INTRA-CARDIAC THROMBUS FORMATION INDUCED BY CARBON MONOXIDE POISONING: A CASE REPORT

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Carbon monoxide (CO) is one of the leading causes of poisoning substances. It can inhibit the delivery of oxygen and cause sequential ischemic change, ending with death by multiorgan failure. And there are few cases about thromboembolic accidents by CO poisoning. However, intracardiac thrombus formation is rarely described as of yet. A previously healthy, 24-year-old woman was referred for carbon monoxide poisoning. She attempted suicide and her initial mental state was drowsiness with focal memory loss. Her initial carbon monoxide fraction was 16%. In the initial laboratory data, CK-MB 90.6 ng/mL (upper limit 5 ng/mL), Troponin I 1.9 ng/mL (upper limit 1.5 ng/mL) were observed. Transthoracic echocardiography (TTE) was done 24 hours from the accident. It revealed 30 x 15 mm nodular echogenic mass in the right atrium (RA). Anticoagulation with enoxaparin was started with hyperbaric oxygen therapy. After 7 days of heparinization, the large thrombus in RA disappeared. This report describes an intracardiac thrombus formation induced by CO poisoning. Because intracardiac thrombus can lead to pulmonary embolism and cerebral embolic infarction, the consideration of it in CO poisoning is important.
EPIDEMIOLOGIC CHARACTERIZATION OF POISONING BY ALDICARB IN RIO DE JANEIRO, BRAZIL

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Aldicarb is a systemic carbamate pesticide used to control nematodes in soil and insects and mites on a wide variety of crops, grain, including citrus fruits, potatoes, peanuts, soy beans, sugar-beet and tobacco. Nowadays, the commercialization of aldicarb has been controlled in several countries and others have been banned, but in Brazil this product may still be found. With his extensive use in Rio de Janeiro, Brazil, we can see a great number of human acute poisoning, a lot of these fatal, because the aldicarb has been illegally used (as rodenticide) since the 80’s. Monthly arrive at the Forensic Institute about 4 suspected cases of poisoning by aldicarb. This study found that, in the period between 1999 and 2011, were received at the Laboratory of Forensic Toxicology 637 suspected cases of aldicarb poisoning, of which 79,9\% were positive (509 cases). The contentious issue is of great relevance to public health and aims to draw the attention of government authorities so that this pesticide is finally banned in our country.
PSP (PARALYTIC SHELLFISH POISONING) TOXINS IN PHYTOPLANKTON OF THE GULF OF THAILAND

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The occurrence of PSP toxins (as saxitoxins equivalent) was investigated from 387 phytoplankton samples representing 21 localities in 5 regions of the Gulf of Thailand. Receptor Binding Assay (RBA) demonstrated PSP toxicity in 19 localities (86 samples). The total toxin contents varied between 13.3 and 1387.7 with the median of 92.5 ng STX equivalents L\textsuperscript{-1} SW. Two samples from 2 localities contained more than 1000 ng STX equivalents L\textsuperscript{-1} SW (1032.2 and 1387.7 ng STX equivalents L\textsuperscript{-1} SW, respectively). Both two located in the Upper Gulf of Thailand with PSP constituting more than 70\% of the total toxin content. In contrast, the highest frequency of phytoplankton found PSP positive (40\% of 43 samples) were in the Andaman Sea. The second most frequent found were in the Eastern Gulf (28\% of 86 samples); followed by the Upper Gulf (20\% of 194 samples), Southern Gulf (15\% of 34 samples) and Central Gulf (6\% of 30 samples), respectively. Temporal variations showed no significant correlation between toxin contents and seawater physical and chemical properties i.e. dissolved oxygen, pH, salinity, temperature, and transparency. Toxin contents peaked in dry season from February to April then increased again but at a lesser extent in July to August. PSP concentrations in toxin test positive phytoplankton showed no correlation with those in bivalves (from our previously investigation) with the correlation coefficients $R^2=0.001$. 

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TOXICOLOGY FINDINGS OF BLOOD METHAMPHETAMINE CONCENTRATIONS AND MANNER OF DEATH IN BANGKOK

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Methamphetamine (MA) is the major illicit drug in Thailand. The blood MA concentrations represent the symptomatic of MA appearance and intoxication such as hallucination, abnormal excitement, poisoning and finally death. Seventy MA-related deaths out of total of 2,018 unnatural autopsy cases (3.46%) of Institute of Forensic Medicine were collected from April to August 2011. The concentrations of MA in blood were analyzed by GC/MS/MS Triple Quadrupole (Agilent 7000B GCMS Triple Quadrupole, USA). In this study, the mean age for 67 males and 3 females was 32.3 years. Mean blood MA concentration was 12.8 µg/mL (range from 59 ng/mL to 717 ug/mL). The high concentrations of blood MA over 1500 ng/mL (24 of 70 cases) were found in manner of death which due to violence and crime (homicide 41.7%, suicide 8.3% and accident 16.7%). On the other hand, 33.3% of undetermined group occurred as a consequence of MA-related death. These findings indicated the importance of social problems due to MA abuse and MA-related death in Bangkok.
A CASE OF METHEMOGLOBINEMIA AFTER INGESTION OF NAPROXEN

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To report a case of acute methemoglobinemia in a patient treated with naproxen for the common cold. A 42-year-old asian woman received atenolol 25mg and atorvastatin 20mg for 6 years for hypertension and hyperlipidemia; lorazepam 1mg, trazodon 50mg, and paroxetine 20mg for 3 years for alcohol dependence and depression from a local psychiatric clinic, and acamprosate 333mg for 6 months for alcohol dependence. Yet she continued to ingest alcohol (20%) 300~600mL every day. Three days prior to visiting the ER, the patient began taking Naproxen sodium and Methocarbamol for mylagia, chills and coughing. One day prior to visiting the ER, the patient was presently taking lorazepam, trazodon, paroxetine in addition to the Naproxen and Methocarbamol prescribed for the cold symptoms and ingested approximately 300mL of alcohol (20%) and then went to sleep. She soon developed dyspnea and dizziness. She was found to have severe methemoglobinemia (serum methemoglobin fraction 49%; reference range 0–0.2). Her symptoms improved substantially, and serum methemoglobin levels decreased after the initiation of methylene blue therapy. 10 days after visiting the ER, she was discharged without any complications. Currently there has been no report of Naproxen intake causing methemoglobinemia. However, Naproxen is known to cause oxidative stress. In particular, in G6PD deficiency, oxidative stress has been reported to cause hemolysis or methemoglobinemia. Furthermore, alcohol is known to cause G6PD deficiency and thus it is hypothesized that the administration of naproxen in an alcohol dependent patient caused methemoglobinemia. Care must be taken when prescribing Naproxen to an alcohol dependent patient.
ASSOCIATION BETWEEN P53 CODON 72 POLYMORPHISM AND GASTRIC CANCER RISK IN THAI POPULATION

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Gastric cancer is a new public health problem in Thailand since the incidence and mortality rate of this cancer are increasing yearly. P53 codon 72 polymorphism has been reported to be associated with various cancers including gastric cancer. The objective of this study was to evaluate an association between P53 codon 72 polymorphism and gastric cancer risk in Thai population. The hospital based case-control study was conducted in 96 gastric cancer patients and 148 healthy controls (age-matched) by using real-time polymerase chain reaction with a TaqMan probe assay. The frequencies of Arg/Arg, Arg/Pro and Pro/Pro genotypes of the P53 codon 72 polymorphism were 33.8 (50/148), 47.3 (70/148), and 18.9 (28/148) % in the controls and 22.9 (22/96), 50.0 (48/96) and 27.1 (26/96) % in the gastric cancer patients, respectively. The Pro/Pro genotype was associated with an increased risk for gastric cancer development [odds ratio = 2.11, 95% confidence interval (CI) = 1.01-4.39, P = 0.04]. However, the significant interactions between the P53 codon 72 polymorphism and smoking and drinking were not observed. The results of this study suggest that P53 codon 72 polymorphism is associated with gastric cancer risk and the Pro/Pro genotype may be a useful risk factor for prediction of gastric cancer development in Thai population.
MULTIPLE ORGAN FAILURE AFTER OXALIC ACID INGESTION

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INTRODUCTION: Oxalic acid ingestion, available as laundry bleach, is an emerging agent among self-poisoning cases referred to the poison center with a high case fatality. CASE PRESENTATION: This is a case of 28 year old man who presented with systemic complications after intentional oxalic acid ingestion. Patient was seen with abdominal pain following ingestion of 10 g oxalic acid mixed with water. Caustic injury was ruled out normal endoscopic findings. Acute kidney injury evidenced by acute oliguric renal failure ensued within 6 hours. Patient underwent five sessions of hemodialysis and before renal function indices returned to normal and calcium oxalate in the urine was no longer evident. Other systemic manifestations noted were metabolic acidosis with elevated anion gap with persistent hypocalcemia, and episodes of QT prolongation. Respiratory distress developed on the third day with signs of acute lung injury. Supportive management was given with hemodialysis, supportive mechanical ventilation, hydration, and electrolyte correction were given. Use of antidotes such as N-Acetylcysteine as nebulization to address lung injury and potassium citrate postulated to inhibit calcium oxalate supersaturation in the renal tubules were included in the treatment regimen to address organ specific injury from oxalate. Patient was discharged after intensive care. DISCUSSION: Pathophysiologic findings following oxalic acid ingestion results from intraluminal crystal deposition with renal biopsy specimen showing the degeneration of the renal tubular epithelial cells associated with intracellular calcium oxalate crystal deposition resulting to acute renal failure. Systemic deposition resulting to widespread oxalosis, is postulated to cause the multiorgan failure exhibited in the course of the patient. LESSONS LEARNED: Early identification of systemic complications of a caustic substance is imperative with adequate supportive management to avoid morbidity. It is recommended that oxalic acid ingestion be included in the continued toxicovigilance and promotion of regulation controls on availability of toxic household chemicals be implemented.

Keywords: Oxalic acid ingestion, Acute renal failure, Household chemical
MERCURY INDUCED OXIDATIVE STRESS AND THE ROLE OF N-ACETYL CYSTEINE AND SELENIUM SUPPLEMENTATION DURING CHELATION: A POSSIBLE APPROACH

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Mercury toxicity is also considered the second-most common cause of acute heavy metal poisoning, with 3,596 cases reported in 1997 by the American Association of Poison Control Centers. Mercury and its derivatives have become an alarming environmental problem, necessitating the search for effective companion formula, which are generally used in micro doses and are devoid of any palpable side-effects. This study was undertaken to study the protective effect of N-acetyl cysteine and selenium alone or in combination against mercuric chloride toxicity in rats. Male Sprague Dawley albino rats (150 ± 10 g) were randomly divided into five groups. Group 1 served as control. Group 2-4 were administered HgCl₂ (12 µmol/kg, i.p.) once only and group 2 served as experimental control. Animals of group 3, 4 and 5 received NAC (NAC: 2 mM/kg, i.p.), Se (Se: 0.5 mg/kg, p.o.) and NAC + Se. Compared to the control, HgCl₂ treatment provoked significant increase (P ≤ 0.05) in of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), bilirubin, γ-glutamyl transpeptidase (γ-GT), cholesterol, triglycerides (TG), protein, urea, creatinine, uric acid, blood urea nitrogen (BUN) content with a decrease albumin concentration in serum. The results demonstrate that treatment with NAC, Se and NAC+ Se provided protection against mercuric chloride treatment caused the altered indices to return to near normal levels. Histopathological analysis was consistent with the biochemical observations and led to conclude that combination therapy provided protection against mercury toxicity.

Keywords: Mercury, N Acetyl Cysteine, Selenium, Oxidative stress
ANTIOXIDANTS WITH CHELATING AGENTS IN THE DIAGNOSIS AND TREATMENT OF PUTATIVE MERCURY POISONING

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Mercury commonly used in industrialized countries, adversely affects human and animal’s physiological and biochemical functions. Mercury exposure is the second-most common cause of toxic metal poisoning. Male albino rats were administered a bolus dose of dimethylmercury (1.0 mg/kg) orally for 12 weeks (5 days/week). The chelation therapy with NAC alone and combination with antioxidants as zinc and selenium was given for (2 days/week) after toxicant administration. Animals of all groups were sacrificed after 48 h of last treatments and various blood & biochemical parameters were performed. In the present study demonstrated that chronic exposure of dimethylmercury led to mark a significant rise in bilirubin, $\gamma$-GT, cholesterol, triglycerides, urea, creatinine and uric acid content with a concomitant decline in albumin concentration. Significant elevation was observed in LPO and mercury concentration in liver, kidney & brain however a concomitant decline was observed in GSH level after toxicant administration in the same organs. A noticeable fall was observed in the brain marker enzyme acetyl cholinesterase. Combined treatment of zinc and selenium with N-acetyl cysteine to dimethylmercury-exposed rats showed a substantial reduction in the levels of DMM-induced oxidative damage and comet tail length. In conclusion, the results of this study support that the supplementation of zinc and selenium with N-acetyl cysteine can improve theDMMinduced blood and tissue biochemical oxidative stress and molecular alterations by recoupment in mean DNA damage.

Keywords: N-acetyl cysteine, zinc, selenium, lipid peroxidation, reduced glutathione, acetyl cholinesterase
HEMATURIA, AN UNUSUAL SYSTEMIC TOXICITY, IN FORMIC ACID INGESTION: A CASE REPORT

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Systemic toxicities occur in some caustic ingestion patients, however hematuria is a rare toxicity reported. In this report, we describe a case of a 1-year-old female child who accidentally ingested liquid formic acid. This patient had severe local corrosive effect included upper respiratory tract compromise and developed gross hematuria during the hospital admission and resolved without specific treatments. The investigations worked up for the cause of gross hematuria were done but could not find any abnormalities. Hematuria might be one of the systemic effect from caustic ingestion.
JUGLANS REGIA L. (WALNUT) EXTRACT AMELIORATES CYCLOPHOSPHAMIDE INDUCED ACUTE LUNG INJURY IN MALE RATS

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Cyclophosphamide (CP) is an alkylating antineoplastic drug widely used in cancer chemotherapy. Among the various side effects of CP, lung toxicity is a major deterrent in its clinical use. *Juglans regia* L. commonly known as walnut has been proven as a good protective agent against pulmonary toxicity because it is rich in antioxidants content. We wanted to study the prophylactic effect of total methanolic extract of *J. regia* on the toxicity profile of CP with special focus on pulmonary toxicity. An acute study was conducted on male Wistar rats. In a 7 day of treatment schedule, rats were exposed to CP (250 mg/kg b.wt. *i.p.*) and plant extract (200mg/kg b.wt. *per os*) Antioxidant profile in lung tissue and enhancement in the level of inflammatory markers in the bronchoalveolar lavage fluid (BALF) was measured along with histopathological examination. A marked decrease in the activities of antioxidant enzymes such as glutathione peroxidase, glutathione reductase, glutathione S-transferase, superoxide dismutase and catalase were observed in the lung tissue which was significantly restored by *J. regia* extract. *J. regia* extract significantly decreases the protein carbonyl content which was significantly increased by CP indicating protein oxidation. Treatment of *J. regia* also caused significant decrease in lipid peroxidation and increase in reduced glutathione content in rat lungs. In BALF, a marked enhancement in the level of inflammatory markers such as alkaline phosphatase, lactate dehydrogenase, myeloperoxidase and total cell count was observed which was diminished by *J. regia*. Histological findings strongly support these biochemical observations. Histological examination of lungs showed changes such as inflammation and fibrosis in CP exposed rat lungs which was attenuated by plant extract. CP exposure to rat lungs showed a toxic effect, especially disruption of lung antioxidant profile and inflammatory response in BALF. *J. regia* proved as a powerful protective agent against CP induced acute lung toxicity in rat lungs.
POISON CENTRE’S IN AFRICA: A ONE YEAR COMPARATIVE STUDY (2011)

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Aim: According to the World Health Organization there are currently 14 Poison Information Centre’s in Africa. The aim of this pilot study was to comparing the spectrum of consultations dealt with by African Poison Centre’s. Methods: Questionnaires were sent to Centre’s. Information required: number and time of communications, interlocutors, patient demographics, intentional/accidental, substance categories, substances most commonly encountered. Results: 44% responded. Two centre’s use the INTOX Database provided by WHO. Kenya and Zimbabwe provided estimations of communications. Morocco received the largest number of communications (36681) of which 57% were by mail. South Africa 6232, Kenya 469 and Zimbabwe – (%estimation due to incomplete recording) all received only telephonic consultations. 92% of Moroccan calls were received within office hours, other centre’s calls varied between 10h00 and 22h00. Age distribution was similar (±50% vs ±50%) except in Zimbabwe where 82% were due to adult exposures. 82% of exposures in Morocco were accidental whereas when compared to the other centre’s the ratio of accidental to intentional were ±58% vs ±42%. South Africa and Morocco dealt with similar percentages of exposures in children and adults (52% vs 48%). 82% of exposures dealt with in Zimbabwe were adults. Pharmaceutical exposures varied between 7% to 45%, non-drug chemicals between 15% and 69% and biologicals between 8% and 75%. 74% of cases in Morocco were due to scorpion sting, pesticide exposures were highest in Kenya (42%) and Zimbabwe (36%). In South Africa analgesics, e.g. paracetamol, was responsible for most exposures. Conclusion: An important finding was the lack of reliable data collection. Morocco receives most communications by mail. An interesting observation was the high number of scorpion sting dealt with by the Moroccan Centre. The other Centre’s deal mostly with pesticide exposures. Further analysis of comprehensive PIC data is needed before a meaningful conclusion can be made.
EFFECTS OF LAMOTRIGINE, LEVETIRACETAM AND TOPIRAMATE ON SERUM TRACE ELEMENT STATUS AND OXIDATIVE STRESS IN RATS

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Background and Objectives: Experimental and clinical studies indicate that conventional antiepileptic drugs (AEDs) can alter the homeostasis of trace elements, electrolytes and increase membrane lipid peroxidation at the expense of protective antioxidants. This information is lacking for the newer AEDs. We therefore studied trace metal status and oxidative stress in rats treated chronically with, lamotrigine, levetiracetam and topiramate in comparison with valproate.

Methods: Thirty male wistar rats were randomly divided into 5 groups and treated orally with vehicle (controls), sodium valproate (370 mg/kg), lamotrigine (50 mg/kg), levetiracetam (310 mg/kg) and topiramate (100 mg/kg) for 45 days. The level of serum zinc, selenium, copper, iron, manganese, cobalt and aluminium were determined using inductively coupled plasma-atomic emission spectrometry (ICP-AES) at baseline and at the end of treatment. Oxidative stress parameters [malondialdehyde (MDA), reduced glutathione (GSH) and superoxide dismutase (SOD)] were also estimated in the rat brain.

Results: Serum iron and cobalt levels were significantly reduced with all the three newer AEDs (P < 0.05) while copper levels were reduced in the rats treated with valproate (P < 0.05) and levetiracetam (P < 0.01). Animals treated with levetiracetam had significantly increased aluminium levels (P < 0.05) while zinc levels were reduced (P < 0.01). Serum selenium levels were reduced in the valproate, levetiracetam and topiramate treated groups. In comparison to control group, MDA was higher in the levetiracetam (P < 0.01) and topiramate (P < 0.05) groups. GSH and SOD activity were significantly reduced by valproate, levetiracetam and topiramate treatment.

Conclusion: Treatment with dose equivalent to maximal therapeutic doses of AEDs can produce significant alterations in the trace element status. Reduced levels of iron, cobalt and copper may be responsible for some of the hematologic adverse effects of newer AEDs while reduced selenium levels may be associated with increased oxidative stress as seen with valproate, levetiracetam and topiramate in this study.
There is a considerable discrepancy between the number of identified occupational-related bladder cancer cases and the estimated numbers particularly in emerging nations or less developed countries where suitable approaches are less or even not known. Thus, within a project of the World Health Organisation Collaborating Centres in Occupational Health, a questionnaire of the Dortmund group, which has been applied in different studies, was translated into more than 30 languages (Afrikaans, Arabic, Bengali, Chinese, Czech, English, Finnish, French, Georgian, German, Greek, Hindi, Hungarian, Indonesian, Italian, Japanese, Kannada, Kazakh, Kirghiz, Korean, Malay, Persian (Farsi), Polish, Portuguese, Portuguese/Brazilian, Romanian, Russian, Serbo-Croatian, Slovak, Spanish, Spanish/Mexican, Tamil, Telugu, Thai, Turkish, Urdu, Vietnamese). The bipartite questionnaire asks for relevant medical information in the physician’s part and for the occupational history since leaving school in the patient's part. Furthermore, this questionnaire is asking for intensity and frequency of certain occupational and non-occupational risk factors. The literature regarding occupations like painter, hairdresser or miner and exposures like carcinogenic aromatic amines, azo dyes, or combustion products is highlighted.
ASSOCIATION BETWEEN HLA GENETIC POLYMORPHISM AND PHENYTOIN-INDUCED SEVERE CUTANEOUS ADVERSE DRUG REACTIONS IN A THAI POPULATION

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Aromatic antiepileptic drugs (AEDs) including carbamazepine (CBZ), phenytoin (PHT) and phenobarbital (PNB) are the common culprit drugs for severe cutaneous adverse drug reactions including Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Cross hypersensitivity between these AEDs, particularly between CBZ and PHT, have been reported. Recent evidences suggest that HLA-B*15:02 allele associate with the CBZ-induced SJS/TEN in certain ethnics. Although association between HLA-B*15:02 and PHT-induced SJS/TEN have been demonstrated in Han Chinese and Thai patients, the number of patients enrolled in those studies were very small. The aim of the present study was to determine the degree of association between PHT-induced SJS/TEN and HLA-B*15:02 as well as to explore the association between other HLA allele and PHT-induced SJS/TEN. Twenty five PHT-induced SJS/TEN and 74 PHT-tolerant patients were recruited in this study. Genomic DNA of each patient was extracted from peripheral blood. The HLA genotypes were determined using specific sequence oligonucleotide method. We found that the heterozygous HLA-B*15:02 was present in only 20% (5/25) of PHT-induced SJS/TEN patients whereas 14.86% (11/74) of PHT-tolerant patients carried this allele. There was no statistical significant association between HLA-B*15:02 allele and PHT-induced SJS/TEN which conflicts with previous studies. However, PHT-induced SJS/TEN were statistical significant associated with HLA-B*51:01, HLA-B*56:04 and HLA-C*14:02. In conclusion, HLA-B*51:01, HLA-B*56:04 and HLA-C*14:02 but not the HLA-B*15:02 allele may be a good genetic marker for PHT-induced SCAR in a Thai population. However, due to limited number of patients enrolled in this study, these association warrant to be confirmed in larger population.