Hybrid Webinar

2022

INTERNATIONAL SYMPOSIUM FOR POISON CONTROL AND RESEARCH DEVELOPMENT

Novel Aspects in Clinical Toxicology

Date

18 Nov. 2022 (Fri)

08:00 - 17:40 (Taipei Time/GMT+8)

19 Nov. 2022 (Sat)

08:00 - 17:30 (Taipei Time/GMT+8)

Venue

Taipei Veterans General Hospital

指導單位：衛生福利部

主辦單位：臺北榮民總醫院臨床毒藥物諮詢中心

臺北榮民總醫院內科部臨床毒物與職業醫學科

財團法人毒藥物防治發展基金會

TWPCC

2022 International Symposium for Poison Control and Research Development

Novel Aspects in Clinical Toxicology

- **Venue**：**Taipei Veterans General Hospital**
- **Date**：**2022/11/18 08:00-17:40 (Taipei Time/GMT+8)**
  2022/11/19 08:00-17:30 (Taipei Time/GMT+8)

Hybrid Webinar

Friday, November 18th

08:00 - 08:10	Registration
08:10 - 08:20	Opening Remark
	Moderator: Dr. Jou-Fang Deng (VGHTPE, Taiwan)
08:20 - 09:00	**Acetaminophen intoxication** Dr. Richard C. **Dart** (U.S.A.)
09:00 - 09:35	**The problem solver for urgent important unmet medical needs- hepatotoxicity-free acetaminophen** Yoa-Pu **Hu** (NDMC, Taiwan)
09:35 - 10:05	**Drug abuse** Dr. Richard C. **Dart** (U.S.A.)
10:05 - 10:30	**E-commerce causing unusual poisonings** Dr. Winai **Wananukul** (Thailand)
10:30 - 10:40	Coffee Break
	Moderator: Dr. Kenneth Hartigan-Go (Philippine)
10:40 - 11:05	**Acute arsine poisoning in a cluster of Indian lead-refinery workers: challenges in diagnosis and management** Dr. Ravikar **Ralph** (India)
11:05 - 11:30	**Serial murder using intravenously administered benzalkonium chloride in Japan** Dr. Yoshito **Kamijo** (Japan)
11:30 - 11:55	**Food safety and toxicology in the Philippines: a regulatory challenge** Dr. Kenneth **Hartigan-Go** (Philippine)
11:55 - 12:00	Panel Discussion
12:00 - 13:30	Lunch Break
	Moderator: Dr. Chih-Yu Yang (VGHTPE, Taiwan)
13:30 - 14:10	**Extracorporeal membrane oxygenation (ECMO) to treat acute poisoning** Dr. Bruno **Megarbane** (France)
14:10 - 14:50	**Application of pharmacogenomics to clinical toxicology** Dr. Bruno **Megarbane** (France)
14:50 - 15:00	Coffee Break
	Moderator: Dr. Winai Wananukul (Thailand)
15:00 - 15:40	**Naloxone pharmacokinetic considerations in the treatment of opioid poisoning in a mass casualty incident** Dr. Luke **Yip** (U.S.A.)
15:40 - 17:30	**Chemical incidents** Dr. David **Russell** (UK)
17:30 - 17:40	Panel Discussion
	Closing Remarks

2022 International Symposium for Poison Control and Research Development

Novel Aspects in Clinical Toxicology

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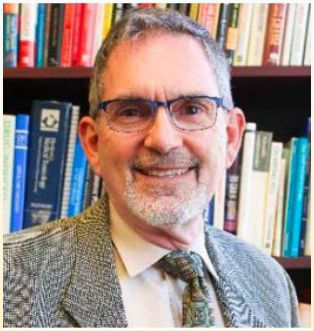
Hybrid Webinar

Saturday, November 19th

08:00 - 08:10	Registration
08:10 - 08:20	Opening Remark
	Moderator: Dr. Chen-Chang Yang (VGHTPE, Taiwan)
08:20 - 08:50	Delayed neuropsychiatric sequela of carbon monoxide poisoning in Taiwan Dr. Chen-Chang **Yang** (VGHTPE, Taiwan)
08:50 - 09:20	Chlorfenapyr Dr. Luke **Yip** (U.S.A.)
09:20 - 09:50	Severe borax poisoning Dr. Hsien-Yi **Chen** (CGMH, Taiwan)
09:50 - 10:20	Cardiac toxicity following the use of cosmetic filler Dr. Uyen Vy **Doan** (Vietnam)
10:20 - 10:30	Coffee Break
	Moderator: Dr. Ahmad Khaldun Ismail (Malaysia)
10:30 - 10:50	Lepidopterism: an interesting clinical-case discussion Dr. Ravikar **Ralph** (India)
10:50 - 11:30	Venomous snake antivenom production Dr. Richard C. **Dart** (U.S.A.)
11:30 - 12:00	The conception of rapid diagnosis for venomous snake bites Dr. Dong-Zong **Hung** (CMUH, Taiwan)
12:00 - 12:10	Panel Discussion
12:10 - 13:30	Lunch Break
	Moderator: Dr. Chih-Chuan Lin (CGMH, Taiwan)
13:30 - 13:55	Uncommon defibrinogenation and coagulopathy caused by Trimeresurus stejnegeri stejnegeri envenomation Dr. Yan-Chiao **Mao** (TCVGH, Taiwan)
13:55 - 14:20	Interesting points of snake envenomation: experience from Thailand Dr. Satariya **Trakulsrichai** (Thailand)
14:20 - 14:45	Clinical presentation and outcome of Naja species injuries consulted to remote envenomation consultancy services Malaysia Dr. Ahmad Khaldun **Ismail** (Malaysia)
14:45 - 15:10	Research on Micropechis ikaheka bites in West Papua Indonesia: limitation of antivenom and special geography in reduction of cases Dr. Tri **Maharani** (Indonesia)
15:10 - 15:20	Coffee Break
	Moderator: Dr. Jou-Fang Deng (VGHTPE, Taiwan)
15:20 - 16:05	Antivenoms: clinical assessment of their effectiveness and safety Dr. David A. **Warrell** (UK)
16:05 - 16:50	Therapeutic innovations in toxinology: the gulf between an idea and its implementation Dr. David A. **Warrell** (UK)
16:50 - 17:20	Interpretation of the blood gas – a simplified approach with a special focus on the metabolic acidosis Dr. Knut Erik **Hovda** (Norway)
17:20 - 17:30	Panel Discussion
	Closing Remarks

Curriculum Vitae



Richard C. Dart

- Citizenship: United States of America
- Affiliation:
  - ✓ **Director**, Rocky Mountain Poison & Drug Center
  - ✓ **Chief**, Medical Toxicology Service, Denver Health Medical Center
- Academic & Administrative responsibilities:
  - ✓ **Professor**, Department of Emergency Medicine, University of Colorado Health Sciences Center
  - ✓ **Chair**, PoisonHelp.org Committee. American Association of Poison Control Centers
  - ✓ **Manuscript Reviewer** for *New England Journal of Medicine*, *Journal of the American Medical Association*, *Annals of Emergency Medicine*, *Toxicon*, *Clinical Toxicology*, etc.

ABSTRACT

Acetaminophen intoxication

Acetaminophen poisoning remains a leading cause of poisoning in many countries. This presentation will address advances in diagnosis and treatment that are available or are expected to be available soon. In addition, the new 2022 National Consensus Guidelines sponsored by US and Canadian toxicology societies will be presented. The latest findings are the discovery of metabolomic markers that predict hepatic adaptation to therapeutic dosing of acetaminophen. Here, a relevant information is briefly attached for your reference.

Background:

Drug induced liver injury (DILI) remains a prominent global issue and acetaminophen (APAP) overdose represents a common cause of hepatic injury and DILI. Transient alanine aminotransferase (ALT) elevations have been documented while adhering to recommended daily dosing. However, no metabolites have been identified in pre-treatment samples predicting which patients will develop these transient increases.

Methods:

This was a secondary analysis of samples collected from a parent study describing the course of ALT levels in subjects receiving therapeutic APAP dosing. Two hundred and four subjects recruited from Denver, Colorado received 4 g APAP/daily for at least 16 days. Subjects were grouped by ALT at any monitored time point above 60 units/L (n = 25) vs. no increase (n = 179). Serum samples from days 0, 7, 16, and 31 were run on ultra-high performance liquid chromatography mass spectrometry. We report the metabolomic results of samples analyzed prior to APAP administration and over time. Significant changes in metabolite and demographic variable expressions were explored using t-tests with false discovery rate correction, chi square, and partial least squares discriminant analyses.

ABSTRACT

Acetaminophen intoxication

Results:

Within pre-treatment day 0 samples, allantoate and ornithine were significantly elevated in subjects of the ALT elevation group ($p = .032$). Baseline ALT ($p = .011$) and alkaline phosphatase ($p = .006$) were also significant. These metabolites were significant independent of race, ethnicity, gender, or BMI.

Conclusions:

Allantoate and ornithine are directly involved in pathways related to nitrogen release and urea production. Further investigation into alterations in the glutathione metabolism and urea cycle pathways may lead to a greater understanding of the mechanisms associated with hepatic adaptation for a variety of pharmaceuticals.

ABSTRACT

Drug abuse

Substance abuse has plagued humankind for thousands of years. Recent years have seen an explosion in misuse, abuse and mortality from drugs in the United States and many developed societies throughout the world. This presentation will address the process of developing dependence and addiction, emerging new drugs that are abused and strategies for measuring and assessing abuse rates. Recently, we confirmed that rescheduled hydrocodone combination products could reduce nonmedical use and diversion. Here, a relevant information is briefly attached for your reference.

Background:

In 2014, the Drug Enforcement Administration rescheduled hydrocodone combination products to Schedule II to reduce nonmedical use and diversion.

Methods:

The impact of rescheduling was assessed using quarterly data from 2011 through 2019 from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System Poison Center Program and IQVIATM Longitudinal Prescription Data. Trends and immediate changes in prescriptions dispensed and misuse exposures before and after rescheduling involving hydrocodone, oxycodone, and other Schedule II opioid analgesics were calculated using segmented regression.

ABSTRACT

Drug abuse

Results:

Hydrocodone prescriptions were stable pre-rescheduling, decreased by 2.7% (95% CI: -3.6%, -1.8%, $p < 0.0001$) per quarter post-rescheduling. Misuse exposures involving hydrocodone were decreasing by 3.2% (95% CI: -3.9%, -2.4%, $p < 0.0001$) per quarter pre-rescheduling and decreased by 4.9% (95% CI: -5.5%, -4.2%, $p < 0.0001$) post-rescheduling. Immediate decreases in hydrocodone prescriptions and misuse exposure rates in 2014Q4 compared to 2014Q3 were significant and different from oxycodone or other Schedule II opioids. Schedule II opioid analgesics prescriptions in aggregate were stable prior to rescheduling, decreased by 10.8% (95%CI: -14.0%, -7.6%, $p < 0.0001$) immediately after the rescheduling, and decreased by 2.3% per quarter (95% CI: -3.1%, -1.5%, $p < 0.0001$) subsequently. Misuse exposures involving these opioids were decreasing by 3.3% (95% CI: -4.1%, -2.5%, $p < 0.0001$) prior to rescheduling then by 2.8%, (95% CI: -3.4%, -2.2%, $p < 0.0001$) after rescheduling. The immediate change in misuse was not significant.

Conclusions:

Rescheduling corresponded with changes in hydrocodone prescribing and misuse not offset by increases in other Schedule II opioid analgesics. Misuse exposures for hydrocodone and comparators were decreasing prior to rescheduling with little change post-intervention.

ABSTRACT

Venomous snake antivenom production

Antivenoms have formed the mainstay of treatment for venomous snake envenoming for over 100 years. This presentation will address the methods for production of antivenoms and the inherent limitations of antivenoms. Finally, potential alternatives to antivenoms will be presented. We recently conducted a clinical trial with copperhead snakebite patients. To compare the differences between F(ab') 2 and Fab antivenom in controlling venom-induced tissue injury. Here, a relevant information is briefly attached for your reference.

Introduction:

Fab antivenom (FabAV) halts progression of tissue injury and improves recovery in copperhead snakebite. It is unknown if F(ab')2AV does as well. The objective of this study was to compare control of tissue injury in copperhead snakebite patients treated with F(ab')2AV versus FabAV.

Methods:

We performed a post hoc analysis of copperhead envenomated patients in a clinical trial comparing F(ab') 2AV to FabAV. The outcomes for this analysis are the number of repeat doses required to obtain initial control, the number of patients requiring unscheduled doses during maintenance, and the time from antivenom administration to initial control.

ABSTRACT

Venomous snake antivenom production

Results:

Twenty-one (13 F(ab') 2AV, 8 FabAV) were copperhead patients. Median age was 46 years with a male predominance. Baseline severity was similar. One (8%) F(ab')2AV and 2(25%) FabAV patients required repeat initial dosing, difference = 17%, (95%CI -18, 57%). One (8%) F(ab')2AV and 1(13%) FabAV patients required additional doses after maintenance, difference = 5%, (95%CI -27, 45%). Median time to initial control was 2.7 range (2.0, 9.3) hours and 3.5 range (2.0, 7.4) for F(ab') 2AV and FabAV respectively, difference -0.8 h (95% CI -2.6, 0.9).

Conclusions:

This exploratory analysis suggests that the available measures of the control of venom-induced tissue injury are similar between antivenom subgroups.

Curriculum Vitae

Yoa-Pu Hu

- Citizenship: Taiwan
- Affiliation:
  - ✓ **Emeritus Professor**, School of Pharmacy, National Defense Medical Center, Taipei, Taiwan
  - ✓ **Chair Professor**, Taipei Medical University
- Academic & Administrative responsibilities:
  - ✓ **Distinguished Visiting Chair**, Institute of Biomedical Sciences, Academia Sinica
  - ✓ **Fellow**, National Academy of Inventors, USA (FNAI)
  - ✓ **Fellow**, American Association of Pharmaceutical Scientists, USA (FAAPS)
  - ✓ **Consultant**, Center of Pharmacovigilance, WHO

ABSTRACT

The Problem Solver for Urgent Important Unmet Medical Needs---Hepatotoxicity-Free Acetaminophen

Introduction:

Acetaminophen (AAP) is the leading worldwide cause of drug-induced acute liver failure. This is due to the hepatic cytochrome P450-mediated formation of a highly reactive toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI). We have developed a novel acetaminophen formulation, SNP-810 can significantly reduce the formation of NAPQI by inhibiting the responsible liver enzymes.

Method:

The following studies have accomplished including: (1) Quantitative measurements of AAP and its nine metabolites including NAPQI (represented by AAP-Cysteine adduct using liquid chromatography/tandem mass spectrometry (LC/MS-MS); (2) Development of selected modulators in vitro to screen hundreds of safe compounds for inhibiting CYP enzymes using both rat and human liver microsomes; (3) Prove eradicating AAP-induced toxicity in rats and mice through various pharmacodynamics and pharmacokinetic studies; (4) Confirm the above findings in over fifty normal healthy subjects with single and multiple doses of SNP-810.

ABSTRACT

The Problem Solver for Urgent Important Unmet Medical Needs---Hepatotoxicity-Free Acetaminophen

Results and Conclusion:

The hepatic injury caused by high dose of acetaminophen including ALT, AST, GSP, and abnormal pathological findings could be eradicated by novel SNP-810 in rats and mice. SNP-810-treated rats and mice showed normal liver biochemistry and all survived with acetaminophen doses up to 8000 mg/kg (equivalent to 90 g for a 70 kg person). SNP-810 formulation significantly reduced the generation of NAPQI in rats as indicated by the level of acetaminophen-Cys adduct, the biomarker of NAPQI. In normal healthy subjects, single and multiple doses of acetaminophen based on the SNP-810 versus Panadol® supported the hypothesis that SNP-810 is a safe acetaminophen formulation. Considering that acetaminophen is the most commonly used analgesic and antipyretic worldwide, SNP-810 may have global health implications and dramatically change the severe side effects of pain relief treatments. Currently, we are applying this finding not only developing safe acetaminophen drug but developing better antidote for AAP overdose patients by inhibiting the toxic metabolite formation instead of eliminating toxic metabolite.

Curriculum Vitae

Winai Wananukul

- Citizenship: Thailand
- Affiliation:
  - ✓ **Head/ Director**, Department of Emergency Medicine and Ramathibodi Poison Center, Faculty of Medicine Ramathibodi Hospital, Mahidol University
- Academic & Administrative responsibilities:
  - ✓ **Councilor**, the Medical Council of Thailand
  - ✓ **Committee member**, the Royal College of Physician of Thailand
  - ✓ **Past-President**, Asia Pacific Association of Medical Toxicology (2008-2010)

ABSTRACT

E-commerce causing unusual poisonings

In management of patients with unknown poisoning, initial diagnosis is based on signs, symptoms and initial laboratory tests. History of occupation, recreation and geographic location are also important additional information for making the diagnosis. It would suggest toxic substances which the patient having exposed. Recently, unusual poisoning without this information consulted to poison center have been increasing. The examples are such as sudden cardiovascular collapse in young adult, hypotension and cardiac arrest in a middle-aged man; young man with severe vomiting and abdominal pain after taking white powder. Finally, the toxic exposures were identified as potassium cyanide, sodium azide and powder of rosary bean, respectively. We found that the patients got these toxic substances by ordering online while their families and friends did not aware.

E-commerce, nowadays, is explosively expanding. The good side is to facilitate customers to buying almost all things easily and without limitation. But toxic or dangerous substances also easily reaches patients who want to harm themselves. This fast convenience service combined with information via internet facilitate deliberate self-poisoning.

This concern should be raised. It will cause more variety of poisoning that clinical toxicologists and poison centers have to encounter. For a preventive measure, these potential harmful goods should be controlled for sell. Though, there has been no appropriate measure yet, responsible sectors should find an action to lessen this problem.

Curriculum Vitae

Ravikar Ralph

- Citizenship: India
- Affiliation:
  - ✓ **Professor**, Clinical Toxicology Unit & Poisons Information Center, Department of Medicine, Christian Medical College & Hospital, Vellore
- Academic & Administrative responsibilities:
  - ✓ **Member (2021):** WHO Global Roster of Experts and Technical Advisory Group on the Prevention and Control of Snakebite Envenoming.
  - ✓ **Lead Member (2019):** WHO-SEARO drafting group on a Regional Guidance Document on the Prevention and Control of Snakebite Envenoming in the South-East Asia Region.

ABSTRACT

Acute arsine poisoning in a cluster of Indian lead-refinery workers: Challenges in diagnosis and management

Arsine is a highly-toxic colourless, non-irritant gas with a mild, garlic-like odour. Its presence in industrial settings can easily go undetected. Acute exposure results in severe hemolysis and renal injury, with case-fatality of 25%. Most instances occur when arsine is generated as a by-product of a chemical reaction involving metals with arsenic as an impurity or alloy. When water or acids come in contact with these ores, arsine is released. We describe acute arsine poisonings of varying severity in three workers at a lead-acid battery recycling plant located in southern India.

Patient-1 developed headache, dizziness, abdominal pain, nausea and recurrent vomiting followed by jaundice and passage of tea-coloured urine, 30-minutes after inhaling a colourless gas with a mildly unpleasant odour, generated after lead-dross containing enriched antimony, aluminium and arsenic/arsenic oxide was inadvertently placed in contact with acid-covered battery plates. He developed worsening oliguria two hours later and was noted to have severe intravascular hemolysis and anuria at a regional tertiary center. A diagnosis of acute lead poisoning was considered and he was treated with blood transfusion, dialysis, and d-Penicillamine for two days. He was subsequently referred to our Poison Center due to progressive worsening of renal parameters. On arrival, active hemolysis had ceased but the patient continued to be anuric with laboratory evidence of a secondary toxic nephropathy. In this clinical and occupational setting, we considered differential diagnoses of acute arsine or stibine poisoning. Whole-blood and 24-hr urinary arsenic levels were markedly elevated suggesting acute arsine exposure. The patient declined parenteral BAL chelation and was alternatively treated with DMSA in conjunction with CRRT using an in-house protocol. His renal function gradually improved and he was discharged in a stable condition.

ABSTRACT

Acute arsine poisoning in a cluster of Indian lead-refinery workers: Challenges in diagnosis and management

Patients-2 and 3 were exposed to arsine while unloading a large quantity of lead-dross exposed to rain while being transported in an open-back vehicle between units. Patient-2 developed severe abdominal pain and multiple vomiting episodes 6-hours post-exposure, followed by jaundice and tea-coloured urine 6-hours later. On arrival at our Poison Center 48-hours after the incident, his vital parameters were stable. He had pallor, icterus and normal systemic examination. Laboratory investigations revealed anemia, reticulocytosis, indirect hyperbilirubinemia and high serum LDH suggesting intravascular hemolysis, and features of mild renal tubular injury. Patient-3 also passed dark urine but had no other symptoms. Whole-blood and 24-hour urinary arsenic levels were elevated in both patients. Both survived following management with DMSA chelation, adequate hydration and renal function monitoring.

These cases highlight critical lacunae at levels of industrial safety, correct diagnosis and appropriate management of arsine poisoning. While it is generally accepted that chelators are unlikely to be of any immediate benefit once hemolysis has begun, we chose to treat our patients with oral chelation to aid clearance of the “fixed” arsine in the body and that of other inorganic arsenicals, since environments predisposing arsine exposure would also be expected to present a likely exposure risk to other inorganic arsenicals.

ABSTRACT

Lepidopterism: An interesting clinical-case discussion

Lepidopterism is a systemic illness caused by direct or aerosol contact with the urticating scales, hairs or spines and/or toxic body fluids of moths, butterflies or their caterpillars. The resulting syndrome, characterised by generalised urticaria, headache, conjunctivitis, pharyngitis, nausea, vomiting, bronchospasm and wheezing, can progress to clinical complications and in some cases even death. In many instances, patients with lepidopterism are erroneously diagnosed and treated as infectious fevers due to lookalike symptoms. Consequently, physicians must gather a detailed history and maintain a high index of suspicion to arrive at the correct diagnosis and avoid unnecessary medications.

We present a clinical case of severe lepidopterism following cutaneous contact with the larval stage of Olepa ricini (family Erebidae). A systematic review of recorded clinical cases was also conducted. A computerised literature search of MEDLINE and EMBASE was undertaken using the MeSH terms lepidopterism, erucism, caterpillar dermatitis. Textbooks on clinical toxinology were searched and further reports of cases of were located. All cases of lepidopterism and erucism fulfilling pre-specified clinical definitions were included. All reports were evaluated and the following data extracted: patient demographics (age, sex, geographical location, season), local and systemic effects and causative species. Clinical effects were classified as local and mild or severe systemic.

ABSTRACT

Lepidopterism: An interesting clinical-case discussion

A 7-year-old girl presented to the paediatric clinic with generalised urticarial rash involving the face, trunk and lower limbs, 12-hours after a black insect fell over her leg while she was sitting in her garden, under a tree. The child brushed the insect away and ran to her parents for help. She was brought to the emergency department six hours after the event when her parents noted a progressive itchy red rash over both legs and trunk. At presentation, the child was febrile with tachycardia, and complained of central abdominal pain, nausea and headache. She vomited twice and had scattered rhonchi bilaterally. She was treated with intramuscular adrenaline, intravenous hydrocortisone and antihistamines and nebulised bronchodilators following which her symptoms gradually resolved over a period of five days. A home visit was conducted to identify the culprit species. Numerous black caterpillars were noted on a Moringa olifera tree adjoining the house. Specimens were collected, confirmed by the patient and morphological characteristics recorded. The caterpillars were allowed to pupate and metamorphosise into the adult moth to aid species identification. This is the first case of associated with a member of family Erebidae. Literature search identified 52 studies. Data was reported from six countries and included a total of 92 cases. Commonly implicated lepidopteran families included megalopygidae, nymphalidae, saturniidae, and notontidae. A majority of cases involved children (92%). Common systemic signs included nausea, vomiting, headache and abdominal pain. Anaphylactic shock was rare (4%). Death occurred in two cases.

Curriculum Vitae

Yoshito Kamijo

- Citizenship: Japan
- Affiliation:
  - ✓ **Professor**, Department of Clinical Toxicology, School of Medicine, Saitama Medical University / Clinical Toxicology Center, Saitama Medical University Hospital
- Academic & Administrative responsibilities:
  - ✓ 2015: Professor: Department of Emergency Medicine, School of Medicine, Saitama Medical University / Emergency Center & Poison Center, Saitama Medical University Hospital
  - ✓ 2012: Professor: Department of Emergency and Critical Care Medicine, School of Medicine, Kitasato University

ABSTRACT

Serial murder using intravenously administered benzalkonium chloride in Japan

Benzalkonium chloride (BAC), a positive ionic surfactant, is widely used as a disinfectant in medical facilities. It exerts cellular toxicity as it has cytolytic effect. If administered intravenously (IV), it first injures venous endothelial cells and red blood cells, and second tissues and organs where it distributes and accumulates. An animal study demonstrated that it further more distributes and accumulates in heart, lung, and kidney than in blood, liver, or muscle after IV administered and that it hardly accumulates in brain or adipose tissues. The lethal dose of intravenous administration in huma i n is estimated to be 5 to 15 mg/kg. In Japan, serial murder using IV administered BAC occurred in a hospital located in Yokohama. A young female nurse confessed that she had killed at least 20 aged patients using IV administered BAC. Benzalkonium was detected in three autopsied corpses and the speaker cooperated in the investigation of the three cases and testified in court about the mechanism of three death from BAC.

ABSTRACT

Serial murder using intravenously administered benzalkonium chloride in Japan

Case 1:

An elderly female patient had cardiac arrest approximately 4 hours after the start of the intravenous infusion. During the infusion, she complained of pain in the punctured site, where redness was found and she demonstrated hemoglobinuria and lung congestion. Unfortunately, her corpus had already been cremated. However, 13.3 mg/mL of BAC was detected in her residual blood.

Case 2:

An elderly male patient suddenly died from ventricular fibrillation. At his autopsy, 201.9, 255.0, and 326.0 μg/mL of BAC were detected in her cardiac blood, lung, and myocardium, respectively, but it was not detected in her urine.

Case 3:

Another elderly male patient suddenly demonstrated bradycardia and hypotension 6 hours after the start of the intravenous infusion and died 7 hours after. During the infusion, hemoglobinuria was found. At his autopsy, lung congestion was found and 51.2, 171.0, 349.0 and 410.0 μg/mL of BAC were detected in her cardiac blood, lung, myocardium, and kidney, respectively, and 4.3 and 40.3 μg/mL were also detected in her urine and gastric contents. In the infusion bottle containing about 250 mL of residual extracellular fluid, 6.5 mg/mL of the agent was detected.

Discussion and conclusion: All three patients were diagnosed with lethal BAC poisoning. Rapid intravenous injection of the agent was suspected in case 2. About 1,525 mg of the agent (35 mg/kg) might had been administered through infusion in case 3, which correspond to far more than lethal dose.

Curriculum Vitae

Kenneth Hartigan-Go

- Citizenship: Filipino
- Affiliation:
  - ✓ **Non-Resident Research Fellow** of the Ateneo Policy Center of the School of Government
  - ✓ **Adjunct Faculty** at the Asian Institute of Management
- Academic & Administrative responsibilities:
  - ✓ **member** of the National Advisory Group for Philippine National Police Leadership Transformation and Development
  - ✓ **Honorary Visiting Associate Professor** of the Saw Swee Hock School of Public Health, National University of Singapore
  - ✓ **School Head** of the Stephen Zuellig School of Development Management of AIM (Dec. 2016-Sept 2020)

ABSTRACT

Food Safety and Toxicology in the Philippines: a regulatory challenge

Food is an indispensable part of human capital development and when safety is ignored, human health is adversely affected. How much should Food security and food safety be integrated as part of Health Security?

The Philippines Food Safety Act of 2013 was legislated to create improvements in handling an integrated value chain for the safety of food and hence was very much in the domain of two agencies, the Department of Agriculture and the Department of Health. Many of the problems we saw were often already the adverse end results of unsafe foods in humans.

This talk describes food hazards reported in the Philippines and will present several real live cases of food related toxicity, the challenges of investigations and argue for tighter regulatory oversight in promoting consumer literacy and welfare.

The case examples and the lessons learned will cover local tocino cured meat and methemoglobinemia, unsafe food additives detected in foods sold in public market, red tide and other marine toxicology, natural toxin from cassava, suspected homicide by intentional food poisoning, heavy metal in fishes, contaminated candies, aflatoxin in peanut butter products.

Because of the heavy burden of food safety regulations and the limited resources in government, a proposal for private sector co-regulation in the food sector might be a form of collaborative governance.

Curriculum Vitae

Bruno Mégarbane

- Citizenship: France
- Employment:
  - ✓ **Professor** at Paris University, Paris, France
  - ✓ **Head** of the Department of Medical and Toxicological Critical Care in Lariboisière University Hospital, Paris
  - ✓ EAPCCT past president
- Academic & Administrative responsibilities:
  - ✓ Experimental research at INSERM U1144 (research team leader)
  - ✓ Associate editor of Clinical Toxicology (IF =4.467), Annals of Intensive Care (IF =6.925), Toxicologie Analytique et Clinique (French)

ABSTRACT

Extracorporeal membrane oxygenation (ECMO) to treat acute poisoning

Objectives:

Drug-induced cardiovascular failure remains a leading cause of death. Calcium-channel blockers (CCB) and beta-blockers (BB) account for about 40% of cardiovascular drug exposures, while CCB, membrane-stabilizing agents (MSA) and glycosides represent the first causes of cardiotoxicant-related fatalities. Methods: This presentation will define the aims, usefulness, and possible complications place extracorporeal life support (ECMO) in poisonings. The objective of this presentation is to help the audience understanding the role of ECMO in supporting drug-induced cardiac failure; choosing the optimal antidotes for the usual cardiotoxicants; understanding how to assess refractoriness of drug-induced cardiovascular failure to the pharmacological therapies; understanding the principles of management of the poisoned patient treated by ECMO.

ABSTRACT

Extracorporeal membrane oxygenation (ECMO) to treat acute poisoning

Results:

Severe cardiotoxicity usually appears rapidly after the exposure with the sudden onset of hypotension, high-degree atrioventricular block, asystole, pulseless ventricular arrhythmia. Other critical features include mental status deterioration, seizures, hyperlactacidemia, and renal, liver and respiratory failure. Determination of the mechanism of cardiovascular failure is mandatory. Overdoses with CCB, BB, and MSA result in myocardial negative inotropic effects and arterial dilatation. Prognostic factors remain poorly investigated and seem to be specific for a class of toxicants. Despite optimal supportive and antidotal treatments, management of drug-induced cardiovascular failure is difficult. Ventricular arrhythmia, sudden cardiac arrest, and refractory cardiovascular failure may cause death, despite tight monitoring and aggressive resuscitative measures and vasopressors. Prognosticators of refractoriness to conventional treatments are lacking.

ABSTRACT

Extracorporeal membrane oxygenation (ECMO) to treat acute poisoning

Results:

Due to large volumes of distribution and high protein binding ratios, extracorporeal elimination enhancement techniques are not feasible options. Lipid emulsion has been extensively used but due to the lack of randomized controlled studies, this treatment should be used only in local anesthetic systemic toxicity and lipophilic cardiotoxin intoxication with an immediate threat to life and ineffectiveness of other therapies. ECMO for reversible cardiac toxicity has a sound basis but clinical experience is still limited in toxicology with insufficient evidence to demonstrate its definitive effectiveness. The purpose of ECMO is to take over the heart function during refractory cardiac shock until recovery can occur, thus minimizing myocardial work, improving organ perfusion, and maintaining the renal and biliary elimination of the toxicant. By contrast, ventricular pacing can only be considered if the inotropic heart function is preserved. Interest of intra-aortic balloon pumps is limited due to the need for intrinsic cardiac rhythm for synchronization and diastolic augmentation.

ABSTRACT

Extracorporeal membrane oxygenation (ECMO) to treat acute poisoning

Conclusions:

Supportive and antidotal treatments are usually efficient to treat drug-induced hypotension. However, due to persistent high-rate of mortality, there is a need for more aggressive management in patients not responding to conventional treatments. Clarification of prognosticators of refractoriness is mandatory. Usefulness of ECMO remains a matter of debate and recommendations from the scientific societies are expected.

Conflict of interest:

none.

ABSTRACT

Application of pharmacogenomics to clinical toxicology

Background:

Every year, about 100,000 people die in the US from acute poisonings or severe drug side effects. In a number of cases, gene polymorphism can explain a particular vulnerability of these severely intoxicated subjects to the drug or toxicant involved in their death. The objective of pharmacogenomics is to identify such genetic variants, in order to explain the severity of the clinical features and possibly to prevent them. The aims of this presentation are to discuss the application of pharmacogenomics to clinical toxicology and to illustrate its interest in some specific situations.

ABSTRACT

Application of pharmacogenomics to clinical toxicology

Methods:

Review of the recent medical literature. Results: Genes currently known to explain a particular individual susceptibility to a toxicant code for metabolic enzymes, serum or membrane transporters, and major histocompatibility complex (MHC) proteins. Metabolic enzyme variants or transport protein variants can alter the pharmacokinetic or pharmacodynamic parameters of the toxicants. Thus, the variants of the genes coding for thiopurin-S-methyltransferase and uridine diphosphate glucuronosyltransferase 1A1 increase the risk of myelotoxicity associated with azathioprine and irinotecan treatment, respectively. A variant of the organic anionic transporter SLCO1B1 has been shown to be strongly associated with the risk of drug-induced myopathy. A recent study showed that 60% of simvastatin-induced myopathies are attributable to the SLCO1B1 variant. Gene polymorphism analysis is able to prevent administering high doses of simvastatin to homozygous or heterozygous patients for this allelic variant. In the field of psychotropic drugs, strong evidence supports correlation between gene variants of the D2 and D3 dopaminergic receptors and the risk of late dyskinesia, from variants of serotonin transporter to non-response to serotonin-reuptake inhibitor antidepressants as well as variants of the 5-HT2C serotonin receptor gene to the weight gain observed when treated with antipsychotic drugs.

ABSTRACT

Application of pharmacogenomics to clinical toxicology

Methods:

MHC genes determine the intensity of the hypersensitivity reaction associated with the toxicant behaving like a hapten or an immunogenic compound. The HLA-B1502 variant was thus associated with the increased occurrence of skin reactions with carbamazepine treatment, sometimes progressing to Stevens–Johnson syndrome or scalded skin syndrome. The routine application of pharmacogenomics at the bedside can improve prescription safety and allow understanding the severity of possible side effects or toxicity. Here are well-documented examples: the hemolytic accidents and glucose-6-phosphate dehydrogenase (G6PD) gene polymorphisms; isoniazid overdose and N-acetyltransferase-2 gene polymorphism (determining the speed of acetylation); and hemorrhagic accidents on warfarin and cytochrome P450 2C9 (action on pharmacokinetics) or VKORC1 gene polymorphisms (encoding epoxide reductase, action on pharmacodynamics). Several severe or fatal poisoning case reports have illustrated the role of gene polymorphism (mainly cytochrome P450 2D6) in opioid toxicity including codeine, tramadol and oxydone.

ABSTRACT

Application of pharmacogenomics to clinical toxicology

Conclusions:

The rapidly developing pharmacogenomics and proteomics-based molecular approaches will play an essential role in the next future in predicting drug toxicity (as part of personalized medicine) and better understanding individual variability of features in clinical toxicology.

Conflict of interest:

none.

Curriculum Vitae

Luke Yip

- Citizenship: United States of America
- Employment:
  - ✓ **Medical Officer/ Senior Advisor** for Medical Toxicology, US Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta
- Academic & Administrative responsibilities:
  - ✓ **Clinical Assistant Professor**, University of Colorado Health Sciences Center, School of Pharmacy
  - ✓ **Consultant Emergency Physician**, Calvary Health Care Tasmania, Hobart, Australia
  - ✓ **Attending Staff Physician**/ **Consultant Clinical Toxicologist**, Department of Medicine, Division of Medical Toxicology, Denver Health Medical Center, Colorado

ABSTRACT

Naloxone pharmacokinetic considerations in the treatment of opioid poisoning in a mass casualty incident

Most public health experts are familiar with media reports on the incident that occurred 23 October 2002 during the “Nord-Ost” musical performance in Moscow’s Dubrovka Theater where 40 terrorists took 914 people hostage. In response, Russia’s Federal Security Service staged an operation to liberate the hostages. The operation involved delivery of aerosolized opioids through the Theater’s ventilation system as part of a military offensive. Over 400 people were hospitalized and 115 deaths were related to opioid poisoning. This event demonstrates the feasibility of a health security threat by the deliberate release of opioids resulting in mass casualties.

The medical management of opioid toxic patients from a deliberate opioids release causing mass casualties is a challenge. The primary medical countermeasure to opioid toxicity is active airway management (e.g., bag valve mask and endotracheal intubation) and mechanical ventilation. This requires commensurate number of skilled healthcare providers and sufficient equipment to perform such procedures with the number of casualties. Naloxone antagonizes the effects of opioids in the central nervous system and is an important acute pharmacologic treatment of opioid toxicity. However, treatment of opioid toxicity with naloxone is not a substitute for the primary medical countermeasure. Naloxone can be administered by different routes (e.g., intravenous, intramuscular, and intranasal), and their respective pharmacokinetic profile has clinical implications that should be considered when administering naloxone to patients in a mass casualty situation. We will discuss the pharmacokinetics of naloxone when administered by different routes and its clinical implications to help understand the limitations of naloxone when administered to patients in a mass casualty situation.

ABSTRACT

Chlorfenapyr

Introduction:

Chlorfenapyr, an N-substituted halogenated pyrrole, is a broad-spectrum insecticide. The insecticidal activity of chlorfenapyr depends on its biotransformation by hepatic mixed function oxidases to tralopyril, which uncouples mitochondrial oxidative phosphorylation and disrupts adenosine tri-phosphate production. Although chlorfenapyr's mechanism of action has been elucidated, human chlorfenapyr poisoning is not well characterized and the management of chlorfenapyr exposure is unclear. The purpose of this work is to characterize human chlorfenapyr poisonings, its laboratory and imaging findings, and propose a management plan for human chlorfenapyr exposure.

Methods；

We systematically searched EMBASE, Google Scholar, PubMed, and Web of Science from inception to March 2021 across all languages. Non-English publications were translated using either Google Translate or primarily translated by our authors. The search strategy included "human," "chlorfenapyr," and "tralopyril." We excluded in vitro studies, animal studies, and environmental impact studies. Abstracts from scientific conferences with sufficient description of exposure and clinical course were included. Conversely, abstracts from scientific journals were excluded if we were unable to subsequently obtain the full text article. We then performed a review of the citations of included studies, culling articles which met inclusion and exclusion criteria. The study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.

ABSTRACT

Chlorfenapyr

Results:

Our systematic search identified 1143 publications of which 23 met study inclusion criteria. One of these studies did not include sufficient information for analysis and was excluded yielding 22 studies with patient level data and 34 cases of human chlorfenapyr poisoning. Chlorfenapyr poisoning occurred via ingestion (91%), inhalation (3%), dermal exposure (3%), and intra-abdominal injection (3%). The mean time from exposure to symptom onset was 3.3 days (range 0-14 days) for all patients, though this was shorter amongst those who died (2.6 days) than in those who survived (7.0 days) (Table 1). The most frequently reported symptoms at presentation were diaphoresis (44%), nausea and/or vomiting (26%), and altered mental status (24%). Fever (≥38° C) was uncommon at presentation (9%) but developed in 55% of the patients. Elevated creatinine kinase was the most frequently reported abnormal laboratory result (44%) during hospital course, and neuroimaging studies were notable for diffuse bilaterally symmetrical white matter changes in the central nervous system (33%).

Chlorfenapyr poisoning is associated with a high mortality (73%). Fever was an ominous clinical sign and it often preceded hemodynamic collapse and death. Amongst patients who died, mean time to death was 7.9 days (range 2-20 days). Of the survivors, 38% incurred neurological sequelae (e.g., paraparesis and vision loss). Management of chlorfenapyr exposure and treatment of chlorfenapyr toxicity were highly variable between cases, and the effectiveness of any specific treatment is unclear.

Conclusion:

Human chlorfenapyr poisoning is characterized by a latent period as long as 14 days, deterioration over hours to days, variable abnormal laboratory results, and distinctive neuroimaging findings, and is associated with high mortality. We propose a management algorithm for patients who are exposed to chlorfenapyr based on characterization of chlorfenapyr poisoning.

Curriculum Vitae

David Russell

- Citizenship: British
- Employment:
  - ✓ **Head** of CRCE-Wales and Co-Head of WHO Collaborating Centre for Chemical Incidents
  - ✓ **Consultant** of Environmental Toxicology for the United Kingdom Health Security Agency
- Research Interest/Specialty:
  - ✓ Public health management of chemical incidents
  - ✓ Maritime transport
  - ✓ Air quality and public health
  - ✓ Chemical terrorism

ABSTRACT

Chemical incidents

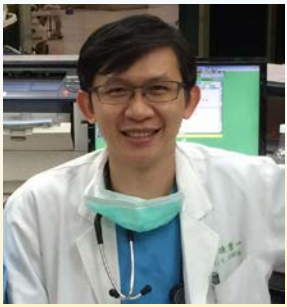
Chemical incidents can happen at any time and at any place and result in both acute and chronic health consequences. The large number and volumes of chemicals synthesised, stored, transported and utilised and subsequently disposed of by a myriad of industries and the general public may leads to potential community exposure. Such incidents may result from contamination of air, water, soil and/or food and result in both acute and chronic systemic health effects, mutagenicity and concerns about carcinogenicity. In addition, chemical incidents may result in mental health consequences including stress, anxiety and depression.

This short seminar will provide an introduction into the role of the health sector in the various phases of the disaster management cycle, starting with prevention and working through emergency planning, preparedness response and recovery. It will illustrate key points by means of case studies based on global examples of chemical incidents and culminate in a short interactive exercise.

Curriculum Vitae

Chen-Chang Yang

- Citizenship: Taiwan
- Employment:
  - ✓ **Distinguished Professor**, Institute of Environmental & Occupational Health Sciences, School of Medicine, National Yang Ming Chiao Tung University
  - ✓ **Adjunct Attending Physician**, Division of Clinical Toxicology & Occupational Medicine Taipei Veterans General Hospital, Taipei, Taiwan
- Academic & Administrative responsibilities:
  - ✓ Advisory Expert, Global incidence alert network for food safety
  - ✓ Editor, Clinical Toxicology (Phila), Asia Pacific Journal of Medical Toxicology, Journal of the Chinese Medical Association, etc.



Curriculum Vitae

Hsien-Yi Chen

- Citizenship: Taiwan
- Affiliation:
  - ✓ **Head,** Department of Emergency Medicine Chang Gung Memorial Hospital Taoyuan Taiwan Republic of China
- Academic & Administrative responsibilities:
  - ✓ School of Medicine, Chang Gung University, Taiwan, Adjunct lecturer
  - ✓ Member of Toxicology & Hazmat Incident Committee, Society of Taiwan Emergency Medicine

ABSTRACT

Severe borax poisoning

Borax, also known as sodium borate ($Na_2B_4O_7 \cdot 10H_2O$), was widely used as household cleaners, pesticides, laundry detergent boosters, flame retardants, and food addictive. Following ingestion, borax reacts with hydrochloride acid and forms boric acid. Acute borax or boric acid ingestions are not uncommon and produce minimal or no toxicity in most patients. Severe and systemic toxicity following borax poisonings were rarely reported.

ABSTRACT

Severe borax poisoning

A 56-year-old female ingested 200-300 g of borax, developed severe vomiting and diarrhea, and was sent to a local hospital 13 hours after ingestion. She underwent gastric lavage and was then transferred to our Emergency Department. On arrival, she was awake and oriented, and her vital signs were: heart rate 114 beats/min, blood pressure 97/59 mmHg, respiratory rate 18 breaths/min. Physical examinations were unremarkable. Laboratory data were as follow: WBC 23800 /μL, BUN 18.8 mg/dL, Cr 1.25 mg/dL, Na 153 meq/L, K 2.9 meq/L, pH 7.46, pCO2 37.7 mmHg, bicarbonate 26.4 mmol/L. She developed sustained hypotension and received 1500 mL normal saline bolus and norepinephrine infusion. She was admitted to ICU, where an emergent hemodialysis (HD) was initiated 13 hours after the patient's arrival. Endoscopy examination revealed a Zargar's classification 3A caustic injury at stomach. She still had intermittent hypotension even after HD, and we added on vasopressin infusion and initiated forced diuresis to enhance the elimination of borate. On the third day, her blood pressure improved and inotropic agents were discontinued on the 4th day. She gradually recovered and was discharged after 12 days. We did quantitative analyses (by LC-MSMS) for her serum samples, which showed the boric acid concentration before and after HD were 1071.43 μg/mL and 113.73 μg/mL respectively. We also analyzed boric acid concentrations in both urine and dialysate samples, and found that HD effectively removed boric acid.

Severe borax poisoning is rare but can be life-threatening. HD effectively removes boric acid from the blood and should be considered in patients who ingested large amount of borax and developed severe toxicity.

Curriculum Vitae

DOÃN UYÊN VY

- Citizenship: Vietnam
- Affiliation:
  - ✓ **Deputy Head** of Division of Medical Toxicology, Cho Ray Hospital, Ho Chi Minh City, Vietnam
- Academic & Administrative responsibilities:
  - ✓ **Guest Clinical Lecturer** (Medical Toxicology), Department of Critical Care – Emergency – Medical Toxicology, University of Medicine and Pharmacology, HCMC

ABSTRACT

Cardiac toxicity following the use of cosmetic filler

Introduction:

Lidocaine toxicity has been seen during cosmetic surgery and cases of fatalities have been reported following local anesthetic use. Lidocaine toxicity during the use of body fillers however, has not been reported.

Case report: We report a case of a patient presenting to the emergency department in systemic shock after body filler injection in her breasts and face was performed in a private practice cosmetic practice. She was injected with 150 ml of Alisa Body Filler® into her breasts and 6 ml into her chin and outer corners of both eyes. After 30 minutes, the patient had a mild fever, then developed fatigue gradually over 12 hours. Later she complained of chest tightness, difficult breathing and was admitted to the local hospital. The first diagnosis was of a grade 3 anaphylactic reaction related to the body filler product. The patient was treated with 0.5 mg of adrenaline IM followed by an adrenaline infusion, and she was transferred to CRH. Within one hour of presentation to the Emergency department, the patient became hypotensive, confused, and tachycardic at 120 bpm. Echocardiography showed general hypokinesis of the left ventricle with an EF of 30%. An arterial blood gas showed a metabolic acidosis with pH 7.3, HCO3- 16.1 mmol/L, PO2 55 mmHg, PCO2 32.3 mmHg. Other labs were: AST 99 U/L, ALT 80 U/L; BUN 20 mg/dL, creatinine 1.65 mg/dL, lactate 9.7 mmol/L, Troponin I 6.75 ng/mL. She had a cardiac arrest while preparing to perform ECMO, but she was successfully resuscitated in the CCU with continuous advanced cardiovascular life support. The patient required VA-ECMO for 72 hours until she stabilized. After ECMO was discontinued, she was still bradycardic (50 – 60 bpm), so we decided to administer Lipofundin® emulsion 20% 100 ml, and she further stabilized. Her left breast was swelling and inflamed, and surgery was performed to remove the body filler.

ABSTRACT

Cardiac toxicity following the use of cosmetic filler

Discussion:

Alisa Body Filler® is Korean commercial products for cosmetic use and is easy to purchase on the internet. It composed of 20 mg/ml hyaluronic acid and 3 mg/ml Lidocaine, mixed in a 50 mL. bottle. The staff of small private practices use this product for their customers who wish to enhance their physical appearance. In our case, the patient was injected with 150 ml in each breast and 6 ml in her chin and the outer corner of the eyes by her colleagues who worked with the patient in the cosmetic shop. Her friend also injected more than 4 ml of lidocaine before the body filler injection into each breast. The total dose of lidocaine that the patient was given equaled 508 mg and her body weight is about 50 kg. While the regional anesthesia is 4 mg/kg, the maximum dose of lidocaine is 200 mg (in Europe) and 300 mg (in the US). In this case, the patient had 508 mg, double the normal dose. She had lidocaine – induced systemic toxicity (LAST). The main target of organs are the central nervous and cardiovascular system. Lidocaine was injected into her breasts locally but because this was done on each side, and with the large volume of body filler injected subcutaneously and the proximity to the heart, it was absorbed, systemically within 12 hours. All local anesthetics directly produce a dose-dependent decrease in cardiac contractility. Lidocaine serum levels were not measured after presentation because a relative did not provide any product information initially. After 24 hours of VA-ECMO, we determined the cause of her cardiac shock. In this case, grade 3 anaphylactic reaction with hyaluronic acid or lidocaine were not consistent with her presentation because this patient has previously used this kind of body filler in her face on several occasions with no affect. Also, the administration of adrenalin at the local hospital with no response, and her condition continued to deteriorate. This presentation was consistent with the diagnosis of LAST due to the concentrations present in the product and the total dose administered.

Conclusion: The use of body filler that has lidocaine mixed with hyaluronic acid

ABSTRACT

Cardiac toxicity following the use of cosmetic filler

Conclusion:

The use of body filler that has lidocaine mixed with hyaluronic acid must be used with caution. The total dose of lidocaine must be calculated. Large doses of these products injected for cosmetic fill it could be fatal, producing LAST, and ECMO may be required for resuscitation and stabilization.

Curriculum Vitae

Dong-Zong Hung

- Citizenship: Taiwan
- Affiliation:
  - ✓ **Director,** Toxicology Center, China Medical University Hospital, Taichung, Taiwan
- Academic & Administrative responsibilities:
  - ✓ **Associate Professor**, Institute of Clinical Medicine and Research, China Medical University
- Research Interest/Specialty:
  - ✓ Clinical Toxicology
  - ✓Environmental and Occupational Medicine
  - ✓Internal Medicine
  - ✓Emergency Medicine

ABSTRACT

The Conception of Rapid Diagnosis for Venomous Snake Bites

Venomous snakebite is one of the major public health issues of global concern. There are a large number of people, in some developing or under developing countries or regions of Asia, Africa and South America, suffer from lethal result or physical disability after poisonous snake envenomation due to the inconvenient of correct diagnosis and specific antivenom treatment.

It is an impossible mission to have a universe test and a unique drug or antivenom that can be applied to diagnose and treat venomous snake bites anywhere in the world under the impact of great variance and difference of snakes on distribution and venom components. In order to recognize snake species quickly and to be able to cope with the needs of most of the regions in Asia, we have established a long-lasting and efficient platform for the production of highly specialized avian IgY, which can assemble a rapid diagnostic kit for snake bites in any specific region in a short period of time.

ABSTRACT

The Conception of Rapid Diagnosis for Venomous Snake Bites

In Taiwan, the rapid test ICT-Cobra® could differentiate cobra from hemorrhagic venomous snake bites, with 100% specificity, and the detection limit is 5 ng/ml of cobra venom in serum. We also performed clinical trial in northern Vietnam, the sensitivity of patient's blood of symptomatic envenomation was more than 95%, and the sensitivity of the swabbed fluid on the bite wound was as high as 98%. This kit can detect other Naja species in Southeast Asia, although this reagent only reached a positive detection rate of 54.3% in a small trial in Bangladesh. We have also demonstrated that different snake venoms (cobra & Russell's viper) can be assembled on the ICT-kit at the same time with good discrimination. Therefore, it is technically feasible and can be customized to design an ICT-kit for any regional snake species to improve the quality on the management of poisonous snake envenomation.

Curriculum Vitae

Yan-Chiao Mao

- Citizenship: Taiwan
- Affiliation:
  - ✓ **Director** of Clinical Toxicology, Department of Emergency Medicine, Taichung Veterans General Hospital
- Academic & Administrative responsibilities:
  - ✓ **Deputy secretary**, Toxicology society of Taiwan
  - ✓ **Clinical consultant**, Department of Emergency Medicine, Taichung Armed Forces General Hospital
  - ✓ **Assistant Professor**, National Defense Medical Center, School of Medicine

ABSTRACT

Uncommon defibrinogenation and coagulopathy caused by Trimeresurus stejnegeri stejnegeri envenomation

In Taiwan, Trimeresurus stejnegeri stejnegeri (green pit viper) is responsible for more than half of all the venomous snakebites annually. Envenoming syndromes are primarily affect the local tissue, leading to tissue swelling and pain, occasional local ecchymosis, bullae and blister formation, and lymphangitis and lymphadenitis. Defibrinogenation and coagulopathy have rarely been reported, and the treatment remains unexplored. Herein, we described the case of a man who was bitten by T. s. stejnegeri on his right big toe, which later developed into grade 2 limb swelling. Severe hypofibrinogenemia (fibrinogen level <50 mg/dL), low activities of factors V and XI, plasminogen, and α2-antiplasmin, as well as prolonged prothrombin time were observed. However, a favorable outcome was achieved by administering the antivenom specific for treating the patient without systemic bleeding or thrombosis. Therefore, knowledge of specific coagulation factor deficiencies and further biochemical evaluation of the venom's effects on coagulation factors may improve our understanding of the relationship between hemotoxins and the resulting envenoming syndromes.

Curriculum Vitae

Satariya Trakulsrichai

- Citizenship: Thailand
- Employment:
  - ✓ **Attending staff and consultant**, Department of Emergency Medicine and Ramathibodi Poison Center, Faculty of Medicine Ramathibodi Hospital, Mahidol University
- Academic & Administrative responsibilities:
  - ✓ **Secretary**, the Thai Society of Clinical Toxicology
  - ✓ **Committee and a working group** on venomous marine animals in Thailand
- Received awards
  - ✓ **The best original research Award** at the 16th Annual Scientific congress of APAMT
  - ✓ **The Outstanding and Excellent Researcher Award 2020** from Thai College of Emergency Physicians

ABSTRACT

Interesting points of snake envenomation: Experience from Thailand

World Health Organization stated snakebite envenomation as a high priority neglected tropical disease that is accountable for enormous morbidities and mortalities in many areas and countries around the world.

In Thailand, snakebite envenomation is endemic and one of important health problems. The venomous snakes commonly affect either hematologic or neuromuscular systems such as green pit viper (Trimerusurus spp.) or cobra (Naja spp.). Many patients with snakebite were consulted and referred to the Ramathibodi Poison Center (RPC) approximately 1,000 cases/year.

This topic covers the general data of snakebite envenomation in Thailand including the rare venomous species such as Ovophis spp. or Rhabdophis subminiatus. Some interesting points of snake envenomation from RPC's experience such as some interesting clinical manifestations or laboratory findings, were described and reviewed.

Curriculum Vitae

Ahmad Khaldun Bin Ismail

- Citizenship: Malaysia
- Academic Affiliation:
  - ✓ Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur
- Academic Position:
  - ✓ Associate Professor & Consultant Emergency Physician
- Academic & Administrative responsibilities:
  - ✓ UKM Ethics and Medical Research Committee (2017-)
  - ✓ Honorary Consultant, National Poison Center, Universiti Sains Malaysia, Pulau Pinang, Malaysia (2021-2022)
  - ✓ Resource Person (Expert), Malaysian Biodiversity Information System (MyBIS), Ministry of Energy and Natural Resources (2022-)

ABSTRACT

Clinical Presentation and Outcome of Naja Species Injuries Consulted to RECS Malaysia.

Snake related injuries (SRI) remains an important but under-reported public health hazard in Malaysia. Previous studies have identified Naja species as the most common venomous SRI in Malaysia. This presentation discusses on the clinical profile, the geographical distribution, the pattern of injury and management outcome of the two Naja species in Malaysia, namely Naja kaouthia and Naja sumatrana. This was a retrospective cross-sectional study of all probable and confirmed Naja species related injuries consulted to Remote Envenomation Consultation Services (RECS) from 2015 to 2019. Data was extracted into standardised data collection form and were descriptively analysed. A bivariate analysis using Chi square test or Fisher's exact test was used to measure clinical pattern of injury and outcomes between the two Naja species. An independent t-test was used to measure the duration of hospitalisation and amount of antivenom used between the two Naja species. The outcome of this study may help clinicians to better prepare and provide the optimal management to patients.

Curriculum Vitae

Tri Maharani

- Citizenship: Indonesia
- Employment:
  - ✓ **Emergency Medicine Specialist** at the Department of Emergency Medicine
  - ✓ **President** of Indonesia Toxinology
- Academic & Administrative responsibilities:
  - ✓ **Advisor Temporary**, WHO of snake bite
  - ✓ **Leader**, policy and programme, bite and sting animal venomous and toxin plantation
  - ✓ Program zoonosis and porgramme animal venomous and toxin plantation in ministry of health
  - ✓ **Coordinator** of RECS Indonesia

ABSTRACT

Research Micropechis ikaheka bites in West Papua Indonesia limitation antivenom an speciel geography to reduction cases

Background:

Indonnesia unique country ,west Indonesia same asia animal ad platation species and east Indonesia same Australia animal and plantation ,West Papua have snake name microphecis ikaheka.in 2012 until 2022 Indonesia toxinology habe report many cases microphecis ikaheka bites and most of cases death.In 2022 research about why many cases death collaboration Indonesia toxinology and new program bite and sting national program in Ministry of health.

Analysis:

Many causes make cases death from microphecis ikaheka death .This research analysis factor factor interna and externa and limitation many cases. Mystic inn papua first causes make delay go to medical and have medication,and geography west papua make difficult transportation and first aid in this cases.Prosentation cases death and life must make policy to help many people in west papua.

Conclusion:

Need good education community in West papua.need rapid transportation to deliver systemic cases , many antivenom and equipment to manajemen emergency condition example equiment airway ,breathing and circulation .All health worker must continue training to first aid and manajemen emergency condition

Curriculum Vitae

Sir David Alan Warrell KCMG

- Citizenship: British citizen
- Employment:
  - ✓ **Emeritus Professor** of Tropical Medicine, Honorary Fellow, St Cross College, University of Oxford
  - ✓ **"Profesor Honorario"** Universidad Nacional Mayor de San Marcos, and Hon.
- Academic & Administrative responsibilities:
  - ✓ WHO: Member, Expert Advisory Panel on Malaria and CHEMAL committee
  - ✓ Hon Consultant: (Malariologist) to the British Army
- Decorations:
  - ✓ **Companion of The Most Exalted Order of The White Elephant** (appointed by His Majesty King Bhumibol Adulyadej of Thailand)
  - ✓ **Knight Commander of The Most Distinguished Order of Saint Michael and Saint George** For services to global Health Research and Clinical Practice (Her Majesty The Queen's Platinum Jubilee Birthday Honours)
- Distinctions:
  - ✓ **Sir Patrick Manson Medal**, Royal Society of Tropical Medicine and Hygiene
  - ✓ **Chalmer's Medal** (Royal Society of Tropical Medicine & Hygiene)

ABSTRACT

Antivenoms: clinical assessment of their effectiveness and safety

Perceptions of the effectiveness of many therapeutic interventions have been based on anecdote. In Vietnam in 1896, two people were bitten by Naja kaouthia. The one treated with Calmette's antivenom survived, while the other untreated case died. The concept of antivenom treatment was launched internationally, based on this insubstantial anecdote. Twelve decades later, nothing has changed, and the wide acceptance that antivenom is life-saving has virtually excluded the possibility of carrying out definitive randomised, placebo-controlled clinical trials in human patients.

Pre-clinical testing of antivenoms has by in vitro antivenomics, but cruel in vivo rodent assays to determine LD50/ED50 remain regulatory imperatives. Species differences in venom susceptibility and the pre-incubation of venom and antivenom used in rodent assays are severe limitations of these tests, but what is the alternative?

ABSTRACT

Antivenoms: clinical assessment of their effectiveness and safety

Conventional clinical evaluation of a drug proceeds through Phase I (in a small number of healthy volunteers to detect common adverse effects and roughly to estimate effectiveness and likely initial dosage), Phase II (in larger numbers, perhaps 100-300, to provide stronger guidance for likely effectiveness hence appropriate dosage in Phase III), Phase III (in substantial numbers, usually more than 300, determined by calculation of statistical power), to Phase IV (post-marketing clinical surveillance). Phase II and III studies should be randomised, double-blinded (to avoid assessment bias), and comparative. In the absence of placebo, different doses or types of antivenoms can be compared, using non-inferiority design. Antivenoms are too dangerous to be given to healthy people, but risks might be justified if they were given under close medical supervision to consenting patients with mild systemic envenoming.

In fact, few antivenoms receive any kind of formal clinical testing before they are marketed, due to the many practical, logistical, clinical and ethical issues in the resource-poor LMICs where they are largely deployed. This is a major obstruction to antivenoms' being accepted as safe and effective drugs. Solutions must be found!

ABSTRACT

Therapeutic innovations in Toxinology: the gulf between an idea and its implementation

Over the last 10 years, there has been a remarkable surge in new ideas about improving the treatment of snakebite envenoming that is most welcome!

It is widely accepted, as a result of decades of clinical use, that some specific antivenoms - hyperimmune sera raised in large animals - the only available antidotes for envenoming, can reverse anti-haemostatic effects, shock and post-synaptic neurotoxicity; and prevent or limit pre-synaptic neurotoxicity, local tissue damage and rhabdomyolysis. However, antivenoms carry the risk of severe adverse reactions, do not cover some medically-important species and geographical venom variants, and have insufficient potency in their current formulations.

ABSTRACT

Therapeutic innovations in Toxinology: the gulf between an idea and its implementation

New strategies include:

1-Improving design, refinement/purification, and concentration of conventional polyclonal animal-derived antivenoms: suggested innovations include the use of lower molecular weight, more diffusible, camelid heavy chain antibodies; and harnessing alternative immunogens such as synthetic peptide epitopes, recombinant toxins/toxoids, DNA strings, etc.

2- Monoclonal or oligoclonal antivenoms: use of these epitope-specific antibodies is complicated by the sheer number/diversity of venom toxins' epitopes that are proven or potentially damaging in human patients.

3- Non-antibody based innovative treatments: these include oligonucleotide aptamers, nanoparticles, peptides, naturally occurring protein inhibitors, and, most promising, small molecule enzyme inhibitors. Venom enzyme inhibitors are directed against phospholipases A2 (e.g. Veraspladib), Zn2+ metalloproteinases (e.g. chelators such as marimastat), serine proteases, and hyaluronidase. Some of these compounds have already been tried, unsuccessfully, in patients suffering from other diseases and may have been registered and are, therefore, "repurposable".

However, none of these promising new ideas will become more that academic notions/hypotheses unless they can be tested in human patients, singly or in combination, to demonstrate their safety and effectiveness, and to derive appropriate dosaging.

Clinical testing will become the bottleneck for advances in snakebite treatment unless more support is provided for what is currently perceived as being far less exciting than the easier task of laboratory-based innovation.

Curriculum Vitae

Knut Erik Hovda

- Citizenship: Norway
- Emplyment:
  - ✓ **CEO** of Orphan Diagnostics A/S (2018-)
  - ✓ **Clinical Consultant** of National Poisons Information Center, Oslo (2011-)
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- Principal research interests:
  - ✓ Methanol and ethylene glycol toxicity
  - ✓ Metabolic Acidosis
  - ✓ Epidemiology of poisonings
  - ✓ Toxicology in the developing world
  - ✓ Critical Care Toxicology

ABSTRACT

Interpretation of the blood gas – a simplified approach with a special focus on the metabolic acidosis

Blood gas machines have an inherent strength in that it can provide a lot of information within minutes at the bedside; and although it seldom reveals the cause of the disturbances, it gives a snapshot of the current respiratory- and metabolic situation. While the respiratory parameters typically requires the analysis to be done on arterial blood, both arterial- and venous blood will be useful in the interpretation of the metabolic parameters. The availability of blood-gas machines is typically very good in the high-income countries, whereas the availability in low- and middle-income countries is more limited.

Depending on the various models, the machines typically provides information on the acid-base status, the respiratory status, lactate, electrolytes (typically Na+, K+, Ca2+, often Cl-), hemoglobin and glucose. Some will also analyze for carbon monoxide and methemoglobin. Some of the parameters are measured (e.g., pH, pO2, pCO2 etc.), while some are calculated (HCO3-, BE, etc.).

The respiratory disturbances is typically easy to interpret, whereas the metabolic disturbances can represent a challenge. The severely ill patients will sometimes have various disturbances on the blood gas simultaneously, and in a stressful situation in a busy hospital, important information can easily be overlooked. The present lecture describes the most important features of the blood gas, especially looking at a simplified and structured way to interpret the metabolic acidosis.

Conflict of interest: The presenter is a co-inventor and co-owner of Orphan Diagnostics (OD), a company dedicated to produce simple, bedside tools for diagnosis, such as a formate strips for diagnosis of methanol poisoning. OD does not at present have any commercially available products on the market.