without any need for treatment, RA-III need of treatment, RA-IV life threatening, RA-V unqualified). Results: 27 cases were matched and compared from hospital admissions (M/F 138/138). The majority of children were 2–3 years old (29%). The toxic exposures were divided into 3 groups: drugs (group A, n = 167), chemicals (group B, n = 103) and substances of abuse (group C, n = 5). In group A 27/167, in group B 2/103 and in group C 1/5 were transferred to the ICU. According to information in the discharge letters, 79% of the poisonings did not result in any further complications. In 20% of the poisonings, the children needed a second clinical check-up after a follow-up laboratory test after discharge. In only 2 cases did the poisoned patients developed complications (one patient was transferred for plastic surgery after exposure to a corrosive drain cleaner, and one patient was transferred for continued gastrointestinal distress due to an industrial detergent). In 237 cases, DPC categorized the poisonings as RA-II (189), RA-IV (25) or RA-V (23). In 13% of RA-II and in 16% of RA-IV assessments, the patients were transferred to the ICU (0 in both RA-I and RA-II). There was a significant relationship between the duration of hospitalization (median days) and the risk categorisation performed by the DPC (RA-I 0.01, RA-II 0.11, RA-III 0.59 and RA-IV 0.92 days). Conclusion: There was a close association between the severity of the DPC RA score and referral to ICU. Furthermore, there was a significant relationship between the duration of hospitalization and the resulting severity of the poisoning according to the duration of hospitalization.
186. Unintentional Overdose with Vitamin D
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Objective: This study evaluates the calls due to overdose of vitamin D (cholecalciferol) in children. The prophylactic dose of vitamin D to avoid rickets is 500 IU p.o. daily during the first year of life. This dose is equivalent to 1 drop of Vigrantol. Vitamin D intoxication may cause hypercalcemia. Methods: A retrospective analysis of the calls due to overdose of vitamin D was performed, using the electronic records database from January 1 to December 31, 2009. The outcome was evaluated based on the telephone lines and discharge report of hospitalized patients. Results: 105 calls (50.5% of all inquiries due to vitamins in 2009) concerned vitamin D. Only children aged 0–3 years were involved, of whom 66.6% children were younger than 1 year. There were 46 boys (43.8%) and 59 girls (56.2%). The most common incorrect dose in 51 children was 5000 IU (about 10 drops) of vitamin D, administered to the mouth directly from the dropper. Nine children older than 1 year ingested approximately 100,000 IU of vitamin D from the bottle. Only 5 children received vitamin D repeatedly in a dose of 5000 IU for 10 days, without the supervision of parents. Only 5% of all incorrect doses were twice 5000 IU, 3–4000 IU, 3x 100,000 IU. Twenty-two children were hospitalized for 2 days. Conclusion: A high percentage of parents did not follow the instructions on the package to give one drop in a meal or on the spoon. About 33.4% of the ingestions were caused by incorrect storage. Nevertheless, overdose up to 100,000 IU did not cause any symptoms, and only in 5 of 105 cases was a mild increase of serum calcium level found. Physicians should carefully educate parents about the correct method of providing the prophylactic treatment and the parents should be more cautious about the storage of drugs. Acknowledgements: MSM021620807.

187. Lead Exposure in the Danish Population as Seen from an Open Poison Centre
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Objective: Exposure to lead has declined significantly over decades.1 Simultaneously the lowest level of health effects from lead has decreased.2 In the present case series we described lead exposure in a post-industrial society. Case series: All contacts to the Danish Poison Information Centre where lead was stated as the toxic agent were identified in the centre’s database and the records evaluated. The time frame was from the poison centre opening to the public on August 1st, 2006 to October 31st, 2010. Information on lead source, lead exposure route, clinicopathological characteristics and, if available, blood-lead level was extracted. Thirty-one cases exposed to lead were identified. Ten were five years or younger and all had eaten lead objects. Six were 5–14 years old and except for one with mixed exposure, all had oral exposures. Among those 15 years or older, four had been exposed by inhalation, two orally, one by a gun shot, five by more than one route and four by unknown route. Exposure to work was the setting for 5 cases, two with inhalation, one with mixed and two with undetermined exposure. Blood lead measurements (BLLs) were available for six cases above 10 μg/dL (9.37–27.3 μg/dL) and 25.7–27.3 μg/dL. Three 14-years old boys had peak BLLs at 1.99, 2.68 and 2.73 μg/dL after having eaten a lead based toy and two of these had chelation treatment. Exposure to lead was found in 2 cases in 2 households, in 2 cases in 2 modern society. In some instances with toxicologically significant lead levels as a consequence. Thus, the goal of primary intervention was to prevent poisonings and secondary education was defined as reducing morbidity and mortality by creating poison center awareness. All calls concerning general information on health and disease prevention questions were classified as general question (GQ). Only calls concerning acute exposure to poisons were defined as poisonings (PQ). Since EPI’s search engine shows first a list of healthy mammals, all poisoning questions were answered via the search engine on October 10, 2008 the monthly number of calls was compared. Results: During the analysed period in total 768 calls were answered. The structure of the calls was as follows: 2008 90 calls (11.1%) GQ, 59(58.9%) PQ; 2009 331 calls: 127(38.4%) GQ, 204(61.6%) PQ; 2010 347 calls: 86(24.8%) GQ, 261(75.2%) PQ. In 2008 3 lectures were held and 2 articles were published; in 2009 6 lectures and 8 articles; in 2010 6 lectures and 6 articles. As a result, the median monthly call volume increased from 30 in 2008 to 38.6 in 2010 (22.2%), the number of PQs increased from 17.7 in 2008 to 29 in 2010 (39%). Conclusion: Active and systematic poisons information education increases the awareness of the population to the poison information centre without an expensive media campaign and has a positive impact on the volume of poisonings handled by the centre. The educational programmes did not have an immediate effect on the call volume and structure but had a positive effect from the second year forward. As the programme was described, combining primary and secondary poison prevention in one initiative may have a small but positive impact on poison centre call volume.

188. The Role of the Slovenian Poison Control Centre in the Prevention of Chemical Poisoning in Children
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Objective: Prevention of poisoning, especially in children, is one of the most important tasks of our National Poison Control Centre (PCC). In the late childhood period (age 11–18 years) drugs of abuse and suicide attempts predominate. In contrast, poisonings of children in the early period (age 0–10 years), are unintentional and as such accessible for poisoning preventative measures. Methods: We analysed the calls register of our 24-hour information and consultation service for the period 2001–2003. In children, age 0 to 10 years, poisonings with chemicals represent 48.9% (n = 863), 56.2% (n = 863), 58.3% (n = 863) and 61.9% (n = 863). Poisons of the most toxicological risk categorisation: (20.8%), organic solvents (14.6%), corrosives (10.8%) and gases (3.8%) predominate. Among non-toxic chemicals, soaps/detergents (23.5%) and others (26.5%) predominate. In 2004 the preventative action plan for children was established in collaboration with Institute for Public Health for the Republic of Slovenia, Ministry of Health and Ministry of Education. The action plan includes an education program for target groups (parents, carers and teachers) as well as collaboration on the legalisation level. The action plan was adopted well; its effectiveness was evaluated by comparison with another analysis for the period 2007–2009. Results: Poisons with chemicals in this period represented 47.5% (n = 863). Poisoning with pesticides was reduced by 47.1%, with organic solvents 39.7%, with corrosives 43.5% and with gases 35.7%. We registered an increase of exposures in children to non-toxic chemicals: by 24.7% for soaps/detergents and 58.5% for others. Conclusion: Co-ordinated efforts and collaboration to non-toxic chemicals should be in accordance with good practice of general chemical management. Our special aim for the near future is also to achieve a restriction of concentrated corrosives used as household products.

189. How to Use the Internet and the Media to the Benefit of Public Health? The Norwegian Poison Information Centre’s Experiences
Ringstad K, Lorentzen HR.
Poisons Information Department, Directorate of Health, Oslo, Norway

Objective: Until 2003 the means the Norwegian Poison Information Centre (NPIC) used actively to reach the public were brochures, posters and a website with limited information. In 2003 we changed direction in order to reach the public in different ways. The pro-active work has increased the awareness of the population to the poison information centre without an expensive media campaign and has a positive impact on the volume of poisonings handled by the centre. The educational programmes did not have an immediate effect on the call volume and structure but had a positive effect from the second year forward. As the programme was described, combining primary and secondary poison prevention in one initiative may have a small but positive impact on poison centre call volume.

Abstracts

Clinical Toxicology vol. 49 no. 3 2011
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191. **Sufficient Product Information Without Exhauating the Poisons Information Centre’s Resources?**

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Objective: To describe the current system regarding product information in the Norwegian Poison Information Centre (PIC), including the Product Information Bank (PIB). Results: A PIC needs immediate access to product information on any product they are asked about. Therefore, an updated database of all products is too time-consuming for most PICs. The Norwegian PIC used to have a database of about 4000 datasets, but not the resources to keep it properly updated. A web-based system forced them to pay extra time registering products we rarely have enquiries about. In 2009 most of our datasets were transferred to PIB. Companies who want the PIC to have access to their material safety data sheets (MSDS) are asked to register them in PIB. PIB is a public website (www.pib.no) run by the Norwegian Product Register (governmental). An offline copy of PIB is made available in the PIC to ensure continuous accessibility. The PIC has been involved in the development of PIB from the beginning. PIB’s vision is to be an official website for efficient exchange of information about chemicals and/or products. It is therefore vital that most products are included and that the information is up-to-date. As yet it is not mandatory and thus, far from all companies are willing to devote resources to registering their products in PIB. The number of MSDS in PIB per November 2010 is 5111. In addition to the MSDS, the PIC has access online to The Product Register’s database with complete composition of about 25,000 products. However, time consuming security measures means that this database is only sporadically used in emergency situations. For most enquiries the PIC relies on the supervision of the chemical product and/ or information from datasets is sufficient. Conclusion: Despite a limited number of MSDS available in PIB it is useful to the PIC. The PIC can devote attention to the products that are most relevant to its work. Even though PIB is our current solution, we follow closely and with great anticipation the ongoing work regarding CLP article 45.

192. **The Federal Institute for Risk Assessment Human Data of Poisonings to the Case Report Database For Poisonings - Standardization of Case Reports, Improvement and Examination for Subject-Specific Access**

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Background: The Federal Institute for Risk Assessment (BfR) Documentation and Assessment Centre for Poisonings (BfR-DCoCen) is part of the German toxicological network. German Physicians and Poison Centres (PCs) report human data of poisonings to the BfR. Every case is assessed on the chemical product involved with the distinct formula provided by BfR products and their relevant toxicological data of the German industry. Data on human poisonings is condensed in a harmonized and standardized data file for analysis. In addition cases of special toxicological and scientific interest (e.g. rare poisonings, high-volume, high-flow, dose exposures, cases with unexpected clinical course, substances of special interest etc.) are prepared for standardized case reports. For better retrieval of human toxicological data a bilingual case report database had been implemented. Methods: The cases are documented in a standardized form (accident/situation of poisoning/age/gender/symptoms/signs/exposure data/clinical development/changes/treatment), indicates substance/product involved and supplemented with important references. After co-checks for correctness, completeness and readability, the German text is translated and transferred to the case report database. In addition, selected case reports from literature were transferred as pdf-files to the same database. Results: Since July 2002 more than 500 cases have been selected, prepared and processed with additional data for case reports. The case reports were written down in uniform documents, provided with keywords and additional information, finally assigned to index words. Starting in 2004, the documents were recorded in a prototype database driven by MS-Access, from 2006 onwards the case record database was transferred to an inhouse MS Access database. At present, the BfR-case database has been provided with additional staff. The BfR is in consultation with specialists in data protection to ask whether the BfR needs additional staff for the future. Conclusion: In the assessment of poisonings and for e-learning there is a great interest in case reports. The BfR intends in future to offer its case reports on poisoning via its Internet portal for subject-specific access.

193. **From Bedside to Bench: Calcium Gluconate is an Effective Treatment in Hydrophobic Acid Skin Burns and Reverses Fluoride Induced Vasocostriction In Vitro**

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Objective: We studied the efficacy and safety of intraarterial infusion of calcium gluconate on hydrophobic acid (HF) skin burns treatment as well as on fluoride effects in rabbit aortic ring contraction in vitro and in modulation of intracellular Ca²⁺ concentration ([Ca²⁺]i) in vascular derived smooth muscle cells in culture. Methods: Calcium gluconate was hypothesized to be mediated by fluoride which was previously identified as a GTP binding proteins activator leading to inositol-phosphate accumulation and increase in intracellular [Ca²⁺]i. Calcium gluconate either topical or in intraarterial infusion is considered the most effective clinical therapeutic approach. In this study, we examined a case series of patients with severe HF burns admitted to the Toxicology Unit of Careggi Florence Hospital, between 2005/2009 and treated with calcium gluconate both in local dermal application and in intraarterial infusion. Moreover, fluoride effects on rabbit aortic ring contraction in vitro and on modulation of [Ca²⁺]i in vascular derived smooth muscle cells in culture were evaluated. Results: Five patients were admitted to the Toxicology Unit of Careggi Florence Hospital with a diagnosis of HF skin burns. They were treated with local dermal application and intra-arterial infusion of calcium gluconate. In all cases there was a complete reduction in fluorescence intensity of two months and an average hospitalization time of six days. In vitro experiments, sodium fluoride (10–30 mM) induced a contraction of rabbit aortic ring preparations (167 ± 25%, n = 4, p < 0.05 one tailed t test) when compared to a standard contraction stimulated by KCl 80 mM. Calcium gluconate (50–100 mM) was able to decrease sodium fluoride induced contractile response (38 ± 17%, n = 4, p < 0.05 one tailed t test). Similar results were obtained on sodium fluoride increase in [Ca²⁺]i, in vascular derived smooth muscle cells in culture. Conclusion: Intra-arterial infusion of calcium gluconate was confirmed as a safe and effective therapeutic approach for wound healing and pain relief in HF skin burns. Calcium gluconate was also shown to be effective in reversing fluoride induced in vitro vasocostriction, assumption may be suggested as a possible mechanism of HF induced skin damage.

194. **Benzydamine: Recreational Misuse of a Non-Recreational Drug**


1Clinical Toxicology Unit and Poison Control Center, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy.

Objective: Benzydamine hydrochloride is an indolic non steroidal anti-inflammatory drug available as mouthwash, vaginal douche, aerosol and pills. Being an over the counter drug it can be easily obtained and recreational use has become a street youth in developing countries. We describe an acute recreational benzydamine intoxication following voluntary ingestion of a commercially available vaginal douche containing 200 mg, per sachet diluted in water. The patient was confused, agitated with mild tachycardia (96 bpm) and hypotension (135/95) with hallucinatory vision and muscle weakness. Toxicological screenings were negative for alcohol and common drugs of abuse. ECG showed QT interval prolongation. Treatment was symptomatic (diazepam i.v.) and supportive. The hallucinations lasted for almost six hours. ECG normalized after 24 hours. The patient remained in hospital for 6 days due to psychiatric comorbidity and was discharged in good health. Conclusion: Benzydamine has structural similarity to dimethyltryptamine and for this reason could cause serotonergic system toxicity. Although the exact mechanism of benzydamine hallucination is still unknown, multiple pharmacological interactions could be hypothesized.
196. Bidirectional Tachycardia During Treatment of Metoprolol Overdose
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Objective: Bidirectional tachycardia is an unusual arrhythmia characterized by beat-to-beat alternation of the morphology and the axis of the QRS-complexes. It is most commonly linked to digitalis toxicity, certain channelopathies, cardiomypathies, seldom in case of phaeochromocytoma, myocariditis. We report the first case of bidirectional tachycardia associated with administration of atropine and dopamine in metoprolol overdose. Case report: A 33-year-old female presented to our clinic with a history of an intentional intake of 1500 mg metoprolol. On arrival her vital signs were: BP 93/57 mmHg, HR 67 bpm, GCS 15/15. Electrocardiogram displayed a normal PR, QRS, QTc interval. After 8 hours she became drowsy, and her electrocardiogram was notable for third degree atrioventricular block and her blood pressure dropped to 70/40 mmHg. She was given a bolus of 1 mg atropine and infusion of dopamine (8 micrograms/kg/minute). Ten minutes later the patient complained of retrosternal chest pain. The ECG revealed a bidirectional tachycardia at 160 bpm with QRS of 88/121 ms which lasted for 2 minutes with spontaneous return to a sinus tachycardia at 100 bpm. The subsequent ECG showed ST-segment elevation in lateral leads. Dopamine infusion was stopped and colloid infusion was administered. The patient’s BP went to 86/62 mmHg. Cardiac troponin was moderately elevated. An echocardiography was carried out showing no regional wall motion abnormalities with an ejection fraction of 38% (by Simpson method). Cardiac MR performing next day revealed anterolateral hypokinesia and an ejection fraction of 48%. Chest pain lasted for 10 hours and ST-segment elevation persisted for 2 days. A second echocardiography performing 5 days after ingestion showed an ejection fraction of 60% with no wall motion abnormalities. The patient refused coronaryography. Stress test was performed. In our case, tachycardia (together with administration of atropine after ingestion of a large amount of metoprolol) seemed to cause: 1. bidirectional tachycardia (perhaps triggered by a burst in coronary artery spasm).

197. The Role of Urgent Esophagogastroduodenoscopy in Prognosis of Acute Esophageal Injury
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Introduction: Ingestion of corrosive substances causes severe lesions to the upper gastrointestinal tract that are manifested with destructive changes of the mucosa and muscle layer and even perforation of the esophagus and the stomach in more severe cases. The gold standard for determination of the grade and extent of the lesion, which at the same time helps in deciding on the therapeutic approach, is urgent esophagogastroduodenoscopy. The aim of this paper was to present our clinical experience with the 4-grade endoscopic classification of injuries in prognosis of the outcome in acute caustic poisonings. Methods: This was a retrospective study comprising 33 patients with grade II B and III injury hospitalized at the University Clinic for Toxicology in Skopje, FYROM in the period 2008-2009. The grade of injury was determined with urgent esophagogastroduodenoscopy performed in the first 2-12 hours after admission and the post-corrosive injuries were classified according to the four-grade classification recommended by Kikendall. After treatment the patients were followed for a minimum of six months. A total of 33 patients were examined. At the time of hospital admission post-corrosive injuries of grade III predominated (n = 22, 66.67%), whereas the remaining patients had post-corrosive injuries of grade II (n = 11, 33.33%). After 6 months of clinical follow-up, the most common late post-corrosive complications of the esophagus were stenosis of the esophagus (n = 19, 57.58%) while normal finding of the esophagus was found in 14 (42.42%) patients (p < 0.001* p < 0.0001*** (N.sig.)). The most common post-corrosive damages of the stomach were: antro-pyloric stenosis (n = 10, 30.30%), pyloric stenosis (n = 6, 18.18%) and antral stenosis (n = 3, 9.09%), whereas in 14 (42.42%) patients a normal finding of the stomach was found (p < 0.05* p < 0.001*** (N.sig.)). Conclusion: Urgent esophagogastroduodenoscopy has to be done in all acute caustic poisonings in the first 12-24 hours and they are to be classified according to Kikendall’s four-grade classification. Patients with confirmed post-corrosive complications of the esophagus and stomach require a high index of morbidity. The classification in four grades of post-corrosive injuries to the upper gastrointestinal tract might help in therapeutic approach and prognosis of the outcome.

198. Mortality Rate in Glycol and Methanol Intoxications in Poland in the Year 2009
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Background: Glycol and methanol poisoning is not common but can be a life threatening condition. In Poland most patients intoxicated with these alcohols are admitted to the hospitals at a late stage, with profound acidosis and multiorgan failure. Because of this, the majority of them must be treated in the Specialized Toxicology Care Units (ICUs). Objective: The aim of our study was to compare the mortality rate among patients treated because of glycol and methanol poisonings in 2009 in all TUs and ICUs in Poland. Methods: All medical interventions provided in TUs and ICUs, in which the main diagnosis was coded as T51.1, and T52.3 according to ICD-10, and all those codes recorded as co-morbidities and positively verified by two toxicologists were included in our study. The state of health as well as the age of both groups were similar. Results: There were 192 patients in Poland in 2009, including 23 methanol and 105 glycol patients hospitalized in TUs, and 20 methanol and 44 glycol patients treated in ICUs. Intoxications with those alcohols were the main cause of death in 44% of all TUs and ICUs in Poland in 2009. In the methanol group the mortality rates in TUs and ICUs were 39.1%, and 55.0% respectively, while in glycol group the mortality rates in TUs and ICUs were 20.9%, and 56.8% respectively. The overall mortality rate in both groups was 24.2% in TUs, and 56.2% in ICUs. The much higher mortality rate in ICUs needs further and exact investigation, however, to some extent, this problem may be connected to delayed diagnosis of intoxication; prolonged supportive treatment; too low dose of intermittent haemodialysis (IHD), and the usage of Continuous Renal Replacement Therapy (CRRT), which is the standard procedure carried out in ICUs, but for which the clearance is much longer than for IHD. Conclusions: There is a strong need for postgraduate education of the ICU staff in which should have its own Toxicological Unit. It is necessary to produce diagnostic and treatment protocols for intoxicated patients in Poland. References: 1. Bayliss G. Dialysis in the poisoned patient. Hemodial Int 2010; 14:158-67.

199. Impact of Direct Admissions to a Poisons Treatment Ward
National Poisons Information Service (Cardiff), Cardiff and Vale University Health Board, Cardiff, UK

Objective: To evaluate the benefits of direct admission to a specialist treatment ward compared to transfer following initial triage in an Accident and Emergency department (A&E). Results: In a 26-bed treatment ward, part of the Welsh National Poisons Unit, is an eight-bedded ward opened in 1983 dedicated to the care of poisoned patients; the only specialised treatment ward of its type in the UK. In April 2005 a policy was introduced to allow patients with uncomplicated paracetamol poisoning to be admitted directly to this ward; previously they would have required triage in A&E and then transfer across the city by ambulance, a distance of 6 miles. Later that year this policy was extended to allow all uncomplicated poisoning cases with a GCS of 14 or above to be admitted directly. Results: Following these changes, the number of direct admissions increased from 6.5% to 50% of total admissions. The policy was revised again in 2008 to allow those with a GCS of 12 or above to be admitted directly; currently direct admissions account for 75% of all patients admitted to the ward. Conclusion: The overwhelming benefit of direct admission is to the patient who has immediate access to specialist care; additional advantages include a reduction in waiting times, inevitable in a busy accident unit. This is particularly important in a group of patients that have self-harmed and tend to readily self-discharge. The ward ensures that all patients have access to early psychiatric assessment - also important as a significant proportion (30%) of patients is discharged within 24 hours. Currently 71% of all patients admitted to the ward are psychiatrically assessed prior to discharge. The calm environment of the ward is conducive to the specialist care required by poisoned patients with trained doctors, nurses and psychiatric staff ensuring a high standard of effective care. Other obvious and quantifiable benefits of direct admission to the poison ward include reduced pressure on the busy A&E department and a decrease in medical emergency referrals; the cost savings are appreciable with 1207 direct admissions in 2009 that would have otherwise utilised considerable human and financial NHS resources.

200. Effective Methotrexate Elimination using High-Flux Haemodialysis
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Background: Methotrexate is a chemotherapeutic agent used in the treatment of childhood acute lymphoblastic leukaemia and sarcoma as well as psoriasis and rheumatoid arthritis. In overdose, toxic effects can be severe, symptoms can include vomiting, diarrhoea, mucositis, haemolytic anaemia, renal failure, hyperkalaemia and bone marrow suppression leading to leucopenia, thrombocytopenia and anaemia. Standard treatment is symptomatic and supportive together with folic acid or glucaricase therapy but results are variable. Enhanced elimination of the drug by haemodialysis is generally considered to be ineffective. We report a case in which serum methotrexate concentrations were high and rapidly reducing of which haemodialysis was invoked. Case report: A 23-year old female patient on treatment with high dose methotrexate for lymphoma was admitted with renal failure. Her serum methotrexate concentration was 81.9 μmol/l upon presentation. She was started on folic acid therapy and also haemodiafiltration using an FX 100 high-flux dialyser. Following a
Table 1. Methotrexate (MTX) concentrations before and after dialysis

<table>
<thead>
<tr>
<th>Day</th>
<th>MTX Dialysis</th>
<th>MTX Dialysis</th>
<th>MTX Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>81.9 g/6 hours</td>
<td>67.6 g/6 hours</td>
<td>11.2 g/6 hours</td>
</tr>
<tr>
<td>24</td>
<td>24.0 g/6 hours</td>
<td>- / g/6 hours</td>
<td>2.7 g/6 hours</td>
</tr>
<tr>
<td>3</td>
<td>3.75 g/6 hours</td>
<td>- / g/6 hours</td>
<td>0.98 g/6 hours</td>
</tr>
<tr>
<td>4</td>
<td>1.26 g/6 hours</td>
<td>- / g/6 hours</td>
<td>0.45 g/6 hours</td>
</tr>
<tr>
<td>5</td>
<td>0.48 g/6 hours</td>
<td>- / g/6 hours</td>
<td>- / g/6 hours</td>
</tr>
<tr>
<td>6</td>
<td>0.2 g/6 hours</td>
<td>- / g/6 hours</td>
<td>- / g/6 hours</td>
</tr>
</tbody>
</table>

6-hour dialysis session, a break of 2 hours and a further 6-hour session, the methotrexate concentration fell to 11.2 g/L. This was reduced to 2.7 g/L following a further 2 sessions of dialysis. Six-hourly sessions of dialysis/day for the following 3 days reduced circulating methotrexate concentrations to 0.2 μmol/L (Table 1).

Each morning there was evidence of a rebound in concentrations. Conclusion: Methotrexate toxicity can be severe and deaths have occurred. In this case high-flux dialysis rapidly decreased circulating concentrations. The use of this means of elimination should be considered in cases of life-threatening toxicity not responding to conventional treatment.

201. Coagulation Tests as Predictive Parameters of Acute Liver Toxicity in Phalloides Syndrome: Thrombin Time and Activated Partial Thromboplastin Time

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Objective: Phalloides syndrome is an urgent toxicological issue demanding early treatment. In countries where measurement of amanitin is not available, estimation and rechecking of the coagulation blood tests in the early phases of poisoning is imperative for making treatment decisions. Prothrombin time (PT) is accepted as an early and prognostic parameter but the tests in the early phases of poisoning is imperative for making treatment decisions. PT(PT) time (aPTT) and thrombin time (TT) can also be considered as valuable markers of acute toxic hepatitis. Methods: The coagulation tests in 6 patients with incubation period of more than 10 hours and proven gastroenterocolitis were analyzed. Admittance at the Clinic was after 17.6 ± 6.02 hours of having the mushroom meal with developed gastroenterocolitis and dehydration. The prothrombin time (PT), activated partial thromboplastin time (aPTT) and thrombin time (TT) were measured on admission. Results: During the stay the patients underwent symptomatic and active treatment with haemofilter sometimes with ACTH-CG. aPTT and TT (Z = 0.97, p = 0.808) was maximally found to be 3520 ± 209 U/L and AST 2383 ± 1589 U/L. TT and aPTT were prolonged before PT. aPTT showed significant correlation with outcome (death/survive) (r = -0.97, p = 0.008), while TT (r = 0.50, p = 0.31) and TT (r = 0.50, p = 0.31) showed a weaker association with the outcome. The comparison of the correlation coefficient for the test/outcome association, showed strong and significant difference between aPTT and PT (Z = -3.23, p = 0.002). The differences between correlations of the test with the outcome, aPTT and TT (Z = -1.89, p = 0.058) and PT with TT (Z = 1.34, p = 0.17) were not significant. Conclusion: In case of inaccessibility to amanitin estimation in biological materials, coagulation tests may be useful parameters of early decision for aggressive and active treatment in phalloides syndromes and prognosis. TT and PT(A) are early signs of acute liver toxicity while aPTT can be used as a more predictive sign of the clinical outcome.

202. Intralipid Treatment of Sedative Hypnotic Drug Overdose: A Case Series

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Objective: Intralipid Emulsion Therapy (ILE) has been advocated as a possible treatment for sedative hypnotic drug ingestion in which endotracheal intubation and ventilation are required and where endotracheal intubation was immediately required or considered likely. Intralipid 20% solution (Presenius Medical Care Ltd) was administered in a dose of 500 mL over 20 minutes in suitable cases after discussion with the clinical toxicologist. Methods: A retrospective chart review was conducted to review the outcomes of this protocol in October 2010. Data collected included demographic details, drug(s) ingested, need for intubation, time for which ventilation was required and length of stay (LOS). Results: During the 12 month period from November 2009 till October 2010, ILE was used in nine cases. Of these 2 (22%) were male and median age was 32 years old (IQR 27–43). Intubation was required in 7 (78%) cases, 5 (71%) of whom received ILE prior to intubation. The median time to intubation was 19 minutes (IQR 13–80) from ILE administration. Median length of ventilation was 31 hours (IQR 28–48h). Median LOS for all 9 cases was 88 hours (IQR 60–93h). Of the 2 cases that did not require intubation one required a naso-pharyngeal airway for several hours and had no significant increase in GCS over this period. Quetiapine was the main ingestant in 6 cases (67%) with 2 cases (22%) due to bacofoen and 1 due to carbamazepine (11%). Coagulation markers of acute toxic hepatitis. The differences between correlations of the test with the outcome, aPTT and PT (Z = -3.23, p = 0.002). The differences between correlations of the test with the outcome, aPTT and TT (Z = -1.89, p = 0.058) and PT with TT (Z = 1.34, p = 0.17) were not significant. Conclusion: In case of inaccessibility to amanitin estimation in biological materials, coagulation tests may be useful parameters of early decision for aggressive and active treatment in phalloides syndromes and prognosis. TT and PT(A) are early signs of acute liver toxicity while aPTT can be used as a more predictive sign of the clinical outcome.

204. Massive Overdose of Meprobamate Treated with Continuous Venovenous Hemofiltration

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Objective: Meprobamate is an old sedative and anxiolytic drug. Overdose with this substance still occurs and may be potentially life-threatening due to cardiovascular collapse and severe CNS depression.1 It is important to have a reliable method of treatment available in cases of severe intoxication in a suicide attempt with meprobamate in a 45-year-old woman treated with continuous venovenous hemofiltration. Case report: The clinical course was complicated by profound CNS depression, respiratory failure, and prolonged hemodynamic instability despite aggressive fluid resuscitation and administration of vasopressors. Orotracheal intubation was performed and multiple dose activated charcoal was administered. Because of the serious clinical condition, continuous venovenous hemofiltration (CVVHDF) was begun in order to enhance meprobamate elimination. Pharmacokinetics during CVVHDF could be described by first order kinetics. The elimination half-life (t1/2) was 6.6 hours, total plasma clearance (CLR) was 87 mL/min and clearance by CVVHDF (CLRcv) was 64 mL/min (74% of CLR). After 36 hours of CVVHDF, extracorporeal assistance was stopped and the patient made an uneventful recovery. Conclusion: CVVHDF was clearly limited by the dialysate flow rate and it could be concluded that meprobamate is a dialyzable and filterable, in accordance with the physico-chemical properties of meprobamate. References: 1. Charon C, Mekontso-Dessap A, Chergui K, et al. Incidence, Causes and Prognosis of Meprobamate Poisoning. Intensive Care Med 2005; 31:1582–6.

205. Predictors of Mortality in Verapamil Overdose: Usefulness of Serum Verapamil Concentrations

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Objective: Verapamil poisoning may result in life-threatening cardiovascular morbidities and fatalities. To date, prognosticators of mortality have been poorly evaluated and used. The purpose of the present investigation for prognosis remains unclear. We aimed to evaluate the ability of usual clinical and laboratory parameters including serum verapamil concentrations and the use of serum verapamil concentration to predict outcome (survival versus death) in verapamil poisoning. Methods: We reviewed the medical records of all intentional and intravenous sodium bicarbonate, hypertonic saline and noradrenaline infusion to maintain haemodynamic stability. Her condition stabilised 12 hours post ingestion and she was extubated after 48 hours. Conclusion: These two episodes of amitriptiline over-dose of the same dosage in the same patient illustrate the importance of early decontamination and supportive management. On her first presentation she was treated with activated charcoal and the use of CVVHDF had an uneventful course. In contrast there was a delay in decontamination and supportive treatment by 3 hours on her second visit which led to recurrent pulseless ventricular tachycardia, seizures and haemodynamic instability.
symptomatic verapamil poisonings admitted over eight years to two medical intensive care units (ICU). Clinical and laboratory parameters were measured in 65 patients and final outcomes of survival or death recorded. A multivariate analysis was conducted to evaluate the prognostic values of recorded parameters. Results: Life-threatening complications of verapamil poisoning included shock (62%), atrioventricular block (24%), sinoatrial block (20%), acute respiratory distress syndrome (19%), and cardiac arrest (11%) resulting in death (8%). Verapamil concentrations measured on ICU admission were the only independent factors associated with mortality (p = 0.001). Comparison of serum verapamil (A), norverapamil (B), and verapamil + norverapamil (C) concentrations measured on admission according to the patient’s final outcome in the intensive care unit are shown in Table 1. The optimal verapamil cutoff point was 5.0 μmol/L (100% sensitivity, 91% specificity), which conferred a 2.8-fold increase in odds of fatality. Conclusion: Cardiovascular monitoring and assessment of respiratory function are vital in survival of verapamil poisoning. The serum verapamil concentration has excellent prognostic ability for predicting fatality in verapamil overdose.

206. Clinical Aspects of Genomics in Poisoning Situations
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Objective: Pharmacogenetics aims to explain the genetic variability in drug response and adverse drug effects. Despite large variability between individuals, in many cases, drug responses to drug exposure are predictable. Treatment is rather oriented towards diseases instead of individual patients. However, the one-dose-fits-all principle has come into question in many fields of drug therapy since we know, for many therapeutic areas, that large variability in drug exposure between subjects is leading to sometimes fatal overdosing and serious adverse effects. Discussion: Drug poisoning depends on many factors, among which variability in drug exposure may be one of the most important. Pharmacogenetic variants in drug metabolizing enzymes lead to differences in drug disposition and drug-drug interactions. In the atonic verapamil poisoning, the serum verapamil concentration has excellent prognostic ability for predicting fatality in verapamil overdose.

207. Genomic, Transcriptomic and Metabolomic Tools as Biomarkers of Paracetamol Hepatotoxicity
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Introduction: The history of research on paracetamol toxicity is an excellent example of the evolution of investigation aims and tools in clinical toxicology in the last few decades. The ability of paracetamol as a potent hepatotoxic producing hepatic cytolyis and, eventually, acute hepatic failure was described in adults and children and led to extensive research on the implied toxic mechanism and the antidotes to be used. In 1975 a treatment nomogram was the result of the study of a large number of cases and established different therapeutic steps for different populations. The basic mechanism of cell lesion was described as follows: at toxic doses paracetamol undergoes an oxidative metabolic pathway, mediated by a member of the Cyt P450 family, producing a reactive metabolite, NAPQI able to be conjugated with glutathione. Following glutathione depletion, NAPQI links covalently to macromolecules, impairing its function and leading to irreversible cell death. A neat and elegant explanation which allowed, on the one hand, the definition of risk populations, such as patients having a history of contact with substances (mainly alcohol), causing probable P450 induction, or with nutritional deficiencies, and, on the other hand, the development of antidotes such as glutathione precursors. Discussion: Nevertheless, many gaps remained to be filled at the molecular level. Many of them have been dealt with in the last decade by means of basic Omics’ tools. We will review some of them: 1.- Genetic and genomic inter individual differences in pharmacologic pathways: The existence of glutathione transference and Cyt P450 2E1 polymorphisms and its influence in paracetamol metabolism have been described in the 90s. 2.- Neverthough much more attention has been focused on the enzymatic induction of the oxidative metabolic pathway. The CYP450 isozyme, currently identified as CYP2E1, was purified and characterized early in the 80s. The enzyme expression in the cell is regulated by transcriptional activation, mRNA stabilization, and increased translatable and protein stabilization. 3. One of the main CYP2E1 inducers is ethanol. Some indications of the role of CYP2E1 from cytosolic degradation through the ubiquitin-proteasome proteolytic pathway, others mention a two-step mechanism related to BAC (Blood Alcohol Concentration): a first step associated with low BACs appears to be post-transcriptional by stabilization and a second step is associated with high BACs and arrest of increased CYP2E1 induction. Recent studies suggest that CYP3A ethanol induction can also play a role in raising acute paracetamol toxicity. 4. It seems that not only CYP2E1 but also CYP2C9 and CYP3A11 may play an important role in NAPQI generation from paracetamol. A transgenic mouse line expressing the human CYP2E1 gene has been developed to study the role of CYP2E1 in acetaminophen hepatotoxicity. This model may also be useful as an in vivo tool for predicting drug metabolism and disposition and drug-drug interactions of chemicals that are substrates for human CYP2E1. 5. Up to now, P450 induction needs to be inferred from the patient’s antecedents from previous exposures. Real time polymerase chain reaction, enzyme-linked immunosorbent assay, and CYP2E1-dependent enzyme activity could be performed in peripheral blood allowing to define, in an objective way, the risk populations. Therefore CYP2E1 over expression could be considered as a biomarker of susceptibility. 6.- Intracellular targets and pathogenic pathways: In the last decade some of the paracetamol intracellular targets and lesional mechanisms have been studied in detail. Besides the role of NAPQI, glutathione depletion by itself gives way to free radical reactive species which causes mitochondrial permeability transition and loss of the ability of the mitochondria to synthesize ATP. The cell death is then supposed to be linked to the production of NAPQI and a concurrent increase in serum lactate after non-toxic and toxic doses of paracetamol. Those changes could be considered as biomarkers of effect. Both monitoring of cell death and susceptibility, can supply very useful information to be taken into account together with the classical exposure biomarker, i.e. paracetamol blood concentration. 7.- Cyt P450 and CYP2E1 genotypes have been studied in detail. Besides the role of CYP2E1, the CYP2E1 KO-derived hepatocytes exhibit more resistance against paracetamol with depressed intrahepatic expression of CYP1A2, CYP2E1, and CYP3A11, impairing paracetamol metabolism. 8.- Conclusions: Transcriptome and metabolomic methods have shown characteristic down regulation of genes involved in oxidative phosphorylation and mitochondrial function in peripheral blood, positively correlated with the production of NAPQI, and a concurrent increase in serum lactate after non-toxic and toxic doses of paracetamol. Those changes could be considered as biomarkers of effect. Both monitoring of cell death and susceptibility, can supply very useful information to be taken into account together with the classical exposure biomarker, i.e. paracetamol blood concentration. 9.- Cyt P450 and CYP2E1 genotypes have been studied in detail. 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Besides the role of CYP2E1, the CYP2E1 KO-derived hepatocytes exhibit more resistance against paracetamol with depressed intrahepatic expression of CYP1A2, CYP2E1, and CYP3A11, impairing paracetamol metabolism. 16.- Conclusions: Transcriptome and metabolomic methods have shown characteristic down regulation of genes involved in oxidative phosphorylation and mitochondrial function in peripheral blood, positively correlated with the production of NAPQI, and a concurrent increase in serum lactate after non-toxic and toxic doses of paracetamol. Those changes could be considered as biomarkers of effect. Both monitoring of cell death and susceptibility, can supply very useful information to be taken into account together with the classic exposure biomarker, i.e. paracetamol blood concentration. 17.- Cyt P450 and CYP2E1 genotypes have been studied in detail. Besides the role of CYP2E1, the CYP2E1 KO-derived hepatocytes exhibit more resistance against paracetamol with depressed intrahepatic expression of CYP1A2, CYP2E1, and CYP3A11, impairing paracetamol metabolism. 18.- Conclusions: Transcriptome and metabolomic methods have shown characteristic down regulation of genes involved in oxidative phosphorylation and mitochondrial function in peripheral blood, positively correlated with the production of NAPQI, and a concurrent increase in serum lactate after non-toxic and toxic doses of paracetamol. Those changes could be considered as biomarkers of effect. Both monitoring of cell death and susceptibility, can supply very useful information to be taken into account together with the classic exposure biomarker, i.e. paracetamol blood concentration.

208. The Use of Genotyping in a Specific Oncology Patient Population to Avoid Drug Toxicity

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Discussion: Pharmacogenetics covers the genetic variations that affect pharmacokinetics and -dynamics, in general. In many cancer-affected patients, metabolism, excretion, cellular transport, targets and target pathways, and their influence on drug-response phenotypes. In childhood acute lymphoblastic leukemia (ALL) pharmacogenomics has in the recent years become a major field of research. The genetic variation includes insertions, deletions, and variations in gene copy numbers, and not least an estimated 15 million single nucleotide polymorphisms with a minor allele frequency of at least 1%. This genetic variation is of particular importance for drugs with a very narrow therapeutic index such as anticancer agents. Many public databases are available for the purpose, such as the Biotechnology Information (NCBI), the International HapMap project, and The Pharmacogenetics and Pharmacogenomics Knowledge Base (PharmGKB) offer information on single nucleotide polymorphisms (SNPs), including their unique dbSNP ID number, their location in a specific gene, whether they are haplotype-tagged, and for example whether they are synonymous (confer no amino acid change) or non-synonymous (changes the amino acid). The therapeutic outcome for any disease is determined by the interaction between the host genotype and the therapy. Previously the focus was primarily on the effect of a specific treatment on the disease, and treatment failures (not least within oncology) were in general regarded to represent resistant disease. However, numerous studies have strongly indicated that for sensitive diseases, such as childhood leukemia, host variations in drug disposition determined by inherited genetic variants may, as frequently as truly resistant disease, lead to treatment failures. Unfortunately, few studies have actually explored this in depth, and many potential obstacles burden the journey. In oncology, most patients are treated with multiple therapies simultaneously, and relatively steep dose-response relationship for most anticancer agents, and a significant fraction of the patients are treated beyond this limit and experience serious late effects (e.g. reduced auditory or kidney function) or even deaths due to toxicities, mostly life-threatening infections. In children above the age of 1.0 year cancer is the most common medical cause of death in the industrialised countries, and ALL is the most frequent cancer in childhood. Over the last decades the outcome for children with ALL has changed dramatically from being an almost universally fatal disease to 80% cure rates by first-line therapy. However, to obtain these cure rates most of the patients receive up to ten different drugs that target DNA synthesis (i.e. the replication fork), and the therapy. Previous studies have revealed that the diversity in response should be predictable by host genomics. This is the primary focus of most genotype-phenotype association studies but is insufficient for personalised medicine. A crucial and acceptable toxicity must be regarded to outweigh the chances of cure, or the risk of relapse must be regarded to outweigh the risk of toxicity, thus leaving clinical room for dose adjustments. Individualized treatment adjustments by host genomics should have predictable effects in individual patients. This has at least been demonstrated with therapeutic drug monitoring, but not with dose adjustments. In order for dose adjustments must be superior to adjustments by toxicity (this has not been shown, but at least indicated in a few studies). 

Reducing toxicity or increasing efficacy by host genomic based dose adjustments must not be impeded by “reverse” events (i.e. less efficacy or more toxicity) (this certainly remains to be explored). 

To convince clinicians to use genetic markers in their treatment strategies, such host genomic based treatment guidelines must be defensible statistically (including confirmation in independent data sets) and be biologically understood. This is rarely the case with new associations found through genome-wide association studies. 

The conclusion, personalised medicine will certainly change from disease to disease depending on the cure rates and toxicities of the treatments. A wide range of drugs and metabolites, from anticancer drugs to oral hypoglycemic agents, can be simultaneously transported by one or more transporters. These transporters means that there is no single mechanism by which the drug is introduced into a biological system such as the human body. This definition can also be extended to toxicokinetics in overdose or intoxicated patients. Pharmacogenomics is now challenged by the growing importance of transporters, a relatively new and potentially major factor in xenobiotic ADME. The drug transporters in the membranes of cells and organelles of mammalian tissues are members of two superfamilies. Those of the ATP-binding cassette (ABC) superfamily are responsible for active primary transport, while the members of the SLC (solute carrier) superfamily are involved in secondary active transport. The ABC transporters are encoded by 48 genes in humans, and the importance of these genes is increasing. 

209. Opioid Receptor Polymorphism Associated with Drug Overdose Severity: Pilot Results

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Objective: Genetic variations in the mu-opioid receptor mediate individual differences in the human response. A common mu-opioid receptor single nucleotide polymorphism (SNP) A118G has been associated with enhanced drug abuse behavior; however its association with overdose severity in humans is unknown. We investigated the relationship between the A118G SNP and overdose severity in patients presenting to the emergency department (ED) with acute drug overdose.

Methods: In an observational cohort study at an urban ED, we enrolled 480 adult ED patients presenting with suspected acute drug overdose over a 5 month period for whom discarded blood samples were available for analysis. Demographics, clinical and adverse effects, along with hospital outcomes were collected by an abstractor prior to SNP analysis. In-hospital severe outcomes were defined as any of the following: respiratory arrest (mechanical ventilation); cardiac arrest (loss of pulse); and mortality. Blinded high-resolution melt genotyping of the A118G SNP was performed after standard DNA isolation using the QIAGEN Tissue kit (Qiagen Inc., Valencia, CA) and whole genome amplification (QIAGEN REFLUIP). Patients were classified as either wildtype (A/A), heterozygous (A/G), or homozygous mutant (G/G) using the LightCycler (Roche).

Results: We have to date evaluated 54 patients (43% female, mean age 41, 12 A/A, 40 A/G, 2 G/G). Urine toxicology was positive in 39%, of which there were 12 A/A, 30 A/G, and 2 G/G. Using the LightCycler we found a high prevalence of the A118G mu opioid receptor SNP in ED patients with acute drug overdose, with no severe outcomes in wildtypes. Future studies will test larger populations and other mutations for overdose vulnerability. 


210. Relevance of Transport Systems in Clinical Toxicology

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Discussion: Pharmacokinetics has been defined over the past several decades as the study of drug absorption, distribution, metabolism and excretion (ADME) when the drug is introduced into a biological system such as the human body. This definition can be extended to toxicokinetics in overdose or intoxicated patients. Pharmacogenomics is now challenged by the growing importance of transporters, a relatively new and potentially major factor in xenobiotic ADME. The drug transporters in the membranes of cells and organelles of mammalian tissues are members of two superfamilies. Those of the ATP-binding cassette (ABC) superfamily are responsible for active primary transport, while the members of the SLC (solute carrier) superfamily are involved in secondary active transport. The ABC transporters are encoded by 48 genes in humans, only about 9 of which influence drug kinetics. P-glycoprotein (P-gp; ABCB1), several isoforms of the multidrug resistance associated proteins (MRPs; ABC drug efflux transporters), and the breast cancer resistance protein (BCRP; ABCG2) efflux their substrates from cells to the extracellular space. In contrast, 362 genes are presently known to encode SLC transporters, and the number is still growing. Several SLC families, classified by their substrate specificity, like the transporters of organic anions (OAT), organic anion polypeptide (OATP), and organic cations (OCT), mediate the influx or efflux of substrates with complex modes of transport requiring voltage or/and ion gradient co-transport. About 30 of these proteins are involved in drug transport. The recent intrusion of drug transporters means that there is no single mechanism by which drugs permeate through the membranes. All these transporters have polycritical transport properties. A wide range of drugs from conventional organic anions, cations and zwitterions to oligopeptides, can be simultaneously transported by one or more transporters. These transporters are also ubiquitous within the cells of xenobiotics as they are more deterministically governed. For example, the hepatic uptake and biliary excretion of numerous xenobiotics
can be mediated by specific transporters expressed either in the basolateral membrane of the hepatocytes or in the bile canalicular membranes, respectively. In a similar way, renal reabsorption and secretion are highly dependent on the activity of multiple transport systems in both the basolateral and apical side of the proximal tubular cells. Drug transporters are also clinically important. They can modulate the pharmacokinetics of drugs, affecting the serum concentrations and causing toxicity in specific organs due to intracellular drug accumulation. Hepatotoxicity, nephrotoxicity, neurotoxicity can be induced by the drugs in the liver, kidney and other organs, respectively.

The release of poorly water-soluble drugs. In contrast to absorbing the active drug into the body gradually and usually releasing the drug at the site of action, the release of drug from a system can be controlled or altered to achieve specific therapeutic goals. Drug transporters are involved in the absorption, distribution, and excretion of drugs.

Objectives: To review the evidence base for modified-release (MR) preparations delaying the onset of, and prolonging, clinically significant symptoms following overdose; to define the role of activated charcoal (AC) and whole bowel irrigation (WBI) in decreasing the absorption of MR preparations. Modified-release preparations: These include delayed- and extended-release systems for oral administration and oral and intravenous formulations that provide the release of poorly water-soluble drugs. In contrast to immediate release drugs, MR formulations release active drug into the body gradually and usually predictably over a 12- to 24-hour period to maintain plasma concentrations within a therapeutic range, in order to minimize adverse effects. With most MR preparations there is a prolonged absorption phase, so that the onset of symptoms is delayed (as late as 16–20 hr), which leads to a delayed time to maximum plasma concentration (Tmax). The release of drug from the formulation may be further prolonged due to the formation of a concretion of tablets (pharmacobezoar) in the stomach or intestine. Impact of single doses of AC: There is evidence from volunteer studies that AC 25 g administered 1 hr post dosing can reduce significantly (p < 0.001) the absorption of MR preparations of carabamazepine (200 mg), theophylline (200 mg) and verapamil (120 mg). AC 1 g/kg (with sorbitol) administered 1 hr after theophylline MR 10 mg/kg to five children resulted in a 61% reduction (p < 0.01) of the AUC 0–12 h. Impact of multiple doses of AC: In other limits of this study, AC 1 g/kg administered at 6 hr, 9 hr, 12 hr (n = 5) reduced the AUC 0–12 h by 38% (p < 0.02) and by 18% (NS) respectively, AC 20 g administered at 6 hr, 7 hr, 8 hr, 10 hr and 12 hr after theophylline MR 170 kg body weight to volunteers decreased serum theophylline concentrations significantly. In another study, the administration of AC at 1 hr (50 g), 5 hr (25 g) and 9 hr (25 g) after theophylline MR 600 mg in 12 volunteers reduced theophylline absorption by 91.2%. The AUC of theophylline in the control group was 152.8 ± (SD) 14.4 mg·h/L, a reduction of 2.3 mg·h/L. In the same study AC was given at 6 hr (50 g), with further doses at 10 hr (25 g) and 14 hr (25 g). The AUC of theophylline in the AC group was 65.3 ± 1.3 mg·h/L, a reduction of 57.3%. No statistical calculations were undertaken. It is not known whether the impact of AC in the second part of the study was on increasing elimination alone, which it is known to do, or on some other pharmacokinetic or pharmacodynamic impact. Impact of WBI: WBI commenced 1 hr after the administration of lithium MR 0.8 mEq/kg to 10 volunteers reduced the AUC by 67% (p < 0.005) and significantly decreased the mean serum lithium concentration (p < 0.03). Aspirin 2.925 mg was administered to 10 volunteers. WBI, commenced 4 hr after dosing, reduced significantly (p < 0.01) the AUC and peak salicylate concentrations; it was also superior to AC and sorbitol (p < 0.05). WBI started after the administration of AC to volunteers dosed with MR preparations of carabamazepine, theophylline and verapamil did not decrease absorption more than AC alone and in the case of carabamazepine decreased its efficacy. Clinical studies: No controlled clinical studies have been performed, though case reports and single case controlled studies have been performed. In regard to theophylline MR preparations, WBI, which are problematic to interpret. Conclusion: Ingestion of MR preparations may result in a delay in the onset of symptoms and in the pharmacokinetics of the MR preparations, and thus may delay release of drug. In volunteer studies, administration of a single dose of AC up to 1 hr after drug dosing has shown to reduce absorption. Multiple doses of AC, even when commenced at 6 hr post dosing, have reduced plasma drug concentrations significantly in some studies but not others. It is not known whether this is the result of increased drug elimination or reduced absorption. WBI has been shown in volunteers to reduce the absorption of MR preparations significantly. References: 1. Buckley NA, Dawson AH, Reith DA. Controlled release drugs in overdose. Clinical considerations. Drug Saf 1995; 12:73–84. 2. Lapatto-Reiniluoto O, Kivistö KT, Neuvonen PJ. Activated charcoal and whole bowel irrigation in preventing the absorption of sustained-release drugs. Clin Pharmacol Ther 2001; 70:255–60. 3. Lim DT, Singh P, Nourtis S, et al. Absorption inhibition and enhancement of elimination of sustained-release theophylline tablets. Clin Pharmacol Ther 1996; 59:20:536–9. 8. Kirshenbaum LA, Mathews SC, Sitar DS, Halstenson CE. Whole-bowel irrigation as a treatment for toxic ingestions. J Toxicol Clin Toxicol 1999; 37:731–51. 7. Smith SW, Ling LJ, Halstenson CE. Whole-bowel irrigation as a treatment for the ingestion of modified-release pharmaceuticals. Clin Pharmacol Ther 1989; 46:264:9. 7. Tenenbein M, Seger DL, Meulenberg J. American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. J Toxicol Clin Toxicol 1999; 37:731–51. 8. Kirshenbaum LA, Mathews SC, Sitar DS, Halstenson CE. Whole-bowel irrigation as a treatment for the ingestion of modified-release pharmaceuticals. Clin Pharmacol Ther 1989; 46:264–9. 7. Tenenbein M, Seger DL, Meulenberg J. American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. J Toxicol Clin Toxicol 2004; 42:237.
Abstracts

214. Paediatric Overdose with Cough and Cold Medicines: The Irish Experience
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Objective: To describe cases of poisoning with cough and cold medicines in children reported to the National Poisons Information Centre (NPIC) in Ireland over an 8 year period. Methods: The records of telephone enquiries to the NPIC from 2005–2012 inclusive were retrospectively reviewed to identify enquries about paediatric poisoning with these medicines. The limited data collected over the last 5 years, however, do not indicate substantially increased fetal risks. Improved methods of follow up are needed if adequate information is to be made available to support management and provide advice to the women affected.

215. Acute Poisonings Treated at the Outpatient Accident and Emergency Clinic in Oslo, 2008
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Objective: Treatment of acute poisonings at an outpatient around-the-clock accident and emergency clinic (EMA) is common in Oslo. In 2003, the number of patients treated at the EMA equalled that of the five hospitals in Oslo seen as whole. There is a tendency for poisonings by drugs of abuse to be treated at the EMA, while pharmaceutical poisonings are treated in hospitals. Our objectives were to study the poisoning pattern with regards to the intention behind the poisoning, treatment and follow-up. Methods: All presenting at the EMA during one year were included consecutively in a prospective study design. A standardized form was completed by the treating physician, covering the aims of the study. Results: There were 2401 cases during the year. Of these, 1588 (66%) were males and the median age was 35 years. The most frequent main agents were ethanol (44%), opiates (22%), and carbon monoxide/ nitrogen (10%). Of the patients, 83% received no further treatment than observation, 9% received antidote(s), mainly naloxone, and 2% received activated charcoal. The median observation time for discharged patients was 3.6 hours. None developed sequelae or died. Sixty per cent were discharged without follow-up and only 17% were transferred to hospitals. Predictors for hospitalization were pharmaceutical poisonings, respiratory depression, and a suicidal intention behind the poisoning. Poisonings with ethanol or opiates were predictors for discharge. The attending doctors assessed 72% of the poisonings as accidental overdose or therapeutic errors, 15% as accidents other than accidents and 11% as suicide attempts. Of the suicide attempts, 13 (4.8%) were discharged without follow-up. Conclusion: Poisonings with cough and cold medicines were substance abuse related. Outpatient treatment of acute poisonings was both efficient and safe. Whether short and long-term mortality rates are affected by the low referral rate of follow-up, is, however, uncertain and needs further study. It is concerning that some of the suicide attempters were discharged without follow-up. The poisoning pattern was largely unchanged compared to the 2003-study, but the number was increased by two-fold in only five years, which calls for concern. We have no single explanation for this increase. Further studies should focus on possible explanations.

216. The Use of Extracorporeal Techniques in Acute Acetaminophen (Paracetamol) Poisoning
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Objective: Although acetaminophen (APAP) can be removed by extracorporeal removal (ECR) techniques such as hemodialysis, the safety and efficacy of N-acetylcysteine usually make the risks of ECR unjustified. In patients admitted to AEC in April 2005-September 2010, 1588 cases were symptomatic when the NPIC was called, but only 7 of these had moderate features and none was severely poisoned. Conclusion: Only 18% of children who had taken excessive doses of these medications were symptomatic and most of these had minor features only. Severe poisoning from cough and cold medicines was not seen in this study.

217. The Utility of Paracetamol Concentrations Prior to 4 Hours Post-Ingestion in Acute Paracetamol Overdose
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Objective: Risk assessment for possible hepatotoxicity and requirement for antidotal treatment with N-acetylcysteine following acute, non-staggered paracetamol overdose involves plotting the plasma paracetamol concentration (PCC) against the nomogram of recommendations such as hemodialysis, the safety and efficacy of N-acetylcysteine usually make the risks of ECR unjustified. In patients admitted to AEC in April 2005-September 2010, 1588 cases were symptomatic when the NPIC was called, but only 7 of these had moderate features and none was severely poisoned. Conclusion: Only 18% of children who had taken excessive doses of these medications were symptomatic and most of these had minor features only. Severe poisoning from cough and cold medicines was not seen in this study.

References:

Clinical Toxicology vol. 49 no. 3 2011
218. Can AST/ALT Ratio Indicate Recovery after Acute Acetaminophen Poisoning? Mullins ME, Vitkovitsky IV, Jones D. Division of Emergency Medicine, Washington University School of Medicine, St. Louis, Missouri, US Background: Acetaminophen (APAP) is the leading cause of pharmaceutical poisoning in the US and Europe. [AST] and [ALT] rise after hepatotoxicity. [AST] and [ALT] rise in similar proportions but later decline at different rates, with [AST] falling more rapidly than [ALT]. Objective: To determine whether the [AST]/[ALT] ratio can indicate assured recovery after APAP poisoning. Methods: In this retrospective, IRB approved study, we identified cases of patients hospitalized for acute APAP poisoning by querying the electronic medical record. The cases were treated with N-acetylcysteine (NAC) from 2001 to 2009. We included all patients with severe APAP poisoning, defined as [AST] or [ALT] > 1000 IU/L. We reviewed all charts to exclude NAC given for other indications. We then recorded paired [AST] and [ALT] concentrations measured at the same time from the same specimen. We classified each pair as clearly post-peak [AST] or not (the non-peak values included values before or at the observed peak [AST]). We calculated the [AST]/[ALT] ratio for each pair of values until both [AST] and [ALT] were < 100 IU/L. We compared the values of [AST]/[ALT] in increments of 0.1 to find the optimal value that reliably indicated resolved transaminases. Results: We identified 1634 patients who received NAC during the 9-year study period. Of these 292 received NAC for suspected poisoning by APAP and/or other substances. After excluding patients without hepatotoxicity, patients with peak [AST] and [ALT] < 1000 IU/L, and patients without confirmed history or laboratory evidence of APAP ingestion, we had 14 evaluable patients with severe hepatotoxicity after acute APAP overdose with 164 evaluable pairs of AST and ALT. The sensitivity of [AST]/[ALT] = 84% at a cut-off of 1.0, 94% at 0.8, 96% at 0.6, 99% at 0.5, and 100% at 0.4. Conclusion: [AST]/[ALT] ratio < 0.5 following severe hepatotoxicity from single acute APAP overdose appears highly predictive of recovery in patients treated with NAC. This has potential to be an indicator of safe termination of NAC treatment.


Objective: Cleaning and cosmetic products containing anionic and nonionic surfactants are considered widely as minimally toxic. Exposure generally causes limited cutaneous, ocular and gastrointestinal irritant effects. Most common symptoms are nausea, vomiting and diarrhoea, which may result in manageable respiratory distress. One objective of this study was to evaluate the frequency and severity of respiratory events. Methods: Prospective analysis of acute chemical consumer product poisoning in Germany poison centres during a six month period. After a confirmed oral exposure of manual dishwashing detergents, soaps, shampoos, general purpose cleaners or laundry detergents, a follow-up call within 48 h after ingestion was performed. Additional data and follow up information were collected with a structured telephone-interview based on a detailed questionnaire. The interviews were conducted by trained Poisons Information Centre staff. Results: 604 patients were covered. Age groups: 540 children, 40 adults, 24 elderly persons. Respiratory symptoms developed in 99 patients (90 children, 2 adults, 7 elderly persons), most frequently cough (94%). Other minor symptoms were transient mild laboured breathing (2), transient shortness of breath (1). In 5 cases cough persisted for more than 6 hours without further respiratory symptoms. Pulmonary aspiration with hospitalisation on intensive care units was reported 5 times. Bronchial airway obstruction (2), tachypnoea (2), oxygen desaturation/hypoxiaemia (4) were reported in 4 cases (1 toddler, 3 seniors). Mechanical ventilation because of respiratory failure was reported once (94 year old woman). Conclusion: After ingestion of surfactant containing products, pulmonary injury occurred rarely in this study. In spite of initial cough in 15 percent, only 1 percent developed respiratory symptoms requiring emergency health care. Mechanical ventilation was only reported once (measured by hospitalisation and supportive medical therapy (0.2% of all children). Elderly patients have an increased risk of respiratory injury after ingestion of anionic and non ionic surfactants.


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Objective: The pulmonary toxicity of hydrocarbons is well-known, and the ingestion of one swallow of fuel hydrocarbons (FH) (gasoline, diesel, fuel mixture) is a frequent cause of admission to emergency departments (EDs). Studies in the medical literature are generally inhomogeneous, and no prospective studies are available focusing exclusively on acute accidental FH ingestion in adults. We investigated (i) the incidence of acute pneumonia, and (ii) the correlation with some risk factor in patients who ingested one swallow of fuel hydrocarbons (FH). Methods: A prospective study of adult patients referred to Pavia Poison Center in a two-year period (July 2008-June 2010) has been performed. Inclusion criteria were (i) accidental ingestion of one swallowing of FH, and (ii) admission to EDs within 8 hours after ingestion. All the patients were observed for at least 8 hours in hospital; a chest X-ray was performed at the 8th hour after ingestion. A telephone follow-up was performed for patients with negative discharge. Informed consent was obtained from all the enrolled patients. The lack of the results of the X-ray was considered an exclusion criterion. Patients included were: 1. ingested one swallowing of FH, 2. no other ingestion of FH, 3. no other ingestion of gasoline, diesel, fuel mixture), 4. (ii) mortality of ingestion (from glass/bottle or during siphoning), (iii) acute symptoms, and (iv) development of acute pneumonia. Results: Among 250 cases of accidental FH ingestion referred to PCC in the study period, 116 patients were included in the study. Thirty patients (11.2%) developed acute pneumonia within 8 hours (X-ray confirmed), and seven of them were asymptomatic at admission. We found a statistically significant correlation between acute pneumonia and siphoning (12/13, p = 0.003), but not between acute pneumonia and vomiting after ingestion (p = 0.54). Among the 103 patients discharged with negative X-ray, follow-up at day 3 (available for 76/103 patients) and at day 7 (70/103 patients) revealed no occurrence of pulmonary symptoms. Conclusion: Acute pneumonia after accidental FH ingestion in adults is a frequent event and can occur even in the absence of respiratory symptoms at admission. In our case all the pneumonia occurred within eight hours, mostly after ingestion by siphoning.

221. Work-Related Rhinitis and Asthma due to Detergents and Disinfectants: the Role of Occupational Inquiries Laborde-Casterot H, Villa AF, Rosenberg N, Chatagnier D, Lee HM, Garnier R.

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Objective: Detergents and disinfectants are an emerging cause of work-related rhinitis and asthma. The components responsible for these effects are not well known. This study discusses the role of ethylenediamine, propylene glycol and acetic acid (lactate > 10 mmol/L, pH < 6.95) due to accidental exposure. The most common precipitating factor was temporary renal insufficiency owing to a few days of vomiting and/or
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223. Surveillance of Toxic Exposures to Plant Protection Agents and Biocidal Products in Europe

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Introduction: Pesticides are a heterogeneous group of biologically active substances designed to control pests such as insects, fungi, weeds, rodents, nematodes, algae, bacteria, and viruses. Due to their toxicological properties and potential public health impact and adverse effects on human health and the environment. Nevertheless, these chemicals serve many useful purposes and, as a consequence, are widely used in agriculture, other occupational settings, and at home. Considering their large availability for consumers as well as their toxicity, the International Code of Conduct on the Distribution and Use of Pesticides (hereinafter the Code of Conduct) calls for actions to reduce health and environmental risks. Among these actions the Code of Conduct specifically encourages governments to develop reporting systems designed to identify incidents of acute human health effects related to pesticides exposure.1 The main intent of this contribution is to highlight how the European legislation on pesticides complies with this specific commitment. Furthermore, an overview of available data on pesticide poisonings in Europe is provided and, on that basis, prospects for a European programme for surveillance of toxic exposure to pesticides are discussed. Action plans (NAPs) aimed at reducing risks and impact of pesticides on human health and the environment and at developing alternative approaches and techniques to reduce their use. Among the objectives and measures to carry out, NAPs should include the implementation of systems for gathering comparable information on pesticide acute poisoning incidents (Art. 7). The Directive also specifies that these systems should operate according to the indications that will be provided in 2012 by a strategic guidance document developed by the Commission, in cooperation with MSs. Experiences from the Directive, Regulation No 1107/2009, concerning the placing of plant protection products on the market, specifies that MSs shall set out provisions concerning the collection of information and reporting on suspected poisonings related to plant protection agents (Art. 68). With reference to biocidal products, Directive 1998/8/EC requires that MSs forward a report to the Commission every three years to document the activities undertaken to control the products on the market and to provide information on any case of poisoning. European data on poisoning incidents are currently very scarce and there is limited information on surveillance systems active at national level in MSs. In the second Composite Report in accordance with Directive 1998/8/EC, 2003-2006,15,15,39 cases of toxic exposures to active substances were gathered. However, the Commission pointed out that the information on poisonings collected by MSs do not always allow for clear distinction between biocidal products and plant protection agents or other types of dangerous agents, nor could the available data be merged and analysed to provide integrated figures of poisoning incidents. As was rigorously updated. The risk of developing severe lactic acidosis during long-term treatment with metformin is not insignificant and due to the need for a better understanding of the condition, it is unlikely to be revealed in controlled treatment studies. A multitude of case reports in the literature also supports this experience. References: 1. Salpetrier S, Godeau P, Pastore P, et al. Severe lactic acidosis in type 2 diabetes mellitus. Cochrane Database Syst Rev 2010; (1):CD002967.

224. How will Pesticides Centres be Affected by new Developments in Chemicals Legislation?
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Objective: In the last 5 years, the chemicals legislation in Europe was updated by the REACH and CLP regulations. The REACH regulation (EC) No 1907/2006 and the CLP regulation (EC) No 1272/2008 completely renew the rules on the (risk) management of substances and mixtures and will gradually replace various chemicals directives, including the substances directive 67/548/EEC and the preparations directive 1999/45/EC. The Cosmetic products regulation (EC) No 1223/2009 will replace Directive 76/768/EEC on cosmetic products. As these new EU legislations are ‘regulations’ instead of ‘directives’, they apply directly in the same way in every EU member state after coming into force. For Poison Centres centres, the legislation predominantly affect the notification of product information by companies to competent authorities or poison centres. Methods: To participate in the discussions, the EAPCCT Board has activated the ‘Working group on Poisons Centres Activities/European Regulatory Issues’. Various EU poison centres are represented in this working group and, in subgroups, take part in the projects of the European Commission (EC) on the notification of hazardous mixtures and on the notification of cosmetic products. Results: In the CLP regulation, paragraphs 1–3 of article 45 describe the notification of information on hazardous mixtures to notified bodies. However, it does not exactly describe what information is required and how it should be notified. At a late stage in the development of the CLP regulation, under the pressure of all stakeholders, this shortcoming was recognised and corrected with paragraph 4. It states that, before January 20th 2012, the EC shall review the possibility to harmonise product information currently only recommended, including the establishment of a data exchange format. And the final result may be adopted by the EC and added as an Annex to the CLP regulation. In 2010 the EAPCCT Board was approached by the DG Health and Consumers’ Protection of the EU Commission and the group and representatives of competent authorities to discuss the requirements for the notification of product information. The starting document for the discussions was the EAPCCT guideline on product information requirements from 1989. A new updated version of the guidelines was established and endorsed by the EAPCCT Board. Important parts of the new EAPCCT guideline are the requirements on the composition of a product and the concentration of its substances. The newly defined health hazard classes and categories of the CLP Regulation were considered in the discussions. Based on poison centres experience, a selection was made for which health hazard classification and category of a substance an exact concentration is required. Selected were acute toxicity (oral, dermal, inhalation) categories 1, 2 and 3, specific target organ toxicity (single and repeated exposure) category 1 and 2, skin corrosion category 1 and eye damage category 1. In addition, the Poison Centres, the EAPCCT Board, Board, Board and legislative experts agreed on the notification of information (without the use of thresholds) and on the use of defined concentration ranges for other substances, still apply. These are the minimum requirements for poison centres activity. The final result: the EAPCCT guideline is the reference to biocidal products, Directive 1998/8/EC.


Clinical Toxicology vol. 49 no. 3 2011
company information were addressed and integrated into the new EAPCCT guideline. In November 2010, the EC organised a workshop, where all stakeholders were invited and the poisons centres’ point of view was presented. It became clear that stakeholders had different views on the required quality of the product information. Nevertheless, they all favoured working together in an effort to realise harmonisation of product notification to appointed bodies. In 2011, the EC will organise two meetings with all stakeholders to identify the differences and how they can be resolved. After these meetings the EC will undertake a review of the current planning of the EC is to bring CPNP into the available product information. The EAPCCT competent authorities can search, view and download can be uploaded by companies. Poisons centres and competitively charged to the EAPCCT guideline on required product information is expected to be included on the improved product composition. The guideline requires the notification and will be the start of discussions with industry and EU member state representatives. In the near future the results of this discussion will be incorporated by the EC in an Annex to Regulation (EC) No 1272/2008.

226. The NPIS Pesticide Surveillance Project 2004–2010: Acute Pesticide Poisoning in the Older Person (>65 years)

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Objective: To describe pesticide exposures in patients aged >65 during the 6.5 years of the NPIS TOXBASE3 pesticide surveillance project. Methods: The National Poisons Information Service Edinburgh Unit (NPIS) monitors pesticide exposures following Internet (TOXBASE4) or telephone enquiries. All patient related accesses to pesticides on TOXBASE5 between 1/4/2004 and 1/10/2010 were notified electronically to NPIS, and followed up using on-line, email or paper questionnaires. All NPIS telephone enquiries from 1/9/ 2009 were also followed up. Enquiries from outside the UK and those where symptoms were not related were excluded. Exposures were analysed for circumstances and symptoms in patients aged >65 and >65 years using Fisher’s exact test as appropriate. Results: Since 2004 5211 pesticide exposures have been reported to NPIS. Children (<13ys), cases without age and chronic exposures were excluded (2878). Patients >65 comprise 18.8% of adult report patients, 11.4% were >65 years and frequently occurred while the pesticide was in use; 278 (69.1%). The majority of exposures involved amateur products (513, 77.9%). Agents reported following accidental exposures were similar in patients >65 and ≤65, glyphosate and perilmininining. Deliberate self-harm (DSH) was less frequent in patients >65 (18.2%) compared to patients ≤65 (24.0%) (p = <0.001). DSH exposures in patients >65 most frequently occurred between ages 65–71 years, 23 of 36 exposures (63.8%). Few DSH exposures occurred over 85 years (2.5%). This reflects findings from previous work on suicide in the elderly.1 In patients >65 rodenticides were involved in 5 DSH cases (13.9%), ≤65 rodenticides were the most frequently reported agent (158, 36.3%, p = <0.006). Poisoning Severity Scores (PSS) grades for accidental exposures appeared similar for patients ≥65 and ≤65 (60% minor, 7% moderate and 1% severe for both). Eye, nose, mouth and respiratory irritation were frequently reported following accidental exposure in patients ≥65. Conclusion: Older patients comprise a significant proportion of pesticide exposures. Findings in accident- exposed patients are similar in both age groups. Patients in the >65 group DSH is less common and the products used differ. References: 1. De Leo D, Padonai W, Socco P, et al. Attempted and completed suicide in the elderly: a population-based study. Int J Geriatr Psychiatry 2001; 16:300–10.

227. Cytokine and Chemokine Profiles in Acute Carbon Monoxide Poisoning: Marked Elevation of Interleukin-6 in Cerebrospinal Fluid

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Background: We reported that early elevation of interleukin-6 (IL-6) concentration in the cerebrospinal fluid (CSF) may be a predictive marker of delayed encephalopathy (DE) due to acute carbon monoxide (CO) poisoning.1 However, cytokines other than IL-6 in CSF after CO poisoning had not been determined. Objective: To investigate the relationship between outcome of CO poisoning and profile of cytokines/chemokine level in blood and CSF, in order to find any prognostic markers for prediction of the outcome. Methods: We measured 17 cytokines/chemokines in the CSF of 39 acute CO poisoned patients who manifested unconsciousness in their course. The CSF and blood were obtained within 24 hours after the last CO exposure. The cytokines/chemokines in their CSF and sera were determined by a commercial assay method. All patients were observed for at least 3 months, and classified into two groups according to their clinical outcomes. Patients who revealed neurological syndrome or persistent vegetative state were classified into the encephalopathy group (Group E, n = 9), and patients who had no delayed symptoms were classified into the no complication group (Group N, n = 30). The relationship between clinical outcome and levels of cytokines/chemokines was examined by statistical analysis. Results: The CSF levels of interleukin (IL)-1-beta, IL-4, IL-6, IL-10, IL-12, granulocyte colony-stimulating factor, granulocyte macrophage colony-stimulating factor, interferon-gamma, monocyte chemotractant protein-1, macrophage inflammatory protein-1-beta and tumor necrosis factor-alpha were significantly elevated in group E. In that group, the serum levels of IL-6 and granulocyte colony-stimulating factor were also significantly elevated. The difference in CSF IL-6 was the most significant among them. Conclusion: There are differences in cytokines/chemokine profiles of the two groups in CO poisoning. Cytokines/chemokines analysis of CSF is more useful than that of serum in classifying CO poisoned patients. A useful biomarker among these analytes was CSF IL-6 for prediction of encephalopathy. References: 1. Ide T, Kamijo Y. The early elevation of interleukin (IL)-1-beta, IL-4, IL-6, IL-10, IL-12, granulocyte colony-stimulating factor, granulocyte macrophage colony-stimulating factor, interferon-gamma, monocyte chemotractant protein-1, macrophage inflammatory protein-1-beta and tumor necrosis factor-alpha were significantly elevated in group E.

Abstracts
an abnormal QT developing. Methods: The data set included 78 escitalopram overdose events (median dose 140 mg [10–560 mg]). SDAC was administered 1 to 2.6 hours after 12 overdoses. A fully Bayesian analysis was undertaken to determine the model that best fitted the data. Pharmacokinetic analysis of 34 admissions with plasma concentration data obtained by a pharmacokinetic-pharmacodynamic (PKPD) analysis of data for all 78 patients. The PKPD model was used to predict the probability of having an abnormal QT based on the QT normogram. Results: A one-compartment model with first-order input and first-order elimination described the pharmacokinetic data, including uncer-
tainty in dose and a baseline concentration for patients taking escitalopram therapeutically. SDAC reduced the fraction absorbed by 31% and reduced the individual predicted area under the curve adjusted for dose [AUC/dose]. The absolute QT interval was related to the observed heart rate with an estimated individual heart-
rate correction factor (x = 0.35). The heart-rate cor-
rected QT interval was linearly dependent on predicted escitalopram concentration (slope = 87 ms/mg−1, be-
tween-subject CV = 70%) using a hypothetical effect-compartment (half-life of effect-delay = 1.0h). Admin-
istration of SDAC significantly reduced QT prolonga-
tion and was shown to reduce the risk of having an abnormal QT by approximately 35% for escitalopram doses above 200 mg. Conclusion: The pharmacoki-
etics of escitalopram overdose were well described by the model. Escitalopram was associated with a delayed lengthening of the QT interval in a dose-related way. SDAC in addition to escitalopram reduced the observed QT prolongation. A one-compartment model of escitalopram absorbed and reduced the risk of an abnormal QT occurring. References: 1. Friberg LE, Isbister GK, Guffull SB. Pharmacokinetic-pharma-
dynamic modelling of QT interval prolongation follow-

229. Toxicity Profile of Desvenlafaxine
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Background: Very limited toxicity data exists on the serotonergic reuptake inhibitor desvenlafaxine (Pristiq® – extended release tablets). It is the major active metabolite of venlafaxine (Effexor®) and toxicity may be similar (e.g. seizures, serotonin toxicity and death). Methods: Cases were recruited through calls to the NSW Poisons Information Centre (PIC) from September 2009 - November 2010. A 2 page clinical research form was used to collect information from hospital-based calls and was faced at the time of the initial call. A copy of the patient’s medical record for the admission was also requested retrospectively. A follow-up call for accidental ingestions was attempted within 72 hours of the initial call. Results: A total of 31 cases of desvenlafaxine poisoning with outcome information was collected through the PIC. The patients were classified as follows: i) Accidental paediatric ingestions (n = 3) 24 month male ingested 50 mg and experienced 2 episodes of vomiting and mild drowsiness shortly after ingestion, the child was observed in hospital for 4.5 h. Two further cases in 2 year olds with estimated doses of 5 mg and 50 mg remained asymptomatic. ii) Deliberate self-poisoning (n = 28): 13 cases involved desvenlafaxine only (alcohol involved in 6 cases) and of these, 10 (77%) were symptomatic (estimated median dose: Symptoms included: range: 200–2100 mg): nausea (n = 7), tachycardia (n = 4), drowsiness (n = 4; alcohol possible cause in 2 cases; lowest GCS was 14), hyperreflexia (n = 2), hyperten-
sion (n = 3) and altered mental state (n = 2; in the only two patients given charcoal), tremor (n = 1), clumsiness (n = 1), eye deviation (n = 1), mydriasis (n = 1). Two cases (ingesting 1400 and 2100 mg) met the Hunter Serotonin Toxicity Criteria for serotonin toxicity but both were mild-moderate and received no active treatment. No seizures or QRS/QT widening was recorded in any patient. Of these drug ingestions of desvenlafaxine. Three patients remained asymptomatic (dose: 600–700 mg). Conclusion: In this limited series, no serious toxicity was noted from desvenlafaxine in accidental paediatric ingestions of up to 50 mg (estimated) and deliberate self-poisoning of up to 2100 mg. Further surveillance is required, particularly with larger doses.

230. The P-glycoprotein Activity of Drugs Highly Associated with Torsade de Pointes
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Objective: To evaluate the role of an efflux transpor-
er, P-glycoprotein (P-gp), in drug-associated torsade de points (Tdp). Methods: We analyzed the product labels of drugs withdrawn because of association with Tdp in the FDA’s database, to identify contraindicated concomitant drugs that have P-gp activity. We identified other drugs that have been associated with admission parameters (Tdp) to determine if the association was due to P-gp activity. Results: We analyzed individual drugs with top Empirical Bayesian Geo-
metric Mean (EBGM) values for Tdp. We also used MGPS to identify drug-drug pairs having the top EBGM values for Tdp that could not be explained by the association of their individual drug components with Tdp. The top drug pairs by EBGM values were assessed to determine if the drug pair included drugs that were P-gp substrates and/or P-gp inhibitors. Results: The drugs contraindicated for concomitant use with cisapride, terfenadine, and astemizole are almost all known P-gp inhibitors. Data mining of postmarketing drug safety reports identified drugs associated with Tdp. The drugs ranked here in descending order (by EBGM value) are itubilide (236), levacetylmethadol (107), bepridil (96), sotalol (68), disopyramide (47), methadone (44), quinidine (40), flecainide (39), ciprofloxacin (32), terfenadine (30), droperidol (28), astemizole (27), and pimozide (25). Nine of these 14 drugs are known P-gp substrates and seven are also known P-gp inhibitors (based on postmarketing reports of P-gp activity). The drug pairs most highly associated with Tdp were cisapride-erythromycin, erythromycin-
terfenadine, salemeh/methanol/trimeprinopin-methadone, itraclopride-methadone, ketonazole-terfenadine, to-
conazole-terfenadine, atazanavir-methadone, metha-
done-ritonavir, fluoxetine-trazodone, flurazepam-
methadone, amiodarone-loratadine, ciprofloxacin-
sotalol, methadone-nelfinavir, fluoxetine-ondansetron, methadone-terfenadine, and sertraline-terfenadine. With the exception of pairs that included sotalol each of these drug pairs included a P-gp substrate that prolongs the QT interval and a P-gp inhibitor. Many of these drug pairs included drugs that were both P-gp substrates and inhibitors. Conclusion: Further research is needed to evaluate a potential role for P-
glycoprotein (drug efflux) inhibition increasing the intracellular levels of drugs that prolong the QT interval, thereby precipitating Tdp.

231. Prognostic Factors in Methanol Poisoning: A Multi-Center Study
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1Department of Anaesthesiology and ICU, Pärnu County Hospital, Pärnu, Estonia; 2Department of Acute Medicine, Oslo University Hospital, Ullevål, Oslo, Norway; 1Department of Clinical Toxicology, Logmann-Hakkin Poison Hospital, Shahid Beheshti University, Tehran, Iran; 2Department of Intensive Care Medicine and Clinical Toxicology (CAMU), Tunisia, Tunisia

Objective: Prognostic parameters in methanol poisoning are reported from time to other, but reports with a high number of patients with a complete acid-base status on admission are scarce. No comparative studies on prognosis with ethanol vs. fomepizole exist. In order to study the prognostic factors in methanol poisoning with a special focus on antidote, we collected material from four different countries where a blood gas was analyzed on admission, and outcome was known. Inclusion criterion was a history of methanol poisoning or administration of S-methanol. Fomepizole was fomepizole the antidote of choice (n = 51). Methods: The material was collected from two different outbreaks in Norway (1979 and 2002–2004), one outbreak in Estonia (2001), one in Tunisia (2003/2004), as well as material from one referral center in Iran (2004–2009). The patients were separated into three groups: Group I: Survivors without sequelae, Group II: Survivors with sequelae, Group III: The patients who died. Data included age, sex, consciousness on presentation, serum potassium/creatinine, methanol level and blood gas analysis on admission. Results: A total of 302 patients were included in the study. The sensitivity and specificity was used to validate how strongly the different parameters corre-
lated with death. Student’s T-tests were used to separate groups regarding the pH in the dying patients (p =
0.011). Conclusion: The high number of patients with thorough sampling of admission data made it possible to compare prognostic parameters for the two antidote treat-
groups. Overall, in spite of different confounders, there seemed to be a leftward shift in morbidity and mortality between the two groups. With fomepizole was the antidote used, more patients seemed to survive with sequelae instead of dying. Conclusion: Patients dying with sequelae seem to avoid the sequelae to a certain extent.

232. Correlation of Blood Lead Levels and Soil Lead Levels in Pediatric Patients in Sub-
africa
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Objective: The objective of this study was to determine if community Soil Lead Levels (SLL) and resident Blood Lead Levels (BLL) are correlated in a heavily contaminated area in sub-saharan Africa. Pediatric patients in 12 periurban communities were studied. Soil Lead levels were determined by a special focus on the pH in the dying patients (p =

Methods: Venous blood lead levels were collected and analyzed by using LeadCare™ B-Pb assay. Surface soil samples were collected and analyzed by inductively coupled plasma atomic absorption spectroscopy (ICP-AES). Descriptive statistics were used to char-
acterize the variables. Results: A total of 909 venous BLL were collected from 12 communities and compared to SLL in these same communities. The mean age of participants was 4.8 years (range 1–12). The mean venous blood level for the entire population was 19.275 µg/dL (range 7.3–44.6). BLLs collected in these communities ranged from 1.275 to 168 µg/dL. There was a log-linear correlation between BLL and SLL. Data showed an increase in mean BLL as mean soil lead levels increased. This correlation existed for communities with SLL below 1000 ppm. Among communities with SLLs above 1000 ppm, mean BLLs are high however they seemingly plateau and do not
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**235. Analysis of Antidote Stocks in the Hospitals of the Italian Regional Emilia Romagna**

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**Objective:** The Department of Pharmacy of the University Hospital of Ferrara (AUOFE) has been appointed Regional Centre of Reference for the supply of some antidotes by the Region Emilia Romagna (RER). In order to assess their availability, a qualitative-quantitative analysis of antidotes available in regional hospitals was performed. We paid particular attention to antidotes supposed to be used within 30 minutes, namely the A-type, and which should be available in all hospitals. Methods: All 17 regional hospitals were asked for information about the kind and the quantity of stocked antidotes. The number of potentially intoxicated users has been calculated according to the maximum dosage. Results: All 17 regional hospitals provided the required information with the following results. Among the 27 A-type antidotes we analyzed, the stock for the maximum treatment of a patient was the following: 2 antidotes (ticarcillin, nafcillin) were available in all hospitals; 2 antidotes (calcium gluconate and activated charcoal) were available in 5 hospitals, and 5 antidotes (atropine sulphate, flumazenil, sodium thiosulphate, propafenone, sodium thiosulphate, propafenone) were available in 15 hospitals. Seven A-type antidotes (fomepizole, MgSO4, Fuller’s earth, hydroxocobalamin, digoxin-specific antibodies, polylethylene glycol 4000 and alcohol 96%) were available in less than 10 hospitals. The availability of antidotes to be used within 2 hours (B-type) was limited: Prussian blue was found in 5 hospitals with dimercaprol and pralidoxime in 8. Conclusion: Quantities of some antidotes available in regional hospitals are not sufficient to treat a single patient. This is the case for fomepizole, digoxin-specific antibodies and Fuller’s earth. In 5 hospitals only we could identify an emergency stock for cyanide antidotes (‘cyanide’, ‘thiosulfate’ and ‘hydroxocobalamin’). Medical record abstraction included the following data: baseline demographics (age, gender, race); indication for the poisoning (burns, smoke, ingestion) versus non-CN related (ulcers, vitamin deficiency); medical history; blood gas and chemistries. The primary outcome was in-hospital mortality, while the secondary outcome was cost. The cost of fomepizole, digoxin-specific antibodies and pralidoxime was the higher. Conclusion: In the rare cases of CN antidote administration over the past decade at an urban tertiary care center, the minority of indications were to treat suspected CN poisoning. In patients with suspected CN poisoning, the rate of antidote administration was poor and precluded analysis of mortality benefit. Future research should focus on elimination of barriers to CN antidote administration.


**236. A Decade of Cyanide Antidote Administration at an Urban Tertiary Care Center**

Nite M 1, Manni AF 2.


**Background:** Cyanide (CN) is a mitochondrial poison found as a byproduct of structural fires or as an industrial compound that can be intentionally ingested. Two CN antidotes exist, hydroxocobalamin and sodium thiosulfate, although the international medical community lacks consensus about which antidote to use first-line. In order to clarify factors involved with CN antidote choice, we reviewed all CN antidote administration at a large academic tertiary care center to determine: (a) the indication cited and (b) the effects on mortality, if any. Methods: A retrospective review of all hospital affiliated medical records was performed over 10 years of consecutive admissions presenting to a single large academic tertiary referral center from January 2000 to November 2010. The study was performed using an extensive electronic data search for the following terms: “cyanide”, “thiosulfate” and “hydroxocobalamin”. Results: Of 60 patients yielded by the search, 43% were female, the average age was 34.9 years, 43% were under 18 years of age, and subjects were from diverse ethnic backgrounds (33% Hispanic, 27% Hispanic, 20% African American). Overall 760 (12%) died during hospital admission and 860 (13%) patients were suspected of CN poisoning. Of the 8 patients suspected of CN poisoning, only 1 (12.5%) was treated. Conclusion: In the rare cases of CN antidote administration over the past decade at an urban tertiary care center, the minority of indications were to treat suspected CN poisoning. In patients with suspected CN poisoning, the rate of antidote administration was poor and precluded analysis of mortality benefit. Future research should focus on elimination of barriers to CN antidote administration. References: 1. Hall AH, Saires J, Baud F. Which cyanide antidote? Crit Rev Toxicol 2009; 39:54ı–52.

**237. Death After Flumazenil Use**

Prado CC, Carvalho AC, Telini AHS, Maia MLPC, De Capitani EM, Bucaretchi F.

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**Objective:** To report a case of death as consequence of flumazenil use in a pregnant woman. **Case report:** An eight weeks pregnant woman, 19-years-old, intentionally ingested an estimated dose of 50 to 300 mg of clonazepam, two and a half hours before first being seen at a local ER. She presented sleepy and with nausea. Gastric lavage was performed despite the long period since ingestion, and was obviously unsuccessful. Two hours later, the ER team called our Poison Control Center asking for quality of care in the case of death after flumazenil administration. Seven hours later our PCC was contacted again, asking for our agreement about the use of flumazenil as the patient continued to be sleepy. Information about the low risk of problems for the patient and the baby was then given, with information about the baby’s and mother’s...
cardiac monitoring to be performed and continuing with the supportive care. Four hours later the PCC informed the patient had developed respiratory depression, when she was intubated, and died after receiving 0.2 mg flumazenil at home, adding that the patient was a regular carbamazepine user. Conclusion: Benzodiazepine (BZD) intoxications are rarely fatal when not associated with other CNS depressants, in which case severe hypoxia with agitation and coma, and cardiovascular complications can occur, and should be treated accordingly. Flumazenil is a competitive BZD receptor antagonist restoring consciousness but not reversing respiratory depression induced by BZD. It may trigger withdrawal syndrome in BZD dependent patients. It can be used very cautiously in BZD isolated overdoses, but its potential to induce refraction convulsions in concurrent carbamazepine anticonvulsant treatment and antidepressants intoxications can lead to catastrophic outcomes, as seen in the present case. References: 1. Seger DL, Flumazenil - treatment or toxin. J Toxicol Clin Toxicol 2004; 42:209–16. 240. The Toxicity of Liquid Detergent Capsules (Fabric Cleaning Liquid Tablets) Williams H 1, Bateman DN 2, Thomas SHL 3, Thompson JP 4, Vale JA 1. 1National Poisons Information Service (Birmingham), City Hospital, Birmingham; 2National Poisons Information Service (Edinburgh), Royal Infirmary, Edinburgh; 3National Poisons Information Service (Newcastle), Regional Drug and Therapeutics Centre, Newcastle upon Tyne; 4National Poisons Information Service (Cardiff), University Hospital Llandough, Cardiff, UK. Objective: To ascertain the toxicity of liquid detergent capsules. Methods: Between 1 March 2008 and 30 April 2009 the UK National Poisons Information Service collected prospectively 5929 telephone enquiries relating to household products, approximately 12% of all telephone enquiries. Results: The majority of enquiries (65.5%) concerned children five years of age or less and were received predominantly from hospitals (32.1%), general practitioners (29.8%) and nurseries (12%). The mode of exposure was ingestion (97.6%), most exposures occurring at home (97.6%). Ingestion occurred alone (79.5%) or in combination with other exposure routes (20.5%). Most of the commonly reported features were vomiting (58.5%), skin (43%) and eye (40.2%) contact. Conclusions: There were no severe sequelae. References: 1. Rauber-Lüthy C, Kupferschmidt H. Household chemicals: management of intoxication and antidotes. In: Luch A, ed. Molecular, Clinical and Environmental Toxicology. Basel, Switzerland: Karger, 2009: 366:547–8. 2. Fayers T, Munneke R, Strouthidis NG. The Toxicity of Household Products in the UK 2008–2009. London: Germfree Network 2010; 126:509–16. 3. Wood KL, Thompson JP, Vale JA. Liquid detergent capsules causing ocular injuries in children. J Pediatric Ophthalmol Strabismus 2006: 43:250–1. 3. Mathew RG, Kennedy K, Corbett MC. Wave of paediatric eye injuries from liquid detergent capsules. Br Med J 2005; 330:118–9. 4. Thompson JP. Liquitabs - a thorough and comprehensive review of the UK national data. Clin Toxicol 2009; 47:459.

Abstracts

239. Agranulocytosis after Massive Benzene Ingestion - A Case Report Jevic-Sediri E 1, Bajic B 2, Cvetkovic D, Jovanovic M. National Poisons Control Centre, Military Medical Academy, Belgrade, Serbia. Objective: Toxic effects of benzene ingestion are well recognized and primarily include signs and symptoms of CNS depression, gastrointestinal irritation and cardiac arrhythmias. We report a unique case of agranulocytosis following ingestion of an agranulocytosis. Case report: A 52-year old female with a history of depression ingested almost 1000 mL of pure benzene as a solvent in a biochemical laboratory. At admission, she presented with staggering gait, somnolence, agitation, tachycardia, vomiting and profuse diarrhea. The initial blood analysis revealed WBC 36.2 ×10^3/mm^3, RBC 4.4 ×10^12/L, Hgb 144 g/L, platelet 45%, and platelets 247 ×10^3/mm^3. BUN was 9.2 mmol/L, creatinine 64 μmol/L, sodium 136 mmol/L, potassium 3.9 mmol/L, glucose 9.2 mmol/L, AST 63 μU/L, ALT 41 μU/L, CK 204 μU/L, LDH 847 μU/L. Urine analysis revealed a high concentration of phenol (320 mg/L). A few hours later she developed nodal tachycardia characterized by a heart rate of 150–170 per minute, with multifocal ventricular extrasystoles. Arrhythmia was successfully treated with lidocaine, so the next day heart rate normalized. Severe diarrhea with incontinence gradually resolved within a week. However, on the skin in the thoracic and gluteal area which was in contact with vomitus and stool, extensive grade II chemical burns developed. Complete blood count monitoring revealed the fall in neutrophils with minimal number of 0.232 ×10^3/mm^3 twenty days after ingestion. Bone marrow biopsy revealed lowering of granulopoietic precursor cells number and increased number of eosinophilic and mono cytes. The patient received filgrastim for 11 days until normalization of neutrophils in peripheral blood. Conclusion: Chronic benzene exposure has been associated with hematologic disorders (thrombocyto penia, aplastic anemia, pancytopenia, and acute myelogenous leukemia). Acute toxicity of benzene inhalation to hematopoietic precursor cells is demonstrated in experimental animals. This report indicates in similar mechanism of toxicity in a human after a single exposure to an extremely high dose.

241. Toxicity of Household Products in the UK Williams H 1, Bateman DN 2, Thomas SHL 3, Thompson JP 4, Vale JA 1. 1National Poisons Information Service (Birmingham), City Hospital, Birmingham; 2National Poisons Information Service (Edinburgh), Royal Infirmary, Edinburgh; 3National Poisons Information Service (Newcastle), Regional Drug and Therapeutics Centre, Newcastle upon Tyne; 4National Poisons Information Service (Cardiff), University Hospital Llandough, Cardiff, UK. Objective: To ascertain the toxicity of current UK household products. Methods: Between 1 March 2008 and 30 April 2009 the UK National Poisons Information Service collected prospectively 5929 telephone enquiries relating to household products, approximately 12% of all telephone enquiries. Results: The majority of enquiries (65.5%) concerned children five years of age or less and were received predominantly from hospitals (32.1%), general practitioners (29.8%) and nurseries (12%). The mode of exposure was ingestion (97.6%), most exposures occurring at home (97.6%). Ingestion occurred alone (79.5%) or in combination with other exposure routes (20.5%). Most of the commonly reported features were vomiting (58.5%), skin (43%) and eye (40.2%) contact. Conclusions: There were no severe sequelae. References: 1. Rauber-Lüthy C, Kupferschmidt H. Household chemicals: management of intoxication and antidotes. In: Luch A, ed. Molecular, Clinical and Environmental Toxicology. Basel, Switzerland: Karger, 2009: 366:547–8. 2. Fayers T, Munneke R, Strouthidis NG. The Toxicity of Household Products in the UK 2008–2009. London: Germfree Network 2010; 126:509–16. 3. Wood KL, Thompson JP, Vale JA. Liquid detergent capsules causing ocular injuries in children. J Pediatric Ophthalmol Strabismus 2006: 43:250–1. 3. Mathew RG, Kennedy K, Corbett MC. Wave of paediatric eye injuries from liquid detergent capsules. Br Med J 2005; 330:118–9. 4. Thompson JP. Liquitabs - a thorough and comprehensive review of the UK national data. Clin Toxicol 2009; 47:459.
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presented a positive correlation with chronic obstructive pulmonary disease (COPD) exacerbation (beta-coefficient = 0.217; P = 0.003), while those of PM10–2.5 were correlated with heart failure (beta-coefficient 0.151; P = 0.039) and venous thromboembolism (OR 1.49 with 95% CI 1.13–2.53). On the other hand, no significant association was found with cardiovascular or cerebrovascular disease. As regards venous thrombosis risk, interestingly, in a subgroup of subjects without thrombosis and without anticoagulant therapy (n = 103) an inverse correlation between PM10–2.5 and prothrombin time was found (R = −0.226; P = 0.022). Conclusion: The results show that diverse chronic PM air pollution may be associated with different acute manifestations of human diseases (COPD, heart failure and venous thromboembolism). In particular, PM10–2.5 may be related with thrombophilia and venous thromboembolism risk.


248. Poisonings Caused by "Chumbinho," an Illicit Rodenticide Used in Brazil

Bucaretchi F, Metta GM, Mello SM, Southbea PC, Cardoso L, Carvalho AC, Branco MM, Prado CC, De Capitani EM, Madureira PR, Vieira RJ, Hyslop S, Costa JM. Case report: Poisoning Prevention Center, Faculty of Medical Sciences, University State of Campinas, Campinas, São Paulo; Instrumental Analysis Laboratory, Criminalistic Institute of São Paulo, São Paulo, Brazil.

Objective: To describe the profile of poisonings caused by "chumbinho" (cholinesterase inhibitors) followed by the Campinas Police Department, in a transversal study based on data collected prospectively from 07/2009 to 06/2010. Variables analyzed included demographic data, circumstances of exposure, clinical manifestations, length of hospital stay (LOS), treatments performed, identification of pesticides (LC/MS), cholinesterase activity (at admission and after 24 h and 48 h; Elman's method) and classification of severity using the Poisoning Severity Score (PSS; 0–4) based on the overall clinical course. Results: Seventy-six patients were poisoned with "chumbinho" over a 12 month period. Age ranged from 2 to 74 years (median = 36 years), and 53.9% were male. Circumstances of poisoning included: suicide attempt (92.1%), attempted homicide (5.3%), accidental ingestion (2.6%). Most of the patients (96.1%) were symptomatic, with predominantly cholinergic muscarinic manifestations and an average LOS of 7.4 days. Atropine was given in 82.9%, and mechanical ventilation used in 46.1%. Table 1 summarizes the gastrointestinal decontamination procedures. Plasma toxicological analysis (n = 59) revealed: aldicarb (55%), carbofuran (2), aldicarb with carbofuran (1) and undetected (1). In 14 patients with sequential cholinesterase measurements, partial and uniform recovery of enzymatic activity was observed every 24 h, consistent with carbamate poisoning. The cases were classified as asymptomatic (5.3%), mild (11.8%), moderate (35.5%), severe (43.4%) and fatal (4%) (PSS, mean ± SD = 2.3 ± 0.9). Conclusion: Most exposures to "chumbinho" were due to suicide attempts, were severe and were caused by aldicarb, with a fatality rate of 4%. Gastrointestinal decontamination did not affect the LOS and outcome.


249. Intratesticular Injection of Printer Ink: A Case Report

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Background: Inkjet cartridge injection is rarely described in medical literature. Inkjet printer ink contains low toxic ingredients, but could contain potentially harmful ingredients like p-anisidine, organic solvents or lead which may be more dangerous in cases of parenteral administration. Case report: A 24-year-old male, drug abuser, was admitted to hospital due to injection of 10 mL of ink from inkjet printer cartridge into his right testicle. Injection occurred after three days of alcohol and metamphetamine binge. According to anamnestic data, he was under the influence of alcohol and metamphetamine, the patient removed his left testicle with a knife. On admission to the hospital, tremor of hands and tongue was present. The patient complained also of nausea, epigastric and muscle pain. Initial ultrasound demonstrated presence of fluid in the right testicle and gas bubbles in the scrotum. Whole blood count revealed mild leukocytosis of 15.1 G/L. Surgical revision demonstrated puncture of the testicle and no ink inside the scrotum. The examination of patient’s semen performed a week after injection showed black color of semen with 88% of dead, and 1% of mobile sperms. The black color of urine was observed for nine days after the event. Other laboratory tests were within normal range. Control ultrasound made ten days later demonstrated persistent fluid reservoir in the right testicle. The patient was discharged home and the next follow up was scheduled to be done in a month. Conclusion: Intratesticular injection of printer ink resulted in no significant systemic toxicity, however, semen examination showed severe impairment of sperm viability. The clinical symptoms observed in our patient were mainly connected with drug intoxication, and disappeared after diazepam injection. Further examinations must be done to evaluate late toxicity of injected ink. References: 1. Heden F. [Case report. Ink intoxication - a man colored blue] [Article in Swedish]. Lakartidningen 2001; 98:2719–20.

250. Cardiac Dysrhythmia Induced by Perchloroethylene - Acute Poisoning - Case Report

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Objective: The majority of cases of perchloroethylene (PCE) intoxication are due to chronic inhalation. However, the acute effects of PCE vapor inhalation have been poorly described and associated with cognitive, hemodynamic, and renal involvement.1,2 A few deaths have even been reported.3,4 We describe a rare case of acute PCE poisoning (first case in last 15 years), presenting with signs of cardiac toxicity and with favorable outcome. Case report: A 45 year old female was admitted to the Clinic of Toxicology after one hour’s exposure to PCE (CCl2Cl2, carbon tetrachloride C, 1-Chloro-1,1,2,2-Tetrafluoroethane, CFC-113). The patient presented in the dry cleaning machines. The patient was conscious, tachypneic, with blood pressure 160/100 mm Hg, Signs of eye and upper airway irritation were present: swollen and erythematous palpebrae, lacrimation, rhinitis, cough. Nausea, dizziness, malaise, headache, tremor and impaired coordination were present. Laboratory monitoring did not show signs of hepatic or renal compromise. At admission to the hospital tremor of hands and tongue was present. The patient complained also of nausea, epigastric and muscle pain. Initial ultrasound demonstrated presence of fluid in the right testicle and gas bubbles in the scrotum. Whole blood count revealed mild leukocytosis of 15.1 G/L. Surgical revision demonstrated puncture of the testicle and no ink inside the scrotum. The examination of patient’s semen performed a week after injection showed black color of semen with 88% of dead, and 1% of mobile sperms. The black color of urine was observed for nine days after the event. Other laboratory tests were within normal range. Control ultrasound made ten days later demonstrated persistent fluid reservoir in the right testicle. The patient was discharged home and the next follow up was scheduled to be done in a month. Conclusion: Intratesticular injection of printer ink resulted in no significant systemic toxicity, however, semen examination showed severe impairment of sperm viability. The clinical symptoms observed in our patient were mainly connected with drug intoxication, and disappeared after diazepam injection. Further examinations must be done to evaluate late toxicity of injected ink. References: 1. Heden F. [Case report. Ink intoxication - a man colored blue] [Article in Swedish]. Lakartidningen 2001; 98:2719–20.

Table 1. Gastrointestinal decontamination procedures after poisoning with “Chumbinho”

<table>
<thead>
<tr>
<th>Subgroups, time after ingestion</th>
<th>Gastric lavage, N (LOS; PSS)*</th>
<th>Activated charcoal, N (LOS; PSS)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 h</td>
<td>24 (3.0; 2.0)</td>
<td>14 (4.0; 2.5)</td>
</tr>
<tr>
<td>&gt; 1 h</td>
<td>24 (3.5; 2.0)</td>
<td>11 (4.0; 2.0)</td>
</tr>
<tr>
<td>not determined</td>
<td>14 (5.5; 3.0)</td>
<td>12 (6.5; 3.0)</td>
</tr>
<tr>
<td>performed</td>
<td>(PSS)* 0.268; 0.796</td>
<td>0.272; 0.115</td>
</tr>
</tbody>
</table>

*Median values. LOS = length of hospital stay (days); PSS = Poisoning Severity Score (PSS 0–4).

251. Hepatic Dysfunction Following Acetic Acid Ingestion

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Objective: Acetic acid ingestion may result in corrosive injury to the upper gastrointestinal tract. Since 1990, when Hepatic Medicine, we have found only a few reports of hepatic failure in intentional acetic acid poisoning. We present a case of hepatic injury in accidental acetic acid poisoning. A 13-year-old boy was admitted to a regional hospital half an hour after an accidental ingestion of approximately 50 mL of 80% acetic acid. Upon admission he was alert, with signs of respiratory distress (tachypnea, 87% hemoglobin oxygen saturation). His blood pressure was 144/80 mmHg, heart rate 55/min. He had perioral and oral burns, dysphagia with odynophagia and was drooling extensively. Upper gastrointestinal endoscopy showed extensive corrosive injury with oral, pharyngeal, esophageal and gastric necrosis and isolated areas of gastric bleeding. She was transferred to our centre and was put on infusion of crystalloids, analgesics and a proton pump inhibitor. Initial laboratory tests showed abnormal liver tests: aspartate aminotransferase 4.6 µkat/L (normal values <0.58 µkat/L), alanine aminotransferase 1.07 µkat/L (normal values <0.74 µkat/L) and lactate dehydrogenase 4.54 µkat/L (normal values <3.2 µkat/L). The next day the signs of hepatic injury were at their highest: aspartate aminotransferase 12.01 µkat/L, alanine am- notransferase 13.96 µkat/L, lactate dehydrogenase 20.10 µkat/L. Creatinine, urea, creatine kinase, alkaline phosphatase, gamma-glutamyltransferase and bilirubin levels were normal. Ultrasonography and abdominal ultrasound showed a moderately enlarged liver with what appeared to be diffuse parenchymal changes. We ruled out other toxic and viral causes of hepatic dysfunction. Enzyme levels returned to their normal in course of the next couple of days and further recovery was uneventful. Conclusion: Accidental acetic acid ingestion may present with hepatic failure beside corrosive injury to the upper gastrointestinal tract.

252. Phosphoric Acid Poisoning: A Case Report

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1Department of Anaesthesia and Intensive Care, S. Anna Hospital, Ferrara, Italy

Objective: To present a rare case of poisoning characterized by serious cutaneous burns and gastrointestinal irritation as a result of a suicidal attempt. Case report: A 52-year-old-man ingested and spilled approximately 50 mL of 80% phosphoric acid and down his front. Clinical examination revealed chemical burns of 2nd and 3rd degree on 30% and 10% of body surface (head, trunk, arms), respectively. Skin and ocular decontamination was performed with large irrigation of saline. Ocular lesions appeared particularly severe. An esophagogastroscope performed during the initial evaluation showed widespread erosions and ulcera- tions, with a grade 2B esophageal injury. Gastric tube was not inserted. Laboratory results were: metabolic acidosis (pH 7.10 units), hyperphosphatemia (4.87 µmol/L), hypocalcemia (1.61, n=2.6–2.6), hyperglycemia (1.54, n=2.0–2.6), severely hypoglycemia and a lengthened clotting time (INR 6.97, n=0.8–1.2). Hypotension required dopamine and generous filling: intravenous crystalloids, red blood cells and plasma. Electrolyte correction was performed. The main systemic symptoms and signs were due to central nervous system involvement (shiver, spread, excitement). Prolonged sedation and three weeks of mechanical ventilation were necessary. The patient had a good systemic recovery except for a serious sight impairment because of the severe cataract he developed. Conclusion: Chemical burns caused by phosphoric acid are uncommon and data about specific treatment are few. Phosphoric acid spilling or ingestion can quickly lead to death. Double exposure forced us to very aggressive therapy that fortunately has been successful. Early recognition of affected areas and adequate resuscitation are fundamental.

253. Methemoglobimina due to Local Treatment of Skin with Gunpowder: A Case Report

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Objective: Methemoglobimina is a disorder characterized by the presence of a higher than normal level of methemoglobin in the blood. Methemoglobin is an oxidized form of hemoglobin that has almost no affinity for oxygen, resulting in almost no oxygen delivery to the tissues. When its concentration is elevated in red blood cells, tissue hypoxia can occur. Gunpowder is a mixture of sulfur, charcoal and potassium nitrate. Compounds containing nitrates can cause methemoglobimina. This case report presents clinical and laboratory changes (methemoglobin levels) due to local treatment of skin with gunpowder in patients with psoriasis. Case report: We report a 58 year old woman with acquired morphea, hospitalized in the Toxicology Clinic, MHATEM "Pirogov". The patient arrived at the hospital after repeated local treatment of skin with gunpowder on the occasion of psoriatic changes - self-medication. She complained of severe headache, general weakness, muscle aches, dizziness, nausea, vomiting, abdominal pain, shortness of breath. She had cyanosis of the skin and the lips. She reported a history of hypertension and diabetes mellitus. Vital signs were: pulse rate 78/min, RR 110/70 mm Hg, respiratory rate 18/min. On physical examination the patient was conscious, but sleepy and relaxed, she had central and peripheral cyanosis without tachycardia or tachy- cardia. Skin and mucous membranes were cyanotic. The pupils were normally broad. Lungs - clear vesicular breathing bilaterally. Cardiovascular system: heart - rhythmic activity without added noise. The abdomen was soft. Hepatosplenomegaly was not detectable. Extremities were without edema, but with cyanosis to the end- phalanges of the upper and lower limbs. Laboratory data: hematology studies, biochem- ical parameters, acid alkali equilibrium - in the reference values. Arterial blood gas analysis (ABG) showed hypoxia with normal pH. Her methemoglobin levels (in dynamic) were: 31.7%, 23.5%, 7.80%, 4.80% and 2%. (Normal = 0–2%). Treatment consisted of infusion of fluids; corticosteroids, large doses of ascorbic acid, oxygen. The patient remained in hospital for five days. Conclusion: Acquired methemoglobimina is a treatable condition that causes significant morbidity and even mortality. Severe and moderate case can be treated with high-flow nitrate compounds, penetrating the human body through the skin.

254. Healthy Homes for Healthy Children: Preventing Accidental Kerosene (Paraffin) Ingestion in Children in Developing Countries

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1Federal Institute for Risk Assessment, Berlin; 2Berlin School of Public Health (BSPH) at the Charité University of Medicine, Berlin, Germany

Background: Besides house and road accidents, in accidental poisoning in children within the house itself, kerosene poisoning is a major problem. In particular in developing countries, where kerosene is still used daily on a large scale for different purposes such as cooking, lighting and for rural medicine. Over the past 15 years, data from Egypt to Sri Lanka have shown that risk, exposure and consequences of childhood poisoning in Kenya and South Africa. Methods: Analysis of available information and literature in order to: 1. find the main causes for accidental kerosene ingestion in children from developing countries. To obtain a deeper view about the most recent or current scenarios in different parts of the developing world several ‘International Program on Chemical Safety’ (IPCS) offices and Poison Centers in South-East Asia and the African region were contacted. Results: Kerosene was found as the most common cause of accidental poisoning in children among household poisonings. Mortality was found to be low, but morbidity was high. Children aged 1–3 years were most likely to be involved in accidental kerosene poisoning. Improper storage of kerosene was detected as the main contributory factor for these accidents. Kerosene was found to be stored in jars, bottles or containers previously used for beverages and juices and these were in easy access of children and mistaken by children for something to drink. Conclusion: Acciden- tali kerosene ingestion is a problem with wide reaching consequences in the developing world, because children are innocent and parents and are not aware and careful enough about storage of kerosene. There is a need for education and increased awareness regarding the poisonous effects of kerosene. Active interventions such as campaigns in schools and local hospitals, performing dramas on the street especially in rural areas, should educate people about safe storage practices. Also they could be provided with safety information (flyer, stickers, symbols etc) and printed information on the back of the pay receipt each time they buy kerosene. Illegal and unsafe kerosene sale has to be stopped.

255. Thermal and Chemical Skin Burns in the Republic of Benin: An Underestimated Cause of Avoidable Mortality in the Developing Countries

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Introduction: Burns represent a worldwide public health concern with a special issue in the developing countries due to persistent high-rate mortality. The recently funded Senegalese Poison Centre in Dakar was mandated to develop a prevention policy to limit the consequences of thermal and chemical skin burns among the poorest rural populations, including in neighboring African countries. To date, epidemiologi- cal data on burns is missing in Benin. Methods: We conducted a retrospective descriptive study during a 3- year period (2007–2010) including all cases of skin burns admitted into a rural hospital in Benin. Circumstances, clinical, and outcome data were collected. Results are given as median (25–75th percentile). Comparisons were performed using Chi-2 and Mann-Whitney tests. Results: We collected 37 cases (age: 5 years [2–25];
This apparent low ingestion appears responsible for plasma cholinesterase reactivators seems controversial. The antidote of choice is atropine. The indication for mild poisoning has not been presented successful outcome on follow-up. The parameters significantly associated with death were age (p = 0.03), Wallace score (p = 0.0007), burn depth (p = 0.005), and severity of dehydration (p = 0.01).

Conclusion: Skin burns still represent a serious concern in developing countries, particularly in Benin, with an elevated mortality rate among young people. Efficient preventive measures are needed to identify the identification of compounds and behaviors at risk.

256. Criminal Poisoning with Aldicarb

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1Poison Center, CHU, Bordeaux; 2Laboratory of Clinical Pharmacology, CHU, Bordeaux; 3Pediatric and Adult Emergency Unit, CHU, Bordeaux, France

Objective: To report a case of cholinergic toxidrome induced by aldicarb and review the current literature.

Case report: Ten minutes after ingesting coffee in the break room, four paramedics simultaneously developed a cholinergic toxidrome involving blurred vision, muscle weakness, sweating, nausea, vomiting and profuse diarrhea. Clinical examination revealed miosis, but no bradycardia or salivation. Toxicological analysis of the coffee revealed the presence of aldicarb, an insecticide, nematicide and acaricide of the carbamate class. Blood analysis carried out at different times throughout the hospitalization showed a high level of aldicarb nor its metabolites however plasma pseudo-cholinesterase was reduced. Clinical improvement occurred within three hours with symptomatic treatment without atropine or pralidoxime. Discussion: Aldicarb, whose marketing has been prohibited in the EU since 30 April 2007, is a reversible inhibitor of cholinesterase. Toxic effects appear at doses below 0.01 mg/kg with a very steep dose-response curve.1 Biology shows a transient decrease of plasma pseudo-cholinesterase. In severe intoxications serum aldicarb level from 850 to 900 ng/mL and concentrations of 250 to 1000 ng/mL in 24 hour urine have been reported.2 Concentrations for mild poisoning have not been recorded. Symptoms are of short duration due to spontaneous hydrolysis of the AChE-carbamate linkage. The antidote of choice is atropine. The indication for plasma cholinesterase reactivators seems controversial. Conclusion: This case series shows that possible criminal contamination of a beverage with the acutely toxic carbamate aldicarb can cause symptoms of cholinesterase inhibition despite the absence of measurable levels of the compound or its metabolites in blood. This apparent low ingestion appears responsible for plasma cholinesterase reactivators seems controversial. The antidote of choice is atropine. The indication for mild poisoning has not been presented successful outcome on follow-up. The parameters significantly associated with death were age (p = 0.03), Wallace score (p = 0.0007), burn depth (p = 0.005), and severity of dehydration (p = 0.01).

Conclusion: Skin burns still represent a serious concern in developing countries, particularly in Benin, with an elevated mortality rate among young people. Efficient preventive measures are needed to identify the identification of compounds and behaviors at risk.

258. Severe Cobalt Intoxication due to Metal-on-Ceramic Pairing in a Hip Arthroplasty

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Objective: The essential heavy metal cobalt is toxic at high exposures. Severe cobalt intoxication after surgery with metal-on-ceramics hip replacement is described. Slow absorption of the metal by ceramic particles has led to a serious toxicity. Case report: A 56-year-old man underwent total hip prosthesis (ceramics-on-ceramics); 3 years later his ceramic head broke. During a revision of the hip, ceramic fragments were carefully removed and the wound was repeatedly cleaned; then a metal head was used. Alloys in metal implants are mainly slightly elevated lactate (3.1 mmol/L), normal transaminases and urine.

Case report: A depressive 33-year-old male goldsmith deliberately ingested about 80 mL of an electroplating solution containing about 25 g of gold or silver. He presented with typical symptoms and signs of cyanide intoxication. After 3 days his condition improved after treatment with sodium thiosulfate, 1 L of 0.9% saline, and charcoal. The patient's condition improved after treatment with sodium thiosulfate, 1 L of 0.9% saline, and charcoal.

Case report: A depressive 33-year-old male goldsmith deliberately ingested about 80 mL of an electroplating solution containing about 25 g of gold or silver. He presented with typical symptoms and signs of cyanide intoxication. After 3 days his condition improved after treatment with sodium thiosulfate, 1 L of 0.9% saline, and charcoal.

259. Acute Hepatotoxicity Caused by Deliberate Ingestion of Gold Potassium Cyanide with Quantitative Determination of Gold in Serum and Urine

Eyer F, Felgenhauer N, Schrott F, Zilker T.

Toxicological Department, Technische Universität, Munich, Germany

Objective: Poisoning with oral ingestion of gold potassium cyanide is rarely reported. We describe a case of deliberate ingestion of potassium dichromate by a patient who developed severe cholestatic hepatitis. We additionally provide kinetic data for serum and urine.

Case report: A 56-year-old man was transferred to our hospital with acute hepatitis after being found unresponsive in his apartment. He had been drank a cyanide-containing solution approximately 18 hours earlier. On admission, he was comatose and could barely follow any commands. His serum ethanol level was 1.58 g/L and a cyanide-level of 0.19 g/L some 29 h after ingestion and

260. Blood Lead Levels in 6-year-old Sudanese Children
Ageib DMA 1, Kosnett MJ 2.
1Poison and Drug Center, Khartoum, Sudan; 2Medical Toxicology, Denver, Colorado, US
Objective: To conduct the first ever pediatric blood lead surveillance study in Sudan, the geographically largest nation in Africa with a population of 40 million. Sudan has a growing petrochemical industry, and leaded gasoline was used nationwide until 2000. Methods: A cross-sectional survey of blood lead level (BLL) was undertaken in convenience samples of healthy 6 year old children attending well-child visits at outpatient clinics of hospitals in two urban centers, Khartoum and Omdurman, and the rural town of Aldiwaim. Capillary blood samples were analyzed for lead using the ESA Lead Care II system. Lower limit of quantification (LLQ) was 3.4 micrograms/dL. Statistical analysis was done by SigmaStat (version 3.5). A questionnaire on demographic and potential exposure factors was administered to subjects’ parent(s) and in further analysis we will explore association between lead concentration and demographics to identify potential risk factors for lead exposure. Participation was by voluntary informed consent in accordance with a protocol approved by the research and ethical committee of the Federal Ministry of Health of Sudan. Results: In this survey of 209 Sudanese children, BLLs exceeded 5 micrograms/dL in more than 50% of both urban and rural subjects (Table 1), a significant elevation compared to developed countries such as the United States, where less than 5% of children have BLLs > 5 micrograms/dL. Conclusion: Further investigation of potential sources of exposure is warranted. References: 1. Centers for Disease Control and Prevention. Fourth National Report on Human Exposure to Environmental Chemicals. Atlanta, USA. CDC 2009. http://www.cdc.gov/exposurerreport/pdf/FourthReport_EsecutiveSummary.pdf [accessed 24 November 2010].

261. Hemolytic Anemia After Taking Lead Herbal Medicines: A Case Report
Wu ML 1,2, Deng JF 1,2
1Division of Clinical Toxicology, Taipei Veterans General Hospital, Taiwan; 2Department of Environmental and Occupational Medicine, National Yang-Ming University, Taipei, Taiwan
Background: Lead intoxications had been reported in patients who took alternative medicine, but in adults, hemolytic anemia attributable to lead intoxication after taking Chinese herbal medicines has been rarely reported in the literature. Case report: A 45-year-old woman visited a local hospital complaining of anorexia and fatigue. Her blood work was significant for a nonspecific symptoms of inorganic lead intoxication and elevated bilirubin (total: 2.1 mg/dL, direct: 1.0 mg/dL), alanine aminotransferase, aspartate transaminase, alkaline phosphate, gamma-glutamyltransferase. Autoimmune hemolytic anemia was suspected, and she received two-month steroid therapy. She came to our medical center due to persistence of symptoms. Follow-up blood tests showed hemoglobin 10.8 g/dL, with basophilic stippling, mean corpuscular volume 104 fL, platelet 119,000/cumm, and negative Coomb’s test. A blood lead level was obtained, with a value of 75 micrograms/dL (reference range: < 10 micrograms/dL). On further query, the patient had consumed lead containing Chinese Medicine for five months prior to becoming ill. Chelation therapy was started with succimer (2,3-dimercaptopropanesulfonic acid). However, she developed itching and skin eruption. Use of another chelating agent, ethylene diamine tetracetic acid (EDTA) successfully lowered the blood lead level and improved the anemia. Conclusion: This case is presented to emphasize the importance of medication histories, including alternative medicine, while approaching patients with hemolytic anemia.

262. Quantification of Blood Concentration of Mercury and Arsenic in the Healthy Population in Aragon (Spain)
Arevalo Duran M 1, Menao Guille´n S 1, Sorribas Alejandre V 2, Millán Soria P 3, Aranda Arrutu A 4, Ferrer Dufol A 5
1Clinical Toxicology Unit, Clinical University Hospital Zaragoza; 2Toxicology Area, University of Zaragoza; 3Blood and Tissues Bank, Zaragoza, Spain
Objective: Despite their long toxicological history, arsenic and mercury are still a matter of environmental and public health concern. Their ubiquitous presence in food and water produces their persistence in the human body. Their effects at low blood concentrations and their precise threshold in non exposed populations are still contentious. In the particular case of mercury, its toxicity and may be fatal in large overdoses. Treatment tolerated. Methods: We have obtained 121 blood samples from healthy adults attending hospital Emergency Departments (EDs) and from the Spanish Information Toxicology Service (SIT). We have analyzed the characteristics of the occupational cases in the TSP and their particularities versus the total chemical cases. We have also compared the occupa- tional data from the TSP and the SIT sources to assess the differences between them. Methods: We compared the cases’ frequency, sex, chemical agent involved, route of entry and main clinical symptoms in the total and occupational TSP cases in ten years and the occupational SIT cases in one year. Results: TSP has accumulated 6,012 chemical cases between 1999 and 2008, of which 1,042 are occupational cases (17%). Among the total SIT 78,210 in one year, 1,095 (1.4%) were occupational cases. Both TSP and SIT cases are evenly distributed by sex (50%) but the occupational cases from both sources of data are more frequent in men (73% and 63%) than in women (27% and 30%) (p < 0.05). The main differences from both databases are: a higher proportion of occupational cases in men (73% versus 2%) and irritant gases (22% versus 10%) in the TSP than in the SIT cases (p < 0.05) and a lower proportion of cases by pesticides (12% versus 22%) and detergents (2% versus 9%) in the TSP than in the SIT cases (p < 0.05). A higher proportion of respira- tory and ocular routes of entry and of respiratory symptoms in the TSP cases (p < 0.05) have also been detected. Conclusion: These sources of data show some slight but significant differences and have to be analyzed together in order to get a broader picture of acute occupational poisoning in Spain.

263. Occupational Poisoning in Spain as Observed in the Emergency Departments and in the Toxicology Information Service
Ferrer-Dufol A 1, Nogue Xarau S 2, Menao Guille´n S 1, Ruiz F 3, Martinez Arrieta R 4, Ballesteros S 5, Ramon F 6
1Clinical Toxicology Unit, Clinical University Hospital, Zaragoza; 2Clinical Toxicology Unit, Clinical Hospital, Barcelona; 3Toxicology Information Service, National Institute of Toxicology, Madrid, Spain
Objective: Acute occupational poisoning is a human toxic issue difficult to survey due to the different possible organizations involved and the dispersion of the cases among different settings. The aims of the Spanish program for Toxicological Surveillance (TSP) is to focus on the surveillance of acute poisoning by chemicals attending hospital Emergency Departments (EDs). One of the involved groups comes from the occupational field. Another source of information was the Spanish Information Toxicology Service (SIT). We have analyzed the characteristics of the occupational cases in the TSP and their particularities versus the total chemical cases. We have also compared the occupa- tional data from the TSP and the SIT sources to assess the differences between them. Methods: We compared the cases’ frequency, sex, chemical agent involved, route of entry and main clinical symptoms in the total and occupational TSP cases in ten years and the occupational SIT cases in one year. Results: TSP has accumulated 6,012 chemical cases between 1999 and 2008, of which 1,042 are occupational cases (17%). Among the total SIT 78,210 in one year, 1,095 (1.4%) were occupational cases. Both TSP and SIT cases are evenly distributed by sex (50%) but the occupational cases from both sources of data are more frequent in men (73% and 63%) than in women (27% and 30%) (p < 0.05). The main differences from both databases are: a higher proportion of occupational cases in men (73% versus 2%) and irritant gases (22% versus 10%) in the TSP than in the SIT cases (p < 0.05) and a lower proportion of cases by pesticides (12% versus 22%) and detergents (2% versus 9%) in the TSP than in the SIT cases (p < 0.05). A higher proportion of respira- tory and ocular routes of entry and of respiratory symptoms in the TSP cases (p < 0.05) have also been detected. Conclusion: These sources of data show some slight but significant differences and have to be analyzed together in order to get a broader picture of acute occupational poisoning in Spain.

264. Long Term Lead Exposure and Health Effects
Ghasem M, Moradi M, Berjani N
Occupational Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
Introduction: Lead is a poison that affects virtually every system in the body. It has been suggested that the nonspecific symptoms of inorganic lead intoxication are related to the effects of the blood lead level. Methods: A total of 503 battery recycling workers with long-term exposure to inorganic lead between the ages of 36 and 45 years in this study filled out a questionnaire of paraclinical symptoms. The SPSS software version 11.5 and STATA version 8 was used for statistical analysis; the chi-square, Fisher’s exact
265. Cytochrome p450 Enzymes and Their Role in Poison Control Centre Information Supply Groothoff MV1, Hunnault CC2, Meulebeek JM2.
1National Poison Information Centre, National Institute for Public Health and the Environment, Bilthoven; 2Division of Intensive Care Medicine, University Medical Center Utrecht, The Netherlands

Objective: Cytochrome p450 enzymes play a major role in the phase I metabolism of many xenobiotics. Main enzymes involved are CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP3A4, and CYP3A4. Their contribution to adverse events and interactions in therapeutic drug use has been extensively studied, but their significance in clinical toxicology is not well known. Antidepressants and antipsychotics are often involved in suicide attempts, and many of these drugs are metabolized by cytochrome p450 enzymes. To investigate if the information supplied by the Information Centre should be adjusted according to p450 interactions, we investigated to what extent those interactions are suspected.

Methods: All multi-intoxications of at least one antidepressant or antipsychotic, concomitant use of another drug and any other substance, reported to our Poison Information Centre in the year 2009 were included. Ingested compounds were categorized as substrate, inhibitor and/or inducer. The exclusion criteria were: intoxication not centered enzyme-based on the Flachtkarte table and the psychosocial table. Potential interactions were investigated. Results: Of total information requests about 18,169 patients, 3069 patients ingested an antidepressant, and 2224 patients ingested an antipsychotic. Among those patients, 2081 in the antidepressant group and 1545 in the antipsychotic group had a multi-intoxication (n = 2856, overlap in 770 patients). Median ingestion among the 2856 multi-intoxication patients was 3 compounds (range 2–16). Interactions on p450 level were recorded in 1686 out of 2856 patients (57.6%). The order of involvement is CYP3A4 (n = 1331, 46.6%) > CYP2D6 (n = 1034, 36.2%) > CYP2C19 (n = 396, 12.9%) > CYP1A2 (n = 221, 7.9%) > CYP2C9 (n = 88, 3.1%) > CYP2E1 (n = 74, 2.6%) > CYP2B6 (n = 3, 0.1%) > CYP2C8 (n = 1, 0.04%). Conclusion: In the majority of cases of multi-intoxications with antipsychotics or antidepressants, interactions of CYP2D6 and CYP2C19 were the top 3 enzymes. This indicates that their role in clinical toxicology cannot be ignored. However, more research is needed to analyze to what extent these interactions influence clinical outcome after intoxications. References: 1. Zanger UM, Turpeinen M, Klein K, et al. Functional pharmacogenetics/genomics of human cytochromes P450 involved in drug biotransformation. Anal Bioanal Chem 2008; 392:1093–108. 2. Fluckhart DA. Drug Interactions: Cytochrome P450 and Trough. Tulane Public University School of Medicine (2007), http://medicine.tulane.edu/cclinpharm/dids/table.asp. Accessed 4 October 2010. 3. http://www.psychosidelineone.com/CYP450%20drug%20interactions.htm

266. Laboratory Results - When the Figures Don’t Fit the Facts
Dyas J, Thomas A, Krishna C, Thompson JP.
National Poison Information Service (Cardiff), Cardiff and Vale University Health Board, Cardiff, UK

Objective: Information relating to interference in certain biochemical analyses is readily available in the scientific literature, yet the UK National Poisons Information Service (NPIS) still regularly receives enquiries from clinicians struggling to interpret unexpected results. We report three recent cases that serve to illustrate how erroneous laboratory results can confound the clinical picture and even lead to misdiagnosis in cases of poisoning. Case series: 1. A 19-year-old male presented at hospital claiming a deliberate ingestion of methanol. He appeared clinically well but had a serum creatinine of 1.7 mmol/L and a urea of 7.66 mmol/L. He had been admitted 10 days previously with a paracetamol overdose and it was assumed that the elevated creatinine was a consequence of this and his methanol ingestion. However, subsequent creatinine results were normal and further investigations revealed a paracetamol concentration of 176 mg/L. 2. A 76-year-old female presented with symptoms suggestive of meningitis. She had a raised white blood cell count and a serum procalcitonin of 0.86 mg/L. Subsequent investigations revealed a c-reactive protein of 15.8 mg/L and a chest X-ray showed pulmonary consolidation. She was treated for sepsis and a diagnosis of multidrug-resistant tuberculosis was made. The procalcitonin was reassessed and found to be < 0.05 mg/L. 3. A 65-year-old female was admitted with symptoms suggestive of gastrointestinal obstruction. She had a serum lactate concentration of 17.8 mmol/L. She was considered for surgery, but a computed tomography scan revealed no surgical cause. She was treated conservatively and her serum lactate on the following day had dropped to 2.1 mmol/L. Conclusion: This case series highlights the importance of not always assuming a single diagnostic hypothesis, especially when the figures don’t fit the facts.

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Objective: Liquid chromatography-mass spectrometry (LC/MS) is a powerful tool widely used for forensic targeted drug screening. However, the quality of LC/MS methods in their sample preparation methods. Offline solid phase extraction (SPE) and liquid liquid extraction (LLE) are the most often used sample preparation methods. These methods are often quite time consuming. Here we will present an automatic online sample preparation method for the screening of more than 400 acidic, neutral and basic drugs in urine. Liquid chromatography-mass spectrometry sample preparation was performed by an online sample extraction method utilizing the TurboFlow technology. Two TurboFlow columns (Cyclone, C18XL) were connected in series and in parallel extraction. Urine samples were run both natively and after enzymatic hydrolysis. The eluent was then transferred to the LC column (Betasil Phenyl-Hexyl, 100 x 3 mm, 3 μm) for separation. A 30 nm gradient from 1% to 98% organic was employed for separation of the analyte with flow rates of 300 μL/min. All samples were then analyzed on a LQX ion trap mass spectrometer (Agilent 1100) in the positive or negative mode using tandem mass spectrometry. Results: The method using on-line extraction has been fully validated. A minor matrix effect (suppression < 5%) was observed for over 98% of the compounds. 90% of the substances showed a recovery more than 90%. The limit of identification (LOI) was below 10 ng/mL for 60% of the substances and 90% could be identified at a concentration of 100 ng/mL. 103 patient samples were analyzed. A total of 451 substances could be identified using the combination of both established methods (LC/MSD and LC/MS specific methods on a triple stage mass spectrometer) and the new on-line extraction method. When using the new method, 404 substances (88%) could be identified. With the new method, 404 substances (89%) could be identified. Conclusion: The online TurboFlow method with the LQX ion trap mass spectrometer allows the identification of more than 400 compounds with LOIs of 10 ng/mL for the majority of the compounds.

268. Retained Drugs in the Deceased
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Objective: Since gastrointestinal (GI) decontamination is controversial and there is a trend toward less intervention we sought to evaluate the presence of undissolved drugs in the GI tract of fatal overdoses in patients that met inclusion criteria for GI decontamination. Methods: Autopsy reports from the New York City Office of the Chief Medical Examiner were reviewed from 01/01/2009 to 12/31/2009. Inclusion criteria were: deceased of all ages, whose postmortem drug presence. Exclusion criteria: cause of death was established as “overdose” or “intoxication,” from ingestion of drugs in the tablet form. Objective criteria: cause of death attributed solely to drugs in a non-tablet form, or traumatic death. Results: 623 cases were reviewed; 355 cases met inclusion criteria. Dissolved and partially dissolved tablets were present in the stomach of 24 cases (6.7%). Actual tablets were identified as Oxycontin in 2/24 cases, and identified as Norco in 2/24 cases. Modified release venlafaxine was confirmed in one case. Saliclylates were present in one case. The time from ingestion was challenging to determine, since 2323 patients were dead at presentation. Conclusion: Dissolved and partially dissolved tablets were present on autopsies of 24/355 (7%) people, with 22/24 cases (91.6%) containing drugs that are usually eliminated in the stomach and not undergo further absorption, suggesting consideration for GI decontamination in selected patients.
269. Potential Utility of Plasma Butyrylcholinesterase and RBC Acetylcholinesterase Determinations as Rule-Out Testing in the Setting of Nerve Agent or Other Mass Exposure

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Objective: Cholinesterase determinations have been used to identify organophosphate exposed patients and guide duration, and may distinguish patients with mild organophosphate/nerve agent exposure from those who are manifesting stress reactions.

1 An Institutional Review Board (IRB)-approved study on a U.S. population of butyrylcholinesterase (BuChE) and acetylcholinesterase (AChE) evaluated relationships to a number of demographic variables. Methods: 976 patients ranging in age from 0-95 years in 3 hospital settings underwent a standard questionnaire and determination of cholinesterase activities by spectrophotometric analysis using a variety of instruments. Results: The mean (SD; instrument) plasma BuChE was 7 Units/mL (1.6; Ortho DT60), AChE 15.4 Units/mL (3.1; COBAS Integra 800). Although trends were present for age and underlying chronic medical conditions, none of these were predictive for individuals. AChE determinations were independent and were not predicted by low or high BuChE. Conclusion: A large hospital-based population of patients manifested normal values of BuChE and AChE, with a Gaussian distribution of cholinesterase activities, consistent with reports of other geographically and ethnically distinct populations.


270. Beta-hydroxybutyrate, Glucose and Lactate in the Postmortem Diagnosis of Alcoholic and Non-alcoholic Ketoacidosis

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Objective: The aim was to evaluate the importance of beta-hydroxybutyrate (BHB), glucose and lactate in the post mortem diagnosis of alcoholic versus hyperglycemic ketoacidosis as the possible cause of death. Methods: Evaluation of toxicological results in death cases identified in our institute in the study period 2006–2010 with an ante mortem history of alcohol use, without an anatomical or pathological cause of death, and in which BHB, glucose, and lactate were determined in blood, urine, and/or vitreous humor post mortem. Results: Four males and three females (21–59 years of age; mean 40.7 years) in a 4-year study period. The pathogenetic cause of death was found in no anatomical or other cause of death could be detected. Toxicological analysis of alcohol, drugs-of-abuse and prescription drugs did not reveal a toxicological cause of death: alcohol was detected in blood in three cases (0.03 to 1.8 g/L), in urine in four cases (0.06 to 2.4 g/L), and drugs detected were found in four non-fatal cases: cocaine was detected in blood and/or urine in all cases. Based on the combined glucose and lactate levels in vitreous humor, hyperglycemia was concluded in one case (glucose < 0.3 mmol/L; lactate: 47.2 mmol/L), in two other cases (glucose: 6.6 and 55 mmol/L; lactate: 47 and 21 mmol/L, respectively). Acetoacetate which is quickly decarboxylated in the body was detected in one case only, (glucose: 0.3 mmol/L; BHB concentrations were elevated or high in all cases: 1 to 14 mmol/L in blood, and 1 to 31 mmol/L in vitreous humor. In the literature, BHB concentrations in vitreous humor below 0.5 mmol/L are considered to be normal, from 0.5 to 2.5 mmol/L considered to be elevated, and concentrations higher than 2.5 mmol/L are considered as pathological. Based on the combined BHB, lactate, and glucose concentrations, it was concluded that alcoholic ketoacidosis was the likely cause of death in five cases and hyperglycemic ketoacidosis the likely cause of death in two cases. Conclusion: BHB, glucose, and lactate are important parameters to differentiate between alcoholic and hyperglycemic ketoacidosis as the likely cause of death in forensic cases with an ante mortem history of alcohol use.

271. Blood Ethanol Concentrations in Traumatic Emergencies

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Objective: Blood sampling for measuring alcohol is not performed in Bulgaria. The present study is to determine whether type of blood sampling tube (BST) will change blood ethanol concentrations (BECs) and influence clinical interpretation. Methods: Varies in BECs in samples collected from one subject in different BSTs were determined. BECs of 8 volunteers were measured. Four samples at a single point were collected from each: two in BSTs without anticoagulant/preservative (red top), and two in tubes with anticoagulant/preservative (gray top). Effects of some procedures on blood samples, collected in two types of tubes on initial BECs were investigated. Eighteen blood specimens of patients with acute intoxication analysis were analyzed. Results: Half of the samples were taken in red top tubes, the rest in gray top tubes. Initial BEC was compared to concentrations of BECs after mixing blood with a top tube of the sample, after opening/closing mixing of the sample after 24/48 hours at room temperature. Results: In each grey top tube sample, BEC was lower than that in red top tubes. Mean difference was 11.9 ± 4.2% (tubes with over 50% filling) and 15.5 ± 5.5% (with less than 50% filling). Largest deviations were observed in red top tube samples, with high air chamber, stored open at about 30°C. During simultaneous influence of these factors, the average percentage of ethanol recovery was 77.5 ± 7.9%. In red top samples with smaller air chamber, stored at normal temperature, average percentage of ethanol recovery was 95.2 ± 2.1%. In all grey top samples the percentage of ethanol recovery was above 95.5%. Conclusion: Depending on the type of BST and method of processing, BEC vary considerably. These differences do influence clinical assessments. However such deviations are inadmissible for forensic practice and can influence judicial rulings. A standard protocol for sampling for BEC determination has been prepared for legalization in the country.

273. Respiratory Failure Following Inadvertent Administration of Methylergonovine in a Neonate

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Objective: Medication errors can have substantial effects on morbidity and mortality in the hospitalized pediatric patient. We report a case of a newly born neonate with respiratory failure after receiving a 0.1 mg/kg dose of methylergonovine case report. A full-term female infant (1.814 grams) was inadvertently given methylergonovine intramuscularly, instead of a hepatitis B vaccination 1 hour post-delivery. Shortly after medication administration, the patient's extremities became cyanotic and displayed "rhythmic" movements which were interpreted to be seizure-like. The patient was immediately transferred to the neonatal intensive care unit and resuscitated with intravenous fluids. After fluid resuscitation, her symptoms resolved; the patient remained hemodynamically stable and continued to produce urine. Within hours, the patient began to experience significant perinatal depression and was intubated. Twenty-four hours later she was successfully extubated without further sequelae. Upon review, the
274. Therapeutic Error as a Cause of Unintentional Poisoning in Children

Shieffelbien LM, Temple WA.

Objective: To determine how often therapeutic error is the cause of unintentional poisoning in children under six in the Perioperative settings from 1998–2005, 2006, Rockville, MD, United States Pharmacopeia Center and to evaluate the impact of direct-to-consumer-advertising on drug misuse and to support prevention strategies.

Methods: A retrospective review of calls made to the NSW Poisons Information Centre during 1 January 2004 to 15 July 2010 involving therapeutic errors with Infacol Wind Drops. There were 567 therapeutic errors matching the search criteria: 73 in 2004, 52 in 2005, 87 in 2006, 73 in 2007, 103 in 2008, 120 in 2009 and 59 until mid-2010. The median age was 2 months (interquartile range: 1–3 months; range: 5 days–3.5 years). The median dose given in error was 1.5 mL and the most common erroneous dose was 2 mL (range: 0.2–8 mL) instead of the recommended dose of 0.2 mL for under 2 years, and 0.4 mL for over 2 years. Sixteen infants were brought to hospital following ingestion and three patients consulted a general practitioner. There were no cases of toxicity related to hospitalisation.

Conclusion: The most common dosing error was 10 times the recommended dose. Although there have been no reports of serious toxicity associated with simepron, considerable distress occurs when incorrect doses are given to infants. This research highlights the importance of smart dosing device design and labelling to minimise the risk of dosing errors and the importance of trained sales staff ensuring carers are confident in choosing and delivering the correct dose.

275. Ingestion of Benzodiazepine-Containing Vaginal Preparations Before and After a TV Advertising Campaign

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Objective: To provide a preliminary description of therapeutic errors due to misunderstanding of the correct instructions for use of vaginal preparations containing diazepam (Tantum Rosa) observed in Italy before and after a TV advertising campaign. Methods: The database of the national Poison Control Centre (PCC) of Milan was searched retrospectively in order to identify all cases of exposure to Tantum Rosa vaginal preparations occurring between January 1 2004 and December 20 2004, before a TV advertising campaign was launched in Italy during the following months, between December 21 2009 and August 31 2010. The ratio observed/expected (OE) and 95% confidence intervals

(95% CI) were estimated assuming a Poisson’s process in the occurrence of the events. The main characteristics of cases observed in the two periods were compared using Pearson’s χ2 test. Results: Altogether, 201 cases were exposed in the pre-advertising period and 106 in the following one. All cases were accidentally exposed. In both periods the most frequently found preparation was Tantum Rosa. Patients drank the packages to dissolve in water, reported altogether in 185 cases. The ratio O/E in the post-advertising period was 9.8 (95% CI: 8.6–11.8, p < 0.001). In comparison with the pre-advertising period, the post-advertising period was characterised by a higher percentage of female (92% vs. 77%, p < 0.05) subjects exposed for therapeutic error due to oral ingestion of the drug (70% vs. 14%, p < 0.05). Subjects with clinical effects associated to exposure (53% vs. 26%, p < 0.001). Altogether, 82 cases were classified as poisonings. Among these, severity of poisoning was low for 73 cases, including 24 cases occurring in the pre-advertising period and 49 in the post-advertising one. For 9 cases severity of poisoning was moderate. All but one of them occurred in the post-advertising period. Signs and symptoms most frequently reported were: vertigo (24 cases), oesophageal irritation and abdominal pain (18 cases, respectively), vomiting (17 cases), nausea (11 cases), hallucinations and pharyngeal pain (6 cases, respectively). Differences were not found. Signs and symptoms can be used to evaluate the impact of direct-to-consumer-advertising on drug misuse and to support prevention strategies.

276. Medication Prescribing Errors in the Prehospital Setting and in the Emergency Department

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Objective: To describe the incidence and characteristics of medication errors in adults during pre-hospital emergency treatment, and in the emergency department (ED), and to identify risk factors for medication errors. Methods: Retrospective study of adult patients transferred by Emergency Medical Services to the ED of a University-affiliated hospital in Israel. The drugs administered in the pre-hospital setting to the patients enrolled in the ED were reviewed by two reviewers, who independently decided whether an error had occurred. The primary outcome was the number of drug errors per patient. Secondary outcomes were the type and severity of the errors and variables associated with increased incidence of drug errors. Results: During the study period (1,837 patients were brought to the ED by PCCs), patients received medications; of those 12.76% (24 patients) were subject to a medication error. The number of medications administered and long evacuation times were associated with higher risk for an error, P < 0.01 and P = 0.011 respectively. The presence of a doctor in the MICU did not alter the risk of an error (CI = 0.998–11.350). In the ED 332 patients received medications (72.6%). Of those, medication errors occurred in 120 patients (36.1%). The more medications administered, the higher the risk of error (P < 0.01). Fewer errors occurred in trauma patients. (P = 0.041; CI: 1.031–4.566). Of those, medication errors occurred in 120 patients (36.1%). The more medications administered, the higher the risk of error (P < 0.01). Fewer errors occurred in trauma patients. (P = 0.041; CI: 1.031–4.566). Of those, medication errors occurred in 120 patients (36.1%). The more medications administered, the higher the risk of error (P < 0.01). Fewer errors occurred in trauma patients. (P = 0.041; CI: 1.031–4.566). Of those, medication errors occurred in 120 patients (36.1%). The more medications administered, the higher the risk of error (P < 0.01). Fewer errors occurred in trauma patients. (P = 0.041; CI: 1.031–4.566). Of those, medication errors occurred in 120 patients (36.1%). The more medications administered, the higher the risk of error (P < 0.01). Fewer errors occurred in trauma patients. (P = 0.041; CI: 1.031–4.566). Of those, medication errors occurred in 120 patients (36.1%). The more medications administered, the higher the risk of error (P < 0.01). Fewer errors occurred in trauma patients. (P = 0.041; CI: 1.031–4.566). Of those, medication errors occurred in 120 patients (36.1%).
279. Myeloperoxidase Changes in Serum of Subjects Exposed to Irritant Factors Released During Uncontrolled Fire


Objective: Evaluation of the concentration of myeloperoxidase (MPO) in serum from 40 patients hospitalised in the Toxicology Unit due to accidental exposure to smoke from a fire. Methods: 40 patients, hospitalized in the Toxicology Unit after exposure to toxic factors released during an uncontrolled fire participated as a study group. They underwent: spirometry, chest x-ray, arterial blood gases evaluation, basal biochemistry tests: full blood count, urea and creatinine level. The MPO concentration was measured in their serum samples at first day (day of admission), the second day and the day of discharge. The MPO concentration was also measured in the serum of blood samples from 10 unexposed, healthy persons (the control group). Results: The average age of patients exposed to toxic factors released during the uncontrolled fire was 49.75 years. The most frequent symptoms in the study group were complaints associated with lower airways pathology: pharynx or nose related symptoms occurred in 14 patients (35%), whereas symptoms suggestive of upper airways' irritation occurred in 22 (55%) patients. Statistically significantly higher levels of carboxyhemoglobin, thiocyanates, C reactive protein and CC16 were revealed in comparison with the asymptomatic patients. Spirometry at rest revealed significantly lower values of FVC, FEV1 and FEF25–75% within the study group, compared to controls, with p < 0.05. Conclusion: The outcomes presented may indicate the usefulness of CC 16 protein as a marker of lower airways pathology during an uncontrolled fire. References: 1. Halatek T, Opaliska B, Swiercz R, et al. Gutaraldehyde inhalation exposure of rats: effects on lung morphology, Clara-cell protein, and hyaluronic acid levels in BAL. Inhal Toxicol 2003; 15:85–97.

280. Clara Cell Protein Changes in Serum of Subjects Exposed to Irritant Factors Released During Uncontrolled Fire

Krackowski L, Sliwickiwick K, Winnicka R, Halatek T.

Objective: Evaluation of concentration Clara Cell Protein (CC 16) in serum from 40 patients hospitalized in the Toxicology Unit after accidental exposure to smoke from a fire. Methods: 40 patients, hospitalized in the Toxicology Unit after exposure to toxic factors released during an uncontrolled fire participated in the project as a study group. They underwent: spirometry, chest x-ray, evaluation of arterial blood gases, basal biochemistry tests: full blood count, urea and creatinine level. The CC 16 concentration was measured in their serum samples at first day (day of admission), the second day and the day of discharge. The CC 16 concentration was also measured in the serum of blood samples from 10 unexposed, healthy persons (the control group). The average age of patients exposed to toxic factors released during uncontrolled fire was 49.75 years. The most frequent symptoms in the studied group were complaints associated with lower airways pathology - reported by 21 (52.5%) patients, pharynx or nose related symptoms occurred in 14 patients (35%), whereas symptoms suggestive of upper airways' irritation occurred in 22 (55%) patients. Statistically significantly higher levels of carboxyhemoglobin, thiocyanates, C reactive protein and CC 16 were revealed in comparison with the asymptomatic control group. CC16 concentrations measured at the first day were 18.61 microgram/L in the serum samples from the studied group and 10.67 microgram/L in the samples from control group with p < 0.05. Significantly higher CC16 concentrations at the first day were also noted within the group of patients complaining of at least one symptom - 19.65 microgram/L - in a comparison with the asymptomatic patients. Spirometry at rest revealed statistically significantly lower values of FVC, FEV1 and FEF25–75% within the study group, compared to controls, with p < 0.05. Conclusion: The outcomes presented may indicate the usefulness of CC 16 protein as a marker of lower airways pathology during an uncontrolled fire. References: 1. Halatek T, Opaliska B, Swiercz R, et al. Gutaraldehyde inhalation exposure of rats: effects on lung morphology, Clara-cell protein, and hyaluronic acid levels in BAL. Inhal Toxicol 2003; 15:85–97.

281. Risk of Venothromboembolism Associated with Asians using Immunomodulatory Agents

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Objective: Venous thromboembolism (VTE) in patients receiving immunomodulatory agents (iMIDs) like thalidomide and lenalidomide is believed to be uncommon in Asian patients with haemato-oncological malignancies. With limited evidence postulating a negligible risk, VTE prophylaxis is commonly omitted. In this study, we evaluate the incidence and risk factors of drug induced VTE in these patients. Methods: Patients with confirmed diagnosis of VTE were obtained from a Multiple Myeloma registry maintained in a tertiary institution. Their characteristics and exposure to iMIDs and anti-platelets agents (APA) were compared against a control group. Results: Among 320 consecutive and previously untreated patients entered into the registry, and prospectively followed for 12 years, 18 VTE events (5.6%) were diagnosed. 232 patients (72%) were exposed to an iMID. Risk of VTE was not associated with patient or disease characteristics at presentation. Exposure to an iMID was found to be a significant risk factor (17/18 patients developed VTE during or immediately after treatment) giving an iMID-associated VTE risk of 7.4%. The median time to VTE was 16 months. The cumulative incidence of VTE among patients exposed to iMIDs at 5.6 years (median overall survival) was 12%. Conclusion: VTE risk in Asian patients, especially those with haematological malignancies, is substantially higher than postulated and confirms a significant morbidity and mortality risk. Events appear to occur later in the course of the disease and were significantly more frequent when there was significant exposure to iMIDs. As iMIDs are essential for the treatment of such patients, physicians should be cognizant of this potential complication. They should also recommend thromboprophylaxis for our Asian patients. References: 1. Shyu VB, Wang PN, Chu PH. Low incidence of venous thromboembolism in Asian myeloma patients treated with thalidomide plus dexamethasone. APJOH 2010; 2:41–7.

282. Internet Accessibility and Quality of Product Descriptions of Ephedrine Containing Products

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Objective: The illegal trade of ephedrine containing products is an unsolved problem for the Danish health service. A retrospective evaluation of inquiries to the Danish Poison Information Center1 indicated careless consumer behavior with intentional intake of large doses for the purpose of weight loss and training enhancement. We wanted to determine the accessibility of ephedrine containing products for Danish consumers on the Internet, in order to evaluate what extent poor product declarations could contribute to such careless consumer behavior. Methods: We conducted a one day search on the Internet, using as a search engine, with the Danish search terms: Vægtgaff [weight loss], efferin [ephedrine] and efferdin producer [ephedrine containing products]. Limits were set to only include websites in Danish. Pages were only included if it was possible to "go to the cash register". Results: 12 websites (519 hits) offering a total of 101 ephedrine containing products were found. Although we performed our search in Danish, only a minority continued in Danish all the way to "cash register". None informed about the illegal import to Denmark of ephedrine per serving, ranging from 10–75 mg ephedrine (mean 24.5 mg ± SD 12.75). 55.4% warned consumers to be careful. Conclusion: Illegally marketed ephedrine products are easily accessible on the Internet by Danish consumers. Only a minority revealed relevant medical information and most declarations were in English. These products do not fulfill the requirements of declaration for medical products and are easily accessible to a group of people who are not medically screened. Therefore, consumers may be at risk of serious adverse effects. Misleading sales slogans, such as "all natural, beneficial to your health, no side effects, scientifically proven" give a false sense of security and may enhance careless and risky consumer behavior. Reference: 1. Kjærgaard CT, Skanning PG, Jürgens G. Retrospective review of ephedrine exposures. An observational case series. Clin Toxicol 2010; 48:262.
284. Methemoglobinemia is not Associated with Intentional Carbon Monoxide Poisoning

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Introduction: Suicide attempts often involve the inhalation of motor vehicle exhaust. These exhaust fumes are associated with a number of dangerous combustion products, such as carbon monoxide, cyanide, nitrogen oxides, and methemoglobin. CO is the predominant toxin associated with suicide attempts from motor vehicle exhaust. A less commonly reported toxicity associated with this type of exposure is methemoglobinemia (MetHgmg). Objective: To determine the incidence of MetHgmg in cases of intentional CO poisoning associated with motor vehicle exhaust fumes.

Methods: A multi-center retrospective emergency department (ED) cohort. Study setting: 23 New Jersey and New York EDs. Subjects: Consecutive patients with the ED diagnosis of CO toxicity and intentional exposure were identified from January 1, 2000 to October 31, 2006. Results: Out of 4.2 million consecutive patients in the 23 EDs, 52 ED patients were identified with intentional CO toxicity (0.012% of all consecutive patients in the 23 EDs, 52 ED patients were identified with intentional CO toxicity (0.012% of all consecutive patients in the 23 EDs, 52 ED patients were identified with intentional CO toxicity (0.012% of all consecutive patients in the 23 EDs, 52 ED patients were identified with intentional CO toxicity (0.012% of all consecutive patients in the 23 EDs). Mean age was 40.2 yrs and 25% were women. Twenty-two (42%) of 52 ED patients were discharged home. Less than 24 hours later, the child presented more than 36 hours after inhalation of talc-containing baby powder, and following resolution of respiratory complications, including respiratory arrest and acidosis, and cardiovascular collapse. In severe toxicity the use of hemodialysis is reported, but largely unsupported by kinetic analysis. We report the dialysis clearance of glyphosate following a suicidal ingestion of a glyphosate-containing herbicide. Case report: A 62 year-old man presented to an emergency department approximately 8.5 hours after drinking a bottle of commercial herbicide containing a 4% solution of glyphosate isopropylamine, in polyoxyethyleneamine (POEA) surfactant and water. Upon presentation, he was bradycardic and obtunded with respiratory depression necessitating intubation and mechanical ventilation. Initial laboratory results were significant for: pH 7.14, PCO2 64 mmHg, PO2 48 mmHg, potassium 5.8 mEq/L, Cr 291.7 micromol/L (increased from 84.0 m-

285. Delayed Respiratory Distress in an Infant Following Inhalation of Talc-Containing Baby Powder

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Objective: The inhalation of talcum powder, or finely ground magnesium silicate, is associated with severe respiratory complications, including respiratory arrest and death. Despite safe alternatives, talc unfortunately remains a component of commonly available baby powder products. We report a case of severe pneumonitis with a delayed progression of symptoms following inhalation of talc-containing baby powder. Case report: A previously healthy boy was brought to the emergency department 20 minutes after inhaling baby powder (81% talc) during his diaper change. His mother described immediate coughing and cyanosis that imminently endangered the child’s life. Upon arrival, he was crying with a respiratory rate of 40–60/min, an oxygen saturation of 98%, pulse of 104/min, and temperature of 37.1°C. Lung examination revealed clear breath sounds bilaterally, and a CXR was normal. After consultation with the poison center, he was given prednisone and admitted for observation. The following day he was well-appearing without tachypnea, and was discharged home. Less than 24 hours later, the child returned to the same ED with grunting respirations, subcostal retractions, and diffuse cracks on lung auscultation. Vital signs were: respirations 60/min; oxygen saturation 92%; pulse 150/min; temperature 39.7°C. A CXR showed increased bronchovascular markings and thoracic hyperinflation, with focal infiltrate. Nebulized albuterol was given without improvement. The patient was admitted to the pediatric intensive care unit, and received intravenous methylprednisolone and empirical antibiotics. His symptoms slowly resolved over the next two days, and he was discharged in stable condition on hospital day 3 to complete a five day course of corticosteroids. Conclusion: In 2008, the American Academy of Pediatrics reported 2,526 exposures to powders made of talc, 87% of which occurred in children under the age of 6 years. Delayed onset of respiratory symptoms is described up to several hours following suspected talc inhalation. This child developed severe pneumonitis presenting more than 36 hours after inhalation of talc-containing baby powder, and following resolution of his initial symptoms. Clinicians should be aware of the possibility of delayed progression of lung injury following acute talc inhalation.

286. Hemodialysis Clearance of Glyphosate Follows Lower than Expected Prediction of Glyphosate-Containing Herbicide

Garlich FM1,2, Goldman M3, Pepe J3, Nelson LS1,2, Allan MJ, Goldstein DA2, Goldfarb DS2,5, Hoffman RS1,2.
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Objective: Ingestion of glyphosate-containing herbicides can result in renal failure, electrolyte abnormalities, acidosis, and cardiovascular collapse. In severe toxicity the use of hemodialysis is reported, but largely unsupported by kinetic analysis. We report the dialysis clearance of glyphosate following a suicidal ingestion of a glyphosate-containing herbicide. Case report: A 62 year-old man presented to an emergency department approximately 8.5 hours after drinking a bottle of commercial herbicide containing a 4% solution of glyphosate isopropylamine, in polyoxyethyleneamine (POEA) surfactant and water. Upon presentation, he was bradycardic and obtunded with respiratory depression necessitating intubation and mechanical ventilation. Initial laboratory results were significant for: pH 7.14, PCO2 64 mmHg, PO2 48 mmHg, potassium 7.8 mEq/L, Cr 291.7 micromol/L (increased from 84.0 m-

287. The NPIS Pesticide Surveillance Project

2004–2010: Fly and Wasp Killer Exposures Adamic A1,2,3, Gillson AE1,2, Good AM1, Jackson G, McGrory C, Dow M, Bateman DN, National Poisons Information Service (Edinburgh), Royal Infirmary of Edinburgh, Edinburgh, UK

Objective: To describe fly and wasp killer exposures in patients reported during the 6.5 years of the NPIS TOXBASE® pesticide surveillance project. Methods: The National Poisons Information Service Edinburgh Unit (NPIS) monitors pesticide exposures following Internet (TOXBASE®) or telephone enquiries. All patient related accesses to pesticides on TOXBASE® between 1/4/2004 and 1/10/2010 were notified electronically to NPIS, and followed up using on-line, email or paper questionnaires. All NPIS telephone enquiries from 1/4/2004 were also notified electronically. Exposures from outside the UK and those where symptoms were deemed not related were excluded. Exposures were assessed for circumstances and outcome. Results: Since 2004 5211 pesticide exposures have been reported to NPIS. One hundred and eighty-nine (3.6%) of these involved accidental exposure to fly and wasp killer products. These products are normally sold as aerosol sprays but occasionally as powders or foams for use on nests. The majority of exposures involved adults (141, 74.6%) and were acute (184, 97.4%). Just over half of patients were male (100, 52.9%) and accidental poisonings frequently occurred while the pesticide was in use; 99 (52.4%). Exposure occurred while in use by another person in 27 (14.3%) cases and after application in 24 (12.7%). Most products were for amateur use: 155 (82.0%). Top agents reported were tetramethrin (91), permethrin (44) and d-phenothrin (36). Route of exposure: ingestion (68, 36.0%); inhalation (30, 16.0%); dermal (27, 14.3%); skin (17, 9.0%), multiple (47, 24.9%). Commonly reported symptoms were: nausea/vomiting (28); mouth/throat irritation (21); eye irritation (18); skin irritation (17); headache (13); dyspnea (11); chest pain (10); cough (8); abdominal pain (6); oral paraesthesia (6); unpleasant taste (6); diarrhoea (5); dizziness (5). Poisoning Severity Score (PSS) grading: none (73, 37.9%); minor (58, 31.9%); moderate (14, 7.3%); uncertain (5, 2.6%), no serious poisonings or deaths reported. Moderate cases involved 6 patients with prolonged symptoms, 2 with corneal abrasions, 1 with epiglottis and 1 with respiratory depression. Conclusion: Accidental exposures to fly and wasp killers account for a small proportion of pesticide exposures overall, however 70.4% reported symptoms. Most of these symptoms were minor but moderate severity did occur. Many symptoms reported may relate to propellants in aerosol products, such as butane and petroleum distillates.
enquiries. Enquiries where symptoms were deemed not related to the exposure were excluded. Slug killer enquiries were analysed for products, circumstances and symptoms in adults and children. A Poisoning Severity Score (PSS) score was assigned to each incident by information staff. Results: Information on 8832 incidents involving pesticides was collected. Of these 406 (4.6%) involved slug killers (predominantly pellets). In 14 cases 56 incidents involved unidentified slug pellets, 137 metaldehyde, 6 ferric phosphate and 3 aluminium sulphate. Where gender was known (404) the male:female ratio was 1:0.6. Where recorded (394) the median age was 2 years (average 9.5 years; range <1–88 years). Where circumstances were known, in 14 cases the patient was using the product themselves; in 33 cases someone else was using it. Incidents occurred after application; 27 due to unsatisfactory storage; and 5 were occupational exposures. For children aged <12 years (325) PSS0 - 282; PSS1 - 27 (mainly gastro-intestinal upset and/or rash/irritation); PSS2 - 1 (prolonged vomiting); uncertain - 15. Seventy cases involved patients >12 years; 33 were the result of deliberate self-harm (PSS0 - 18; PSS1 - 7; PSS2 - 3; PSS3 - 1; uncertain - 4); 36 were accidental (PSS0 - 20, PSS1 - 14, PSS2 - 2 (of which one of uncertain connection)). Occupational exposures (5) resulted in no more than minor features. The single severe case involved acute ingestion of a liquid metaldehyde preparation resulting in ITU admission. Conclusion: Although slug killers are a common query in the UK, accidents are seldom results in no more than minor features. Deliberate ingestion of liquid preparations may be more serious. References: 1. Person HE, Sjoberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13.

289. Acute Poisoning with Imapzamy Herbicide: Taiwan Poison Center Study

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Background: Imapzamy is an imidazolinone herbicide. The herbicidal activity is derived from its ability to disrupt an enzyme (found only in plants) necessary for protein synthesis, and which interferes with cell growth and DNA and RNA metabolism. It is thought to be very toxic to humans. However, information about clinical effects and toxicity in human poisoning is not well known. Methods: We retrospectively analyzed all imapzamy exposures reported to the Taiwan National Poison Center between July 1985 and June 2009. Results: A total of 59 patients were analyzed. Most exposures (92%) involved suicidal ingestion. Ten out of 54 patients with oral exposure were asymptomatic, whereas the others developed gastrointestinal (48%), neurological (33%), cardiovascular (17%), respiratory symptoms (11%) and miscellaneous effects. Six patients developed severe toxic effects and three patients died. Case fatality rate from ingestion was 5.6%. Profound shock, coma, respiratory insufficiency and aspiration were associated with severe or fatal effects. Conclusion: Imapzamy exposure usually causes mild or insignificant effects. However, coma, cardiovascular insufficiency, aspiration pneumonia, or even mortality may occur. Management for imapzamy poisoning is decontamination and supportive treatment, especially respiratory monitoring and ventilatory support, if needed.

290. Aldicarb: A Case Series of Watermelon Borne Carbamate Toxicity

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Background: Aldicarb poisoning has occurred from ingestion of watermelons and cucumbers illegally sprayed with aldicarb. Watermelons are known to be absorbed by watermelons and cucumbers. Despite prohibitions, this dangerous use continues. Case series: Seven farm workers presented to a rural hospital with varying degrees of confusion, abdominal pain and altered mental status. Symptoms began immediately after sharing a watermelon freshly picked from a field. Toxicology consultation was obtained, a diagnosis of cholinesterase inhibition poisoning was made, and the individuals were empirically treated with atropine and pralidoxime with resolution of symptoms. The remains of the partially consumed watermelon, a second watermelon from the same field, and a watermelon from another source were obtained and frozen at -20 degrees Celsius pending analysis. The Regional Public Health Surveillance Team was contacted and undertook an investigation. Watermelons from the farm were quarantined then destroyed; the farm owner was penalized then destroyed; the farm owner was contacted. Conclusion: Although slug killers are a common query in the UK, accidents are seldom results in no more than minor features. Deliberate ingestion of liquid preparations may be more serious. References: 1. Person HE, Sjoberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13.

291. Clinical Experience of Organophosphate Fungicide Intoxication Patients - Three Cases of Edifenphos and One Case of Iprobenfos

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Background: Patients with pesticide poisoning should be treated as soon as possible, and appropriately, because the mechanism of action is markedly different. For example, organophosphate fungicides have a different mechanism of action to that of organophosphate insecticides, so treatment of poisoning with them should be different. However, edifenphos is a kind of organophosphate fungicide which needs the same treatment as organophosphate insecticides. Case series: 1. A 46-year-old man was poisoned by an unknown agricultural chemical. His mental status was semicoma with pin-point pupils. There was a large amount of saliva in his mouth. He was treated with activated charcoal, atropine, and pralidoxime and identified as edifenphos (organophosphate fungicide). He had SLUDGE (salivation, lacrimation, urination, defecation, gastrointestinal motility, emesis) symptoms with low pseudocholinesterase level (below 200 IU/L). 2. A 91-year-old woman was poisoned by an organophosphate fungicide containing edifenphos. She did not have SLUDGE symptoms but did have respiratory failure owing to muscle weakness with low pseudocholinesterase level (below 200U/L). She was treated with pralidoxime for 3 days. 3. A 62-year-old man was poisoned by an organophosphate fungicide containing edifenphos. His mental status was semicoma with SLUDGE symptoms and pin-point pupils. He had low pseudocholinesterase level (below 200 IU/L). 4. A 74-year-old woman was poisoned by 500 mL of iprobenfos which is also an organophosphate fungicide. Her also had SLUDGE symptoms. Her mental status was alert without SLUDGE symptoms. She was treated conservatively, without using pralidoxime and atropine. Conclusion: Both edifenphos and iprobenfos are organophosphate fungicides. Edifenphos inhibits cell wall synthesis by reduction in chitin synthesis activity. It also has an inhibiting action on acetylcholinesterase. Iprobenfos, on the other hand, does not have an obvious effect on acetylcholinesterase. Although edifenphos is a kind of organophosphate fungicide, it is the only one having an inhibiting action on acetylcholinesterase. Edifenphos should therefore be treated with pralidoxime and atropine, contrary to the treatment of other organophosphate fungicides. References: 1. Din AB, Yarden O. Sodium channel depolarization and causing hyperexcitation. 1. We describe a 19-month-old patient in whom tonic-clonic seizures and coma occurred after type-I pyrethroids ingestion. Case report: A 19-month-old female presented to the emergency department (ED) with recurrent tonic-clonic seizures, bilateral miosis and Glasgow Coma Score 3. Vital signs including blood pressure, oxygen saturation on room air, and body temperature were normal; pulse rate was 100 beats per minute. A further inquiry revealed that 9 hours before she had accidentally ingested an imprecise amount of Formulation-Mayer-Concentrate 4, an insecticide containing piperonyl butoxide and an organophosphate (bifenthrin 5%, esbithion 3%). Orotachial intubation, oxygen administration and benzodiazepine infusion were performed. Thiopental sodium up to 18 milligrams/kg was administered to control convulsions. Gastric lavage, activated charcoal and cathartic administration were carried out. During the following 72 hours she became progressively alert; she was discharged asymptomatic 12 days after hospitalization. Bifenthrin and piperonyl butoxide blood levels at 9, 48, 72 hours after ingestion were 500 and 1,640, 95 and 640, 40 and 165 ngamorphin/milliter, respectively. Bifenthrin, esbithion, piperonyl butoxide were confirmed in gastric aspirate. Conclusion: Type-I pyrethroids ingestion is characterized by depression of consciousness, tremors, seizures, paralysis and pulmonary edema. Piperonyl butoxide is an acaricide frequently found in pyrethroid formulations and may increase their toxicity in animals. In our case coma and seizures represented the principal life-threatening features. Supportive therapy and gastric decontamination were performed; benzodiazepines and high doses of thiopental sodium were successfully administered to treat seizures. Bifenthrin and piperonyl butoxide were confirmed in blood and gastric aspirates. In acute pyrethroid poisoning first-aid treatment is therefore indicated if there is evidence of an airway and control of muscle fasciculation and seizures. References: 1. Bateman DN. Management of pyrethroid exposure. J Toxicol Clin Toxicol 2000; 38:107-109. 2. Goldstein JA, Hickman P, Kimbrough RD. Effects of purified and technical piperonyl butoxide on drug metabolizing enzymes and ultra-

294. Atropine Poisoning: Two Severe Clinical Cases Confirmed by Laboratory Analysis
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Objective: To describe two cases of severe anti-cholinergic poisoning due to atropine ingestion. Case series: 1. A 67 year old female pharmacist was brought to the emergency department (ED) with somnolence, rash, mydriasis, hypertension, tachycardia, and hypothermia. At admission no history was available, and an anti-cholinergic syndrome was suspected. Gastric decontamination was performed and physostigmine (up to 0.8 mg/kg/hour) was intravenously administered. Later, the daughter found a 1% atropa-extract that the mother had probably drunk in unknown amount. Atropine levels 2 hours after admission was 20 nmol/mL. On day 4 the patient was transferred asymptomatic to a psychiatric ward. Case report 2. An 80 year old retired pharmacist was found in a coma at home, with a bottle of atropine powder nearby. The wife said she had seen him putting a white powder in his coffee. The patient was in chronic treatment with oxycodone, amloidipine and erythropoietin for a multiplе myeloma. No admission coma, mydriasis, tachycardia, pulse rate 90 bpm, dry skin and mouth were observed. Gastric decontamination was performed and naloxone was administered with slight improvement of neurologic conditions. As symptoms worsened physostigmine (up to 4 mg bolus) was repeatedly administered. The patient died 3 days later from respiratory arrest. Laboratory screening confirmed atropine in the powder and serum levels of 350 nanograms/mL at admission. Conclusion: To our knowledge many cases of anti-cholinergic poisoning are reported after ingestion of plants containing belladonna alkaloids, some of these also with analytical confirmation. Cases of ingestion of large amounts of pure atropine with laboratory confirmation are less frequently described. In these cases high atropine blood concentrations were detected several hours after ingestion compared to normal levels and half-lives reported.

There are still some doubts about the correlation between serum levels and clinical effects. The clinical picture of atropine poisoning may be so easy to treat even with administration of high doses of physostigmine.


295. A Case of Massive Zonisamide Overdose with a Moderate Clinical Course
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1Swiss Toxicological Information Centre, Zurich; 2Medical Clinic and Intensive Care, Hospital of Uster, Uster, Switzerland

Objective: Zonisamide is an anti-epileptic that acts on voltage-sensitive sodium and calcium channels, with modulatory effect on GABA-mediated neuronal inhibition. The common side effect on carbonic anhydrase. Zonisamide overdose data are limited and no case of zonisamide monointoxication has been published to date. A 26-year-old female developed coma, bradycardia, hypotension and respiratory depression after ingesting an overdose of zonisamide and clonazepam.

Case report: A 25-year-old epileptic female treated with 300 mg zonisamide/d, 5 mg cllobazam/d and 150 mg lacosamide/d was brought to the emergency department 8 h after ingestion of 12.6 g zonisamide with suicidal intention. The patient was asymptomatic (GCS 9) and vomited repeatedly. ECG showed QRS widening (102 ms) and QT prolongation (QTC 506 ms). Pulse rate was 87 beats/min, blood pressure 103/54 mmHg. The patient was intubated and a single-dose of activated charcoal was administered. Arterial blood gas analysis (ABGA) after intubation showed moderate lactic acidosis (pH 7.28, pCO2 5.19 kPa, pO2 20.1 kPa, bicarbonate 28.4 mmol/L, BE -7.3 mmol/L; lactate 5.5 mmol/L). The level of consciousness improved within 8 h and she was extubated. She remained somnolent for another 50 h and transient myoclonus and diploria occurred. The following day, the ECG was normal (QTC 375 ms). ABGA showed a normal-anion-gap metabolic acidosis with respiratory compensation (pH 7.34, pCO2 3.7 kPa, pO2 13.0 kPa, bicarbonate 17.0 mmol/L, BE -9.7 mmol/L; lactate 0.5 mmol/L, chloride 117 mmol/L, sodium 136 mmol/L). This alteration improved over the next 3 days. Polypnea without alteration of other renal parameters was demonstrated and with ABGA analysis at admission revealed a plasma zonisamide concentration of 182 μg/L (therapeutic 10–40 μg/L), therapeutic levels of cllobazam and lacosamide and a positive serum toxicological screening for caffeine. The zonisamide plasma concentration one month earlier had been 26.5 μg/L.

Conclusion: Despite a high plasma zonisamide concentration, the patient showed a moderate clinical course with characteristic symptoms. QRS widening and QT prolongation have not been previously described. Due to the long serum half-life (50–70 h), symptoms can persist for several days, but complete recovery can be expected with supportive care.


296. Milnacipran Poisoning: A Review of the Cases Notified to the Paris Poison Centre
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Paris Poison Centre, Femand Widal Hospital, Paris, France

Introduction: Milnacipran is a serotonin and noradrenaline re-uptake inhibitor (SNRI) available commercially in France since 1997. Only 4 cases of milnacipran poisoning were notified to the Paris Poison Centre from September 2009 - November 2010. A 2 page clinical research form was used to collect information from hospital-based calls and was faxed at the time of the initial call. A copy of the patient’s medical record for the admission was also requested retrospectively. A follow-up call for accidental ingestions was attempted within 72 hours of the initial call. Results: A total of 32 cases of zonisamide poisoning with outcome information were collected through the Poisons Information Centre. The patients were classified as follows: i) Accidental paediatric exposures (n = 21; median age: 3; range: 1–6 years), 20 were symptomatic (estimated ingested dose: median 1 mg, IQR: 1–2 mg; range: 0.25–18 mg): Nausea (n = 7), vomiting (n = 14: 8 involved repeated vomiting), hyperactivity/sleep disturbance (n = 10), pallor (n = 8), lethargy (n = 8), nightmarish experience (n = 2), mild hypotension with bradycardia (n = 1), intermittent twitch (n = 1), sweating (n = 1), diaphoresis (n = 1). Eleven were hospitalised for monitoring, the only treatment required was provided in hospital. One child (5%) remained asymptomatic (estimated ingested dose: 0.25 mg); ii) Deliberate self-poisoning (n = 11), 6 cases involved zonisamide only (± alcohol) and 5 cases (± 500 mg) zonisamide with varenicline for both accidental paediatric ingestions and deliberate self-poisoning. Methods: Cases were recruited through calls to the NSP Information Centre between 1st June 1997 to 30th November 2009. Iterative data collection was performed and milnacipran levels were obtained in four with SID of 1250 mg (175–3000 mg). Outcome was known in 17 cases and was comparable to those reported at therapeutic dosage. This intoxication does not need specific management.

297. Toxicity Profile of Varenicline
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Objective: Limited toxicity data exists on the smoking cessation drug, varenicline (Champix®/Chantix®). This study aims to describe the toxicity profile of varenicline, both accidental and deliberate self-poisoning. Methods: Cases were recruited through calls to the NSW Poisons Information Centre between 1st June 1997 to 30th November 2009. A 2 page clinical research form was used to collect information from hospital-based calls and was faxed at the time of the initial call. A copy of the patient’s medical record for the admission was also requested retrospectively. A follow-up call for accidental ingestions was attempted within 72 hours of the initial call. Results: A total of 32 cases of varenicline poisoning with outcome information were collected through the Poisons Information Centre. The patients were classified as follows: i) Accidental paediatric exposures (n = 21; median age: 3; range: 1–6 years), 20 were symptomatic (estimated ingested dose: median 1 mg, IQR: 1–2 mg; range: 0.25–18 mg): Nausea (n = 17), vomiting (n = 14: 8 involved repeated vomiting), hyperactivity/sleep disturbance (n = 10), pallor (n = 8), letheragy (n = 8), nightmarish experience (n = 2), mild hypotension with bradycardia (n = 1), intermittent twitch (n = 1), sweating (n = 1), diaphoresis (n = 1). Eleven were hospitalised for monitoring, the only treatment required was provided in hospital. One child (5%) remained asymptomatic (estimated ingested dose: 8 mg). No seizures or cardiotoxicity was recorded in association with varenicline overdose. The only treatment required was basic supportive care with symptomatic relief provided included anti-emetics, proton pump inhibitors and IV fluids. Conclusion: In this limited series of 32 cases, no serious toxicity was noted from varenicline in accidental paediatric ingestions of up to 18 mg (estimated) and deliberate self-poisoning of up to 50 mg. Symptoms are very common in all types of exposures and at any dose. The majority of accidental paediatric ingestions did not require treatment in hospital. Further experience is still required.

298. Angiotensin II Antagonists - An Assessment of Their Toxicity
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Objective: The aim of the study was to assess the toxicity of angiotensin II antagonists in overdose, because there is little information in literature on this topic. Methods: In a retrospective study, cases of poisoning by angiotensin II antagonists from seven Poisons Information Centres in Austria, Germany, and Switzerland were analysed. Inclusion criteria were monointoxications, defined dose, and documented follow up. Results: In total, 206 cases of poisoning by angiotensin II antagonists were registered (candesartan 94, eprosartan 3, irbesartan 20, losartan 26, olmesartan 16, telmisartan 18, valsartan 29). Patients involved were 150 children (0.8–13 years) and 56 adolescents (15–17 years) or adults (28–77 years). Dose expressed as a multiple of the maximum daily dose for adults ranged between 0.06–6.5 (median 0.5) in children and 0.5–50 (median 7.8) in adolescents. Most children remained asymptomatic (82.7%), 16.7% developed mild symptoms. Only in one case, hypotension required therapeutic measures after ingestion of the 1.5-fold maximum dose of candesartan by a 2.5-year-old toddler. In adolescents/adults almost half the patients suffered from mild (37.5%) or moderate symptoms (8.9%). Most frequent symptoms were hypotension (48%, usually mild), fatigue (19%), nausea/vomiting (15%), dizziness (12%), and somnolence (12%). In moderate poisonings, collapse, pronounced hypotension were observed in adults after ingestion of a 5–7-fold maximum dose of valsartan or a 20–50-fold maximum dose of eprosartan, irbesartan or telmisartan. Conclusion: After ingestion of the maximum daily dose for adults by children, there is no or only mild toxicity. Higher doses may cause moderate poisoning requiring appropriate treatment. In adults, doses from the S-foq maximum daily dose induced moderate toxicity in several cases. In general, angiotensin II antagonists seem to have a wide therapeutic index. Differences in toxicity within the group of angiotensin II antagonists cannot be assessed in this study because the number of cases for most substances was too small.

299. Toxicokinetics of Quetiapine and its Active Metabolite N-desalkylquetiapine During Deliberate Self-Harm

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Objective: Toxicokinetic data on the atypical neuroleptic quetiapine (Q) is relatively sparse. CYP3A4 metabolizes Q to the main active metabolite N-desalkylquetiapine (NDQ). Peak concentration occurs 2h post-ingestion and t1/2 is 7h. Fatal outcomes have been reported at S-concentrations of 19–48 micromol/L. Toxicokinetic data from a near-fatel case is presented. NDQ was measured using an validated LC MS/MS method. The lower limit of quantification was 0.020 and 0.025 micromol/L for Q and NDQ, respectively. SI conversion factors for Q and NDQ (micromol/mL) are 0.384 and 0.296, respectively. Case report: A 39-year-old woman ingested unknown (large) amounts of Q. She was somnolent, tachycardic (115 bpm), but otherwise stable. ECG was normal. Gastric lavage and activated charcoal regimen was not performed, as the suspected time of ingestion was >2h. Ten hours after admission, status epilepticus developed, treated with diazepam. Respiratory depression and severe bradycardia with broad QRS-complexes (150 ms) followed, requiring intubation and cardiopulmonary resuscitation. After successful resuscitation, mechanical ventilation, vasoressors, diazepam and valproate infusions were necessary. Acute respiratory distress syndrome (ARDS) and rhabdomyolysis, metabolic acidosis and sepsis were treated. Her condition gradually improved, but CCT showed possible hypoxic brain damage. After 39 hospital days, psychiatric follow-up and rehabilitation was initiated. S-concentrations of Q and NDQ peaked 12 and 63 hours post-admission, at 31.81 and 10.34 micromol/L, respectively (Table 1). Conclusion: The late peaking S-concentration could be due to large amounts ingested and her circulatory complications might have delayed the elimination. Data concerning effects have not been reported. As the complications followed the kinetic timeline, a more aggressive decontamination approach might have been beneficial.

Table 1. Quetiapine and N-desalkylquetiapine concentrations after overdose

<table>
<thead>
<tr>
<th>Hours after admission</th>
<th>Quetiapine (micromol/L)</th>
<th>NDQ (micromol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.81</td>
<td>6.49</td>
</tr>
<tr>
<td>12</td>
<td>31.81</td>
<td>7.76</td>
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<td>24</td>
<td>8.54</td>
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</tr>
<tr>
<td>86</td>
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<td>6.96</td>
</tr>
</tbody>
</table>

300. Reviewing Quetiapine: Implications from Poison Information and Analytical Data

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Objective: Quetiapine is a dibenzothiazepine derivative that has been evaluated for management of patients with the manifestations of psychotic disorders. Since its introduction in 2000 it has gained increasing importance in the treatment of schizophrenia, bipolar disorders and psychosis due to dementia. Intoxications are supposed to be mild to moderate with somnolence and tachycardia as the main clinical symptoms. They typically resolve within several hours. Correlation between symptoms and ingested dose was found to be poor. As the S-concentration of quetiapine increases, accumulated data from the Poisons Information Centre (PIC) Berlin were reviewed and completed with analytical results of quetiapine intoxications reported in literature. All relevant cases of quetiapine poisoning reported to the PIC Berlin between 2003 and 2009 were analyzed. In addition the analytical results from 93 intoxicated patients were evaluated and correlations with serum concentrations and elimination kinetics. Results: From 2003 to 2009 Berlin PIC was consulted in 494 (315, 146, 33 unknown) cases of deliberate self-harm with quetiapine. Numbers of inquiries increased almost linearly from 18 (2003) to 133 (2009). Reported doses ranged from 100 to 30,000 mg. On initial contact 420 patients were already in an ER with 369 of them having signs of intoxication. In 434 cases inpatient treatment was advised. Severity of intoxications was estimated as PSS3 in 88 patients and PSS2 in 106 patients. Mean serum concentration of quetiapine from 93 patients was 3.914 mg/L (608–11,814 mg/L), thus exceeding the upper therapeutic level (350 mg/L) more than tenfold. Elimination half-life calculated from consecutive quantification was 10.4 h ± 5.49 h with maximum values at 23.7 hrs indicating a significant delay in elimination of quetiapine compared to population kinetics. Conclusion: Intoxications occurred more often with quetiapine than with any other atypical neuroleptic. A majority of patients had moderate to severe symptoms requiring inpatient treatment. There is a significant risk of prolonged symptoms due to aberrant elimination kinetics. References: 1. Hunsfeld NG, Westerman EM, Bossuyk DJ, et al. Quetiapine in overdosage: a clinical and pharmacokinetic analysis of 14 cases. Ther Drug Monit 2006; 28:185–9.

301. Acute Trimipramine Poisoning: Analysis of Clinical Features and Factors Influencing Severity

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Objectives: Trimipramine is a widely used tricyclic antidepressant and intoxications with this drug are frequently observed. The aim of the present study was to analyse the clinical features of trimipramine poisoning, and to identify a minimum toxic dose and the dose bearing a 50% risk of developing a moderate, severe or fatal outcome. We also investigated the influence of ingested dose, age, gender and weight, and the effect of decontamination measures on the severity of poisoning.

Methods: In a retrospective case study of all acute human trimipramine monointoxications involving adults and reported by physicians to the Swiss Toxicological Information Centre between January 1992 and December 2009. Results: There were 170 (73.9%) females and 56 (24.3%) males; the mean age was 35.5 years (range 16–77). Fifteen (6.5%) patients remained asymptomatic, 137 (59.6%) showed mild symptoms, 54 (23.5%) moderate and 21 (9.1%) severe symptoms (Poisoning Severity Score). In 104 (46%) the patient survived with the outcome was fatal due to refractory cardiovascular collapse, 93% of the cases were suicide attempts or completed suicides. The most common symptoms were central nervous system depression (79.2%), tachycardia (19%), QTc prolongation (13.9%), agitation (12.2%), and dysarthria (10.9%). We found a significant correlation between ingested trimipramine dose and severity of poisoning (p < 0.001). The median dose for moderate symptoms was 250 mg (median dose 1.2 g) and 850 mg for severe symptoms (median dose 2.7 g). The dose for a 50% risk of developing a moderate, severe or fatal outcome was 5.16 g. In 38 (16.5%) patients early gastrointestinal decontamination was performed. Overall, these patients ingested higher trimipramine doses than the late- or not-decontaminated patients (not significant, p = 0.228). The median doses were also higher in the decontaminated group within all severity-categories except in the fatal cases. We found no significant correlation between age, gender and weight, and the severity of poisoning. Conclusion: Trimipramine poisonings mainly occurred as a consequence of suicide attempts in young female patients. Moderate trimipramine intoxications can occur after ingestion of doses in the high range. Poisoned patients have to be monitored for central nervous system depression, dysrhythmias, and QTc prolongation. Early decontamination might be beneficial.

302. Acute Quetiapine Overdose in Adults - Experience in Sweden

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Objective: Quetiapine was introduced on the Swedish market in 2003 for treatment of schizophrenia and bipolar disorder. The prescription rate of quetiapine has increased and an increase in the number of inquiries related to overdose has been observed. In order to assess the acute toxicity of quetiapine, a retrospective survey of hospital case records received by the Swedish Poisons Information Centre (Swedish PC) was carried out. Case series: Since the introduction the Swedish PC has received 493 calls concerning quetiapine overdose in adults and adolescents. During this period 40 cases of pure quetiapine poisoning were available to be analysed in detail by studying hospital case records. In these cases there were 13 to 90 mg quetiapine per dose and 12 males. The ingested dose ranged from 400 mg to 33 g...
(average 6.2 g, median 3.1 g). The reasons for over- dosing were self destructive behaviour/suicidal attempt (33/40), therapeutic error (2/40) and unknown (5/40). The severity of poisoning was graded according to the Poisening Severity Score (PSS) (0–5). Three patients were asymptomatic (PSS 0), 24 patients developed mild symptoms (PSS 1), 10 patients developed moderate symptoms (PSS 2) and 2 patients developed severe symptoms (PSS 3). The severity of poisoning tended to be mild to moderate CNS-depression (29/40), tachycardia (20/40), hypotension (7/40), agitation (5/40), prolonged QTc interval (4/40). Other symptoms seen in a few cases were: seizures, dry mouth, palsied gag reflex, coma and miosis. At doses below 3.6 g most patients had mild symptoms. Treatment with gastric lavage and/or activated charcoal was performed in 16/40 cases. Of these, 3 had a previous gastric bypass. An 84-year-old female was referred to an orthopaedic centre from April 1, 2006–June 30, 2009. Inclusion criteria were: single unintentional ingestion where a mg/kg dose could be calculated (some calculations based on average weight for age) and where medical outcome and the highest level of care was documented.

Conclusion: In this series most cases of quetiapine poisoning were benign. In general, doses below 3.6 g produced minor symptoms. Patients taking a large overdose of slow release quetiapine can be asymptomatic up to six hours after ingestion and then progressively develop severe symptoms.

303. Pediatric Venlafaxine Exposures: Should Current Guidelines Be Re-evaluated? Mink M1, Vicas BM1
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Objective: There is a paucity of literature about pediatric venlafaxine exposures. While current resources suggest that pediatric ingestions of <5.5 mg/kg can be managed at home, these are based on a small (n = 14) sample. We sought to characterize which pediatric venlafaxine exposures reported to a Poison Centre could potentially be managed conservatively. Methods: Retrospective chart review of pediatric (ages 0–17 years) venlafaxine exposures reported to our Poison Centre (1996–2006). All cases were retrospectively reviewed for a single unintentional ingestion where a mg/kg dose could be calculated (some calculations based on average weight for age) and where medical outcome and the highest level of care was documented.

Results: 92/188 cases of pediatric venlafaxine ingestion met inclusion criteria. Ages ranged from 7 months to 17 years. The amounts ingested ranged from 17–150 mg or 1.3–15 mg/kg. Table 1 depicts medical outcomes and highest level of care by dose range ingested. Minor effects included nausea, vomiting, mydriasis, diaphoresis, drowsiness. Major effects included agitation, ataxia, tachycardia, hypertension, tremors, confusion, auditory hallucinations. Major effects were observed only in children ingesting >11 mg/kg. All were asymptomatic within 6–10 hours post exposure. The high number of Emergency Department (ED) visits in the 5.5–11 mg/kg dose range likely reflects existing recommendation. Conclusion: Children ingesting <11 mg/kg as a single unintentional ingestion seem less likely to develop significant symptoms and may be candidates for home observation. Further prospective validation is indicated.

304. Hemodialysis for Carbamazepine Removal Brusin KM1, Mair J1, Nettova OV2, Kochmahshev VF3, Sentsov VG1
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Objective: Severe carbamazepine intoxication with plasma level exceeding 40 micrograms/mL, is often associated with coma, seizures, brain edema and shock. Digestive tract decontamination and charcoal hemoperfusion (HP) do not always decrease plasma carbamazepine concentrations significantly. A few cases of successful hemodialysis (HD) usage were published in the last decade. Methods: Six-hour HD was performed in 20 cases with blood flow rate 200 mL/min and dialysate flow rate 500 mL/min. In 8 other cases HP was followed by HD. The plasma carbamazepine concentration was measured by fluoroscent polarizing immunooassay (TDx-FLX Abbot Laboratories, USA). Results: All patients were comatose on admission and 17 were ventilated. Mean plasma concentration was 38.4 micrograms/mL in the group treated with HD and 39.5 in the group treated with HP and HD. Level of consciousness evaluated by GCS on admission was 5.2 and 4.9 respectively. The time from admission to start of extracorporeal detoxification was 4.9 hours in the HD group and 6.4 hours in the HP-HD group. Carbamazepine was 59.8 ± 3.9 micrograms/mL on average and remained stable during 6 hours of the procedure. Concentration of carbamazepine decreased on average from 28.2 ± 2.1 to 20.6 ± 2.4 micrograms/mL (p < 0.001). Concentration of carbamazepine in outflow dialysis fluid was from 2.1 to 3.2 micrograms/mL, and decreased towards the end of the procedure. The total amount of carbamazepine which was removed was 600 mg on average, with the range of 533–714 mg. The apparent elimination half-life was 19.2 hours from the admission to the beginning of HD, 11.7 hours during HD and 43.9 hours during the observation time after HD. Conclusion: Hemodialysis seems to be an effective method for carbamazepine removal. References: 1. Chetty M, Mair J, Park P, Aggarwal S. Successful carbamazepine poisoning treatment with haemodialysis. Nephrol Dial Transplant 2003; 18:220–1. 2. Tapolayi M, Campbell M, Dailey K, et al. Hemodialysis is as effective as hemoperfusion for drug removal in carbamazepine poisoning. Nephron 2002; 90:213–5.

305. Successful Lipid Emulsion Treatment for Generalized Seizures and Cardiac Arrest Following Epidural Lidocaine Administration Grenc D1, Scar L1, Knafelj R2, Vengus R2
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Objective: We describe a case of tonic-clonic seizures and cardiac arrest after epidural administration of lidocaine. The patient was successfully treated with intravenous lipid emulsion. Discussion: This was the absence of toxic lidocaine level in serum. Case report: An 84-year old female was referred to an orthopaedic outpatient clinic for treatment of chronic lower back pain. Lidocaine 20 mg together with triamcinolone 80 mg was administered epidurally. Approximately two minutes after the administration, generalized tonic-clonic seizures occurred. After 5 minutes, she developed respiratory and cardiac arrest and cardiopulmonary resuscitation (CPR) was initiated by the attending physician. Upon the arrival of the resuscitation team, a further 14 minutes later, she developed bradycardia that quickly progressed to asystole. ACLS was performed, patient required intubation, and received adrenaline 2 mg I.V. and atropine 3 mg I.V. A bolus of intravenous lipemulsion (100 mL, i.e. 1.5 mL/kg) was given. Seven minutes after CPR initiation return of spontaneous circulation was established. ECG showed sinus rhythm, rate 77/min, and QRS complex was normal. Holter monitoring showed sinus rhythm with RBBB, with episodes of non-sustained atrial tachycardia and no ventricular ectopic activity. She was discharged 48 hours after the event without sequelae. Conclusion: Our case supports the clinical efficacy of lipid emulsion infusion in local anesthetic toxicity. A matter of interest, which perhaps could help to better understanding of the mechanism of lipid rescue, is the fact that we could not confirm a lidocaine serum concentration which reached toxic levels, thus strengthening the "lipid sink" concept.

306. Accidental Tiotropium Overdose in a Child: A Case Report Chincholkar VM1, James DA2, Cooper G2, Thomas SHL3
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Objective: Tiotropium is a long-acting anticholinergic agent increasingly used via inhalation in the management of chronic obstructive pulmonary disease. Toxicity following oral ingestion of capsules intended for inhalation was not previously been reported, and has been considered unlikely unless large amounts have been ingested because of low oral bioavailability. We describe a case of an accidental oral overdose of tiotropium in a paediatric patient resulting in an anticholinergic toxidrome. Case report: The National Poisons Information Service (NPS) was contacted about a 2 year old female patient following accidental ingestion of 8 capsules (144 micrograms) of tiotropium (Spiriva®) who had presented with features of anticholinergic toxicity including dry mouth, dilated pupils, tachycardia (133 beats/minute) and localised flushing of the cheek. Conservative management was advised with observation for at least 6 hours post-exposure or until asymptomatic. The patient was discharged after observation for six hours hours with no symptoms, except flushing, had resolved. The flushing was clinically deemed to be unrelated to the ingestion. A literature search did not reveal any reports of oral toxicity with tiotropium alone in any age group. Anticholinergic toxicity due to accidental inhalation has been reported with a dose of 90 micrograms in a 74 year old, who developed tachycardia, urinary retention and dry mouth. Over 5 years the NPS Information Service has received enquiries about 21 episodes of accidental oral ingestion in paediatric patients (0–10 years). The majority were asymptomatic, in spite of ingesting high doses. Six patients (0–10 years) ingested 216 micrograms with no symptoms reported at 6 hours. A one year old referred to hospital was asymptomatic.

307. Pulmonary Hemorrhage in Quinine Toxicity
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Objective: While non-cardiogenic pulmonary edema and acute respiratory distress syndrome are known complications of malaria, the possibility of quinine toxicity causing respiratory failure must be considered. We report two cases of quinine toxicity that resulted in alveolar hemorrhage. Case series: Case 1: A 50 year old female with a history of depression and alcoholism presented complaining of vision loss, dizziness, and tinnitus after taking 9100 mg of quinine as a suicide attempt. On examination, her vital signs were normal except a blood pressure of 147/90. She had decreased hearing; her pupils were 7 mm bilaterally and nonreactive, and visual acuity examination revealed only light perception. The remainder of her physical exam was unremarkable. Her EKG was notable for a QRS interval of 120 ms and ST depressions in multiple leads. She received charcoal, sodium bicarbonate, and nimodipine and showed improved vision and hearing. However, 2 days after admission, the patient suddenly developed respiratory failure requiring intubation. Chest x-ray showed bilateral infiltrates, and bronchoscopy revealed alveolar hemorrhage. Case 2: A 35 year old previously healthy female was transferred to our hospital while being treated with quinine for falciparum malaria that was discovered on blood smear. She was transferred due to worsening thrombocytopenia and anemia. At our institution, she was febrile to 39.3 degrees and tachycardic at 122 BPM. Her EKG showed a QTc of 510 ms. Her hemoglobin dropped to 7 g/dL, and her mental status declined, requiring intubation. Her quinine was replaced with a quinidine infusion. She received exchange transfusion and improved after her parasitemia was <1%. However, she failed extubation multiple times with hemoglobin subsequently falling to 5 g/dL. Chest x-ray indicated diffuse alveolar hemorrhage, confirmed with bronchoscopy. Discussion: Quinine is used as an antimalarial agent, but toxicity is manifested by cinchonism, dysrhythmia and hematologic disturbances. We propose that quinine toxicity may be unrecognized as a cause of respiratory failure from alveolar hemorrhage because it is used to treat malaria, a disease with its own pulmonary complications. Conclusion: Quinine toxicity may be an unrecognized cause of acute respiratory failure from alveolar hemorrhage.