already an alerting system for pesticides as part of a project to improve the reporting of pesticide related incidents. A pilot project has been carried out for some chemicals, particularly those that might be used in terrorist attacks. Web based TOXBASE training is already available and a toxicology module is being added. *Conclusions:* On-line poisons information can reduce the need for telephone enquiries. Maintenance of a large poisons database requires intensive effort to keep it current. Usage rates indicate high user satisfaction. 1. National Poisons Information Service Annual report 2006–7 http://www.hpa.org.uk/publications/PublicationDisplay.asp?PublicationID=103 2. Bateman DN, Good AM, Kelly CA, Laing WJ. Delivery of poisons information to health professionals: telephone or internet? The Scottish experience. *J Toxicol Clin Toxicol* 2002; **40**: 567–9. 3. Bateman DN, Good AM. Five years of poisons information on the internet: the UK experience of TOXBASE. *Emerg Med J* 2006; **23**: 614–7.

120. Propagation of Evidence: Wikitox, Internet Based Opensource Curriculum in Clinical Toxicology

Dawson A. *South Asian Clinical Toxicology Research Collaboration, University of Peradeniya, Sri Lanka.*

Background: Evidenced based clinical practice of toxicology has been hampered by the boutique nature of the speciality and consequent lack of general advocacy. Propagation of expert opinion with well constructed position statements generally published in difficult to access journals are poorly cited. Even if incorporated into policy such guidelines often fail to alter clinical practices especially in the developing world. We sought to assess a novel approach to propagate existing information. *Methods:* In August 2006 we initiated an opensource toxicology curriculum project (www.wikitox.org). The basic principle is that clinicians could use the site as a repository to donate existing or new teaching material (such as Powerpoint presentations) which can be used by other clinicians. The site is open to all and can be edited easily online by any registered user. Contributors are encouraged to use material already created, examples include EAPCCT lectures. This material is supported by monographs. The purpose of the wiki is to provide a free resource for selfstudy and teachers. This source can be utilised online or offline. An offline version is distributed by widernet.org to Africa. The content is also being used to support a Masters distance learning course. *Results:* The wiki was examined for the number and type of contributions. Despite an inital core group of 20 people 95% of the contributions came from 3 people. Another 8 people donated extensive material indirectly through a project officer but without any direct editing of the wiki site. 469 pages were created and 258 files with teaching material uploaded. Topic areas of pharmaceutical and agrochemical poisoning were most extensively covered. Usage had increased dramatically from June 2007 with a large increase in visitors from 5 per day to over 75 per day from more than 109 countries. 13.8% of pages viewed were for educational resources, the remainder were for toxicology monographs. *Conclusion:* Clinical toxicology's underdeveloped evidence base is one of the most compelling reasons for toxicologists to promote and facilitate education. A wiki has the potential to provide teaching tools at low cost but requires expanded involvement.

121. Norwegian Poisons Information Centre - Information Distributed Through the Norwegian Electronic Health Library

Sørlid HK, Ziesler TA, Andrew E. *Norwegian Poisons Information Centre, Directorate for Health and Social Affairs, Oslo, Norway.*

Objective: To introduce the Norwegian Electronic Health Library (NEHL) web site as the distribution channel for information from the Norwegian Poisons Information Centre (NPIC) to health care professionals, as a topic library on toxicology. Contents of the topic library and synergism by choosing NEHL for the publishing are pointed out. *Methods:* NPIC wanted to establish an electronic information channel towards health care professionals. NEHL was chosen mainly because it was assumed to reach the main target group. In addition it had suitable content and planned content and established technical solutions. In 2006 collaboration with NEHL through planning and development of the topic library on toxicology started. *Results:* NEHL's vision is to improve health care quality by providing free access for health personnel to useful and reliable knowledge. The NEHL web site was launched in June 2006. It is owned by the Directorate for Health and Social Affairs and the Regional Health Authorities and hosted by the Norwegian Knowledge Centre for the Health Services. NPIC is organized as a department within the Directorate for Health and Social Affairs. The topic library on toxicology was launched in 2007 and mainly consists of treatment guidelines for acute intoxications. Earlier this information was distributed as written documents, and on need faxed or e-mailed to treating physicians. The topic library guidelines include more than 100 different toxic agents/groups of agents, as well as general information on antidotes and methods for elimination. In addition, the topic library includes actualities on toxicology, relevant literature and journals extracted from the resources provided by NEHL. Examples of resources (free): Evidence based reviews, national and local guidelines, patient information, > 1500 medical journals (BMJ, JAMA, Annals of Internal Medicine, The New England Journal of Medicine, The Lancet etc.), bibliographic databases, PubMed, Clinical Evidence, Cochrane Library, EMBASE, MEDLINE, CINAHL, links to open access resources and important national medical resources. *Conclusion:* NEHL is increasingly used by health care professionals. Gains for NPIC: updated information always available, quality assessed information/guidelines, free resources, several other topic libraries available or in progress: mental health, public health, pharmaceuticals, cancer. *Reference:* www.helsebiblioteket.no (the NEHL web page).

122. On-Line Poison Information in the United States

Bronstein AC. *American Association of Poison Control Centers, Washington DC; Rocky Mountain Poison Center, University of Colorado Health Sciences Center, Denver, US.*

Background: The first United States poison center (PC) opened in Chicago, IL in 1953. A standardized poison information system for PCs did not exist. In 1974, Micromedex (Thomson Healthcare, Denver, CO, USA) launched Poisindex® a microfiche based system for poison centers. The system consists of continuously updated pharmaceutical and non-pharmaceutical product index and medical toxicological managements targeted to the active product ingredients. Now CD-ROM and internet based, all 61 US PCs use this system which interfaces directly with their local computer data entry software and provides a common upload to the US National Poison Data System (NPDS). Uploads of cases from poison centers occur continuously and allow for near real-time surveillance with alerts sent to a 24 hour monitoring team. Because of the detailed coding, data can also be examined for any combination of time period, location, region, or product. The AAPCC database (NPDS) documents over 2.4 million exposures and over 1.5 million information calls annually as published in the AAPCC Annual Report. *Objective:* Characterize the features of the US on-line poison information system. *Methods:* PCs respond daily to a variety of questions from the public and health care professionals. Poisindex® lists over 350,000 pharmaceutical and non-pharmaceutical products. All are identified by a unique product identification number and are categorized into one of 922 American Association of Poison Control Centers (AAPCC) generic codes. Product information is obtained directly from the manufacturers using either the Material Safety Data Sheet (MSDS) in the case of non-pharmaceutical products or the Package Insert (PI) for drugs. Product information includes: active ingredients, excipients, form, packaging, company contact information and in some cases inert ingredients. Product information also includes US EPA regulatory numbers, NDC codes, and Chemical Abstract Service (CAS) numbers. This data allows for the precise linking of one or more clinical toxicology managements to each product. Toxicology managements are written by in-house medical and clinical toxicologists with review by external toxicologists. This process insures accurate up-to date information. With the advent of the personal computer, the data system was transitioned to a CD-ROM format. In the last several years, the system has transitioned to the internet. This allows for weekly system updates. Managements and products can be entered weekly and provides the infrastructure for new or products associated with public health events to be added in a day. *Discussion:* Paramount to the provision of accurate management of PC calls is the correct identification of the products involved in the exposures. Poisindex® allows for near real-time product and toxicological treatment information entry. Future possible enhancements include: user independent notification of products not in the system, automated product information feeds to permit the system to have all licensed pesticides and updates as soon as they are released, and date time stamping of information access, and enhanced auto-population of PC case records. The products database also provides the foundation to aid global harmonization for diverse regulatory codes and reporting as it contains a wide variety of identifiers and synonyms. Since this product and management information is available electronically to PCs, centers can assist industry and regulatory agencies in post marketing surveillance; work in collaboration for new product launches, and assist with events of public health significance. Rapid trending and identification of unexpected outcomes of exposures to new or existing products helps minimize risk and liability and improve the public health. *Conclusion:* Data collection and product surveillance are core competencies of PCs. NPDS, operated by the AAPCC allows US PCs to have rapid access to exposure management and product data. Through this system, Poisindex® can work with manufacturers to provide accurate, timely product information that also permits companies to support their product stewardship functions. The Poisindex® - poison center relationship is a unique example of a public private partnership that works.

123. Sleeping Beauty Disease – An Outbreak of a Neurological Illness of Unknown Aetiology in Luanda Province, Angola

Zilker T,[1] Gutschmid K,[2] Häfliger P.[2] *[1]Department of Clinical Toxicology, II Med Clinic MRI Technical University, Munich, Germany; [2]WHO, IPCS, Geneva, Switzerland.*

Case series: A crisis intervention team from WHO was called in by the Angolan Ministry of Health due to an outbreak of an acute neurological disease. Symptoms reported included drowsiness, weakness, ataxia and coma. Most of the patients were directed to the hospital of Cacuaco. Patients who had improved a little were sent home again. Food supply was brought from home to the hospital. Blood, urine and food samples were taken and send to Munich and London. Between October 18th and November 15th, 371 patients were admitted to Cacuaco hospital between 5 and 25 per day. The clinical examination in 30 patients showed the following: central nervous system depression with a GCS ranging from 7–14 points. Mostly children were severely affected, they woke up to painful stimuli but fell back asleep. Muscle tone was extremely weak. There were no signs of peripheral neuropathy. When patients had woken up they hardly could prop themselves up. They could not walk alone. They could not stand or hop on one leg. Blood pressure and heart rate were normal. Respiration rate was slightly decreased. It was impossible to spot the food responsible by cluster evaluation. It became clear that the symptoms observed fitted best with the uptake of an unknown GABA-ercig sedative. Drowsiness, ataxia, fatigue, hypotonic musculature, duration of coma seemed to be more pronounced than seen in benzodiazepine or GHB poisoning. Urine samples which were send to Munich didn't show any organic compounds in GC-MS. In four of the five blood samples bromide levels between 1002 mg/l and 2451 mg/l (normal – 50 mg/l) were measured. In 5 other samples similar results were affirmed by a second laboratory. Salt samples consisted of sodium bromide. *Conclusion:* A so far unknown mass poisoning is described. Modern analytical measurements failed to detect the origin. Clinical observation helped to make the right diagnosis of a disease that reminded us of the fairy tale of the sleeping beauty.

124. Bromo-Dragonfly, a Life Threatening Designer Drug

Personne M, Hultén P. *Swedish Poisons Information Centre (SPIC), Stockholm, Sweden.*

Objective: The hallucinogenic drug Bromo-Dragonfly (BDF) is an amphetamine derivative first synthesized in the late 1990s. We report pronounced and previously unknown severe vasoconstrictor effects of this new dangerous drug of abuse. *Case 1:* A 20-year-old male drug addict ingested 5–6 blotters soaked with 0.5 mg BDF each. Initial hallucinogenic effects were experienced but two days later cyanosis of peripheral parts of the limbs ensued. Six days after using the drug he sought medical care presenting cyanotic, pulseless and aching extremities. Laboratory signs of rhabdomyolysis were recorded. Initial treatment with nifedipine had some beneficial effects but nitroglycerine was also needed to prevent tissue necrosis. The treatment could be terminated after another four days and the patient was discharged without sequelae. *Case 2:* A 34-year-old man bought BDF via the Internet and tested an undetermined dose together with a friend. Shortly afterwards both collapsed and the friend died instantly. After 17 hours the dazed survivor was found by his brother. At hospital the patient displayed severely impaired peripheral circulation and acute renal failure. No method of vasodilatation therapy, including nifedipine, captopril and sympathetic blockade with guanethidine, was particularly effective. Neither was infusion of nitroglycerine, nitroprusside and iloprost. After nine days the spasm abated but the patient lost several distal phalanges of his fingers. The presence of BDF in

the urine was confirmed. *Discussion:* At least one more person in Sweden and one in Norway have been found dead after using BDF. Laboratory analyses established the presence of BDF in both of these cases. This psychoactive substance which has exceptionally strong 5-HT2A agonistic properties is a hallucinogen with structural similarities to other phenethylamine derivatives. It apparently exercises a potent long lasting vasoconstrictor capacity, which possibly also affects the coronary arteries, hypothetically explaining the sudden deaths. The first Swedish reports of its use came during 2006, and up to October 2007 SPIC has been contacted regarding 22 different cases. In most patients symptoms such as anxiety, agitation, visual hallucinations, tachycardia and mydriasis dominated. *Conclusion:* BDF is a new extremely hazardous drug of abuse that can cause severe vasoconstriction leading to tissue necrosis or even sudden death.

125. Withdrawn

126. Causality Assessment in Poisoning: An Essential Part of Data Quality

Kupferschmidt H. *Swiss Toxicological Information Centre (STIC), Zurich, Switzerland.*

As long as prospective randomized and controlled trials are not available for many aspects in clinical toxicology, Poisons Centre data remain an important and sometimes unique source of information on human poisoning, particularly with rare toxins. It is therefore an obligation of clinical toxicologists in Poisons Centres to collect data on such cases accurately, carefully, and as completely as possible. Data must be accurate if they are reported, published or used in epidemiology (e.g. to estimate the prior probability in the Bayesian approach of the diagnostic process (1)). As in the assessment of adverse drug reactions (ADR), the establishment of a causal relationship between exposure and clinical effects is crucial also in poisoning. The accuracy of the information on exposure and on clinical symptoms/findings must be known in order to be able to evaluate the case data appropriately. In Poisons Centres most clinical information is not at first hand because it is collected via the telephone. Moreover, exposure information is invariably taken from the patient history and therefore never proven. When using human data from Poisons Centres for risk assessment in acute toxicity, for toxicovigilance, and for data exchange, a quantitative measure of the accuracy of the data enhances data quality considerably. The situation is similar to the spontaneous reporting of adverse drug reactions in pharmacovigilance. Guidelines and rules for the evaluation of ADR have been set up in the 1970s and 1980s (2–6). Bayesian-based and algorithm-based systems are used. Criteria for the causality assessment in algorithm-based systems are chronology (temporality), symptomatology, contributing factors and differential diagnoses (exclusivity), and the consequences of dechallenge-rechallenge. Most of these systems are highly specific but have a relatively low sensitivity. The concordance between such systems is generally poor (7), and the inter-rater variability is high if no guidelines are applied. To increase reproducibility of these processes they have to follow a harmonized and standardized protocol (8) which decreases ambiguity of the data, facilitates data exchange, and prevents erroneous conclusions by following, at least in part, the viewpoints on causation by A.B. Hill (9). The assessment of causality in acute poisoning may be similar but not identical to that in ADR. There are important differences in the clinical setting between poisoning and ADR: Rechallenge is ethically not feasible. In addition, the setting of asymptomatic exposure does not exist in ADR but is frequent in toxic exposure, and, other than in the assessment of poisoning, it is always assumed in ADR that exposure has taken place. And finally the history of exposure is more difficult to obtain in poisoning than in ADR due to frequently altered mental status. Therefore, if a system similar to that in ADR reporting should be used, modifications are needed. Here, a dual system is proposed consisting of an assessment of the likelihood of exposure, and a causality assessment (causal relationship between exposure and clinical effect). Likelihood of exposure can be graded into four levels: 1) confirmed exposure with analytical detection of a substance in body fluids or tissue, 2) likely exposure with reliable observation of exposure by bystanders, 3) reliable history taken from the patient, 4) possible exposure with indirect evidence of exposure, 5) unlikely exposure with no evidence of exposure, and 6) the exclusion of exposure by a negative analytical test. Causality can be graded into three levels: 1) likely (probable) causality with symptoms occurring in a timely fashion after exposure according to the pharmacokinetic properties of the substance in question and the underlying mechanism of action, typical (expected/described) symptoms, and no other cause or explanation for the occurrence of the symptoms; 2) possible causality with symptoms occurring in a timely fashion after the exposure, with untypical symptoms but no other cause or explanation for the occurrence of the symptom, or with typical symptoms but other possible causes; and 3) unlikely causality with symptoms not occurring in a timely fashion after the exposure and/or symptoms not typical and with the presence of other causes or explanations for the occurrence of the symptoms. In asymptomatic patients and in cases with unusual symptoms, the likelihood of exposure is particularly important, whereas causality has higher priority in symptomatic cases. Only cases with a high likelihood of exposure and with high causality should be included in reports (10). The number of cases with poor causality may be significant (e.g. 12.5% in the STIC in 2006). However, the scientific value of these causality scoring systems is limited because they are difficult to validate (11). The assessment of exposure and causality can be performed by the Poisons Centre staff at any time during the course of poisoning. The result of this assessment can change with time depending on the information available. A final assessment can be done only after the course of illness is terminated and the maximum of information is available; routine follow-up is required to capture all symptoms including delayed effects. *References:* 1. Buckley NA, *et al. J Toxicol Clin Toxicol* 2002; **40**: 213–22. 2. Karch FE, Lasagna L. *Clin Pharmacol Ther* 1977; **21**: 247–54. 3. Begaud B, *et al. Thérapie* 1985; **40**: 111–8. 4. Moore N, *et al.* Lancet 1985; ii: 1056–8. 5. Jones JK. *Clin Pharm* 1982; **1**: 554–5. 6. Naranjo CA, *et al*. Clin Pharmacol Ther 1981; **30**: 239–45. 7. Benahmed S, *et al*. *Eur J Clin Pharmacol* 2005; **61**: 537–41. 8. Arimone Y, *et al*. *Eur J Clin Pharmacol* 2005; **61**: 169–73. 9. Hill AB. *Proc Roy Soc Med* 1965; **58**: 295–300. 10. Kelly WN, *et al.* Drug Saf 2007; **30**: 367–73. 11. Meyboom RHB, *et al. Drug Saf* 1997; **17**: 374–89.

127. The Effect of Single Dose Activated Charcoal on Drug Absorption During the First 6 Hours After Drug Ingestion - A Metaanalysis

Jürgens G,[1] Graudal NA.[2] *[1]Poison Information Centre, Bispebjerg Hospital; [2]Department of Rheumatology, Copenhagen University Hospital, Copenhagen, Denmark.*

Objective: To estimate the effect of activated charcoal (AC) on drug absorption during the first 6 hours after drug intake and evaluate the influence of physical and pharmacological drug properties and charcoal/drug-ratio. *Methods:* 43 placebo-controlled studies (111 comparisons, 39 drugs, 1527 healthy volunteers) were included. The percentage reduction of drug absorption of AC treated volunteers compared with placebo treated volunteers was calculated at 5, 30, 60, 120, 180 and 360 minutes after drug ingestion. The influence of pKa, molecular weight (MW), volume of distribution (Vd) and charcoal/drug-ratio was analysed using a Spearmann-correlation. *Results:* The effect of AC was significant during the first six hours after drug ingestion (Table). The percentage reduction of drug absorption was correlated with the charcoal/drug-ratio ($R = 0.68$, $p < 0.0001$). A correlation was also demonstrated for MW ($R = 0.54$, $p = 0.0001$) and Vd ($R = 0.43$, $p = 0.0002$). *Conclusion:* AC is most effective when given immediately after drug ingestion. However, 25% of the participants achieved at least a 30% reduction of drug absorption up to 6 hours after drug intake, especially when AC was given with large charcoal/drug-ratio. AC appears to be most effective in drugs with large MW and Vd, where other treatment options, including dialysis, are limited and should be considered in poisoned patients, even when presented late to medical care. *Reference:* Position paper: single-dose activated charcoal. *Clin Toxicol* 2005; **43**: 61–87.

128. A Randomised Controlled Trial of Multiple Dose Activated Charcoal in Acute Self-Poisoning

Eddleston M,[1] Juszczak E,[2] Buckley NA,[3] Senarathna L,[4] Mohamed F,[4] Dissanayake W,[5] Hittarage A,[5] Azher S,[6] Jeganathan K,[5] Jayamanne S,[6] Sheriff MHR,[4] Warrell DA.[7] *[1]NPIS Edinburgh, Scottish Poisons Information Bureau, Royal Infirmary, Edinburgh, UK; [2]Centre for Statistics in Medicine, Oxford, UK; [3]Department of Clinical Pharmacology and Toxicology, Australian National University, Canberra, Australia; [4]Department of Clinical Medicine, Colombo University, Colombo, Sri Lanka; [5]Anuradhapura General Hospital, Anuradhapura, Sri Lanka; [6]Polonnaruwa General Hospital, Polonnaruwa, Sri Lanka; [7]Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK.*

Objective: The case-fatality for intentional self-poisoning in the rural developing world is 10–50 fold higher than industrialised countries, due mostly to the use of highly toxic pesticides and plants. We aimed to determine whether routine therapy with multiple dose activated charcoal to interrupt enterovascular or enterohepatic circulations offers benefit, compared to no charcoal, in such an environment. The RCT was registered as ISRCTN02920054. *Methods:* We conducted an open-label parallel group randomised controlled trial of six 50 g doses at four hourly intervals vs no charcoal vs a single 50 g dose of activated charcoal in three Sri Lankan hospitals. Mortality was the primary outcome. *Results:* 4632 patients were randomised to receive no charcoal (1554), a single dose of charcoal (1545), or six doses of charcoal (1533); outcomes were available for 4629. 2338 (50.5%) had ingested pesticides whilst 1647 (35.6%) had ingested yellow oleander seeds. Mortality did not differ significantly between the groups. 97 of 1531 (6.3%) participants in the multiple dose group died, compared with 105 of 1554 (6.8%) in the no charcoal group (adjusted odds ratio [OR] 0.96, 95% confidence interval [CI] 0.70–1.33). 439 patients were admitted within two hours of poison ingestion and allocated to either MDAC (n=214) or SDAC (n=225). Comparing these 439 patients with 225 who were admitted within two hours of poison ingestion and allocated to no charcoal, there was no evidence of benefit on deaths of early charcoal administration (34/439 vs 15/225; OR 1.18 [exact 95% CI 0.61–2.38]; test of interaction P=0.5). In addition, there was no evidence of an interaction between early charcoal administration and any of the secondary outcomes. No significant differences were noted for patients who took particular poisons, or were more severely ill on admission. *Conclusion:* We found no benefit from routine administration of multiple dose activated charcoal, nor from early administration of charcoal, for patients poisoned by plants or pesticides in resource-poor rural developing world district hospitals. We cannot recommend the routine use of activated charcoal in rural Asia-Pacific; while further studies of early charcoal administration may be useful, effective affordable treatments are urgently required.

Table: The effect of AC at 5–360 mins after drug ingestion

Time to AC after drug intake	Reduction of drug absorption (%)						
	5 min	30 min	60 min	120 min	180 min	240 min	360 min
Median	89	54	30	23	25	27	15
25–75% percentile	64–97	40–64	25–59	12–33	11–40	21–32	9–32
Studies	62	5	18	8	4	4	3
Participants	767	56	266	145	74	71	40
Test for overall effect: Z	23.50	3.87	8.88	4.46	3.69	3.42	1.99
p	<0.00001	0.0001	<0.00001	<0.00001	0.0002	0.0006	0.05