IASP Special Interest Group (SIG) on the Prevention of Intentional Pesticide Poisoning

Bibliography: Study Design - Opinion

Agostini, M. and A. Bianchin (2003). "Acute renal failure from organophospate poisoning: a case of success with haemofiltration." Hum Exp Toxicol **22**(3): 165-167.

Severe organophosphate poisoning (OPP) has a high mortality rate. Respiratory and neurological complications are common in OPP. Multiple organ distress syndrome (MODS) and renal impairment are relatively rare but correlated with death. In previous publications, in patients who did not survive OPP, their deaths were due to MODS or acute renal failure. A case of intentional ingestion of an organophosphate with renal and multiple organ complications is described. In addition to the standard atropine/oxime regimen, continuous venous-venous haemofiltration (CVVH) therapy was started; the patient survived this intoxication. The pathogenesis of renal injury by OPP is unclear and more insight is required. In our experience, CVVH can be a valid therapy, considering in particular the toxicokinetics of the organophosphate.

Albers, J. W., P. Cole, et al. (1999). "Analysis of chlorpyrifos exposure and human health: expert panel report." J Toxicol Environ Health B Crit Rev **2**(4): 301-324.

This report summarizes the deliberations of an eight-member panel of scientists convened by Dow AgroSciences in cooperation with the U.S. Environmental Protection Agency (EPA). The panel was charged with evaluating the scientific literature on the health effects potentially associated with exposure to the insecticide chlorpyrifos. Specifically, the panel was asked to (1) evaluate human experience data available and address the adequacy of the available current literature; (2) develop a list of recommendations for epidemiology studies, including appropriate endpoints and study populations, and strengths and weaknesses of each approach; and (3) draft a report to summarize its recommendations. The panel assessed the quality of the existing epidemiologic literature on chlorpyrifos and specific outcomes such as neuropathy (including organophosphate induced delayed neurotoxicity), behavior (cognition and affect), immunologic, and multiple complaints (also referred to as multiple chemical sensitivities). The majority of panel members (five members) agreed that the literature reviewed provided little or no scientific evidence that chlorpyrifos exposure causes harm to human health other than its known cholinergic effects associated with acute poisoning. Those panel members voting in the minority (three members) agreed that the studies reviewed provided inadequate evidence to preclude the possibility of adverse effects to human health from chlorpyrifos exposure at levels associated with its manufacture or professional application. Those voting in the minority suggested further investigation of cohort(s) of workers engaged in either the manufacture or the professional application of chlorpyrifos, or both. Compared to the general population, these groups have relatively high levels of exposure to chlorpyrifos. The primary health outcomes recommended for study were cognitive and affective disorders, with consideration of the assessment of peripheral neuropathy also suggested for at least a subset of the cohort.

Ambade, V. N. (2004). "Self injection of insecticide." J Assoc Physicians India **52**: 169-170.

Baban, N. K., D. L. Nunley, et al. (1998). "Human sequelae of severe carbamate poisoning." Tenn Med **91**(3): 103-106.

Carbofuran is a carbamate that functions as a cholinesterase inhibitor. Accidental or intentional ingestion can produce a life-threatening syndrome that requires prompt diagnosis and treatment. We describe a case of intentional carbofuran ingestion that resulted in coma, respiratory failure from acute respiratory distress syndrome (ARDS), and cortical blindness.

Bairaktari, E., K. Katopodis, et al. (1998). "Paraquat-induced renal injury studied by 1H nuclear magnetic resonance spectroscopy of urine." Clin Chem **44**(6 Pt 1): 1256-1261.

The herbicide paraquat (1,1'-dimethyl-4,4'-bipyridylium dichloride; PQ), is a poison known to cause delayed mortality due to lung and kidney injuries. High-resolution proton nuclear magnetic resonance (1H NMR) spectroscopy has been extensively applied in evaluating nephrotoxicity by the characteristic perturbations in the excretion pattern of low molecular weight endogenous metabolites. The application of the method allows the rapid localization of the renal injury noninvasively. In this study, we report 1H NMR and conventional clinical chemistry urinalysis in two patients suffering from paraquat intoxication after overdose with suicidal intent. The alterations in the urine NMR spectrum suggest necrosis of the pars recta of the proximal renal tubules. The molecule of paraquat is also clearly detected in the same spectrum. In conclusion, the rapid screening of urine by NMR spectroscopy provides information about both the identity of the poison and the abnormal pattern of endogenous metabolites that characterize the location of the injury in renal tubules and reveals alterations in unusual metabolites that are not commonly measured.

Bardin, P. G., S. F. Van Eeden, et al. (1994). "Organophosphate and carbamate poisoning." Archives of Internal Medicine **154 (13)**: 1433-1441.

Organophosphate insecticides may cause serious poisoning either accidentally or by deliberate ingestion. Toxic symptoms are produced by acetylcholine accumulation at cholinergic receptors. Diagnosis is based on history of exposure or ingestion, symptoms and signs of cholinergic overactivity and a decrease in serum pseudocholinesterase levels. Following diagnosis, grading of disease severity may identify patients with serious poisoning who should receive treatment in intensive care using adequate doses of anticholinergic drugs. Complications, particularly ventricular arrhythmias, central nervous system depression or seizures, and respiratory failure, should be anticipated and treated. Relapse may occur after seemingly successful treatment. Public education with regard to symptoms of toxicity must be encouraged, and physicians must provide skilled treatment for a potentially lethal condition.

Barelli, A., P. M. Soave, et al. (2011). "New experimental Oximes in the management of organophosphorus pesticides poisoning." Minerva Anestesiol **77**(12): 1197-1203.

Organophosphorus compounds (OPCs) are widely used in agriculture as pesticides and occasionally in industrial settings. They have also been developed as warfare nerve agents. OPCs poisoning from intentional,

accidental, and occupational exposure is a major public health problem, especially across the rural developing world. The main toxic mechanism of OPCs is the inhibition of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), resulting in accumulation of acetylcholine (ACh) at the synapse with cholinergic crisis and possible death. Exposure to even small amounts of an OPC can be fatal and death is usually caused by respiratory failure. Standard treatment involves the administration of intravenous atropine and an oxime to counteract acetylcholinesterase inhibition at the synapse, but the usefulness of oximes is still debated. During more than five decades, pyridinium oximes have been developed as therapeutic agents used in the medical treatment of poisoning with OPCs. They act by reactivation of AChE inhibited by OPCs. However, their activity in poisonings with pesticides and warfare nerve agents is different, and there is still no universal oxime sufficiently effective against all known OPCs. The aim of this article was to review the most recent findings in this field and compare the protection conferred by the new K-oximes and sugar oximes with the effect of the four recommended pyridinium oximes (pralidoxime, obidoxime, trimedoxime, and HI-6), in the search for a broad-spectrum AChE reactivator.

Bazylewicz, A., T. Klopotowski, et al. (2010). "[Acute poisoning due to chemical substances inducing methemoglobinemia--two cases report]." Przegl Lek **67**(8): 636-639.

Methemoglobin is an oxidized derivative of hemoglobin. It is generated by oxidization the ferrous form of iron (Fe2+) in the heme molecule to the ferric form (Fe3+). A molecule of methemoglobin is incapable of binding and carrying of oxygen. Methemoglobinemia, an increased concentration of methemoglobin in the blood above 2%, may be congenital due to deficiency or lack of specific enzymes protecting hemoglobin from oxidization or abnormal structure of hemoglobin molecule. More often methemoglobinemia is acquired as a result of accidental or intentional poisoning due to chemical substances oxidizing hemoglobin. Some of them may induce hemolysis. Cyanosis resistant to oxygen therapy and dyspnea occur in patients with the methemoglobin concentration above 20%. Consciousness disorders, respiratory and circulatory failure, liver and kidney damage may occur in patients with high methemoglobin levels greater than 50%. Fatal cases have also been reported. In the paper we present two cases of patients who were admitted to our hospital ward. First of them regards a 21-year-old woman with the methemoglobin level of 38.3% induced by accidental inhalation exposure to aniline. The other case concerns a 49-year-old man who developed methemoglobinemia of 42.7% after suicidal ingestion of an urea-substituted herbicide containing linuron. We observed hemolysis in both of these cases. They were treated symptomatically and with a specific antidote--methylene blue.

Bensaude, R. J., P. Choutet, et al. (1979). "Self poisoning with phosphate and phosphorothioate ester pesticides. [French]." Revue de Medecine de Tours **13 (7)**: 1065-1067.

The ingestion of organophosphates in attempted suicide causes a very severe intoxication due to the slowness of the elimination of the substances ingested, which always gives rise to respiratory complications due to

bronchial hypersecretion, bronchospasm and respiratory paralyses. The 2 cases reported here illustrate the necessity of prolonged monitoring because of the major risk of retarded acute respiratory insufficiency; of course, this monitoring should be clinical, but the electromyographic controls constitute a new aid of prime importance for the indication and stopping of assisted respiration.

Benson, B. E., K. Hoppu, et al. (2013). "Position paper update: Gastric lavage for gastrointestinal decontamination." Clinical Toxicology **51 (3)**: 140-146.

The first update of the 1997 gastric lavage position paper was published by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists in 2004. This second update summarizes the 2004 content and reviews new data. Methods. A systematic review of the literature from January 2003 to March 2011 yielded few studies directly addressing the utility of gastric lavage in the treatment of poisoned patients. Results. Sixty-nine new papers were reviewed. Recent publications continue to show that gastric lavage may be associated with serious complications. A few clinical studies have recently been published showing beneficial outcomes, however, all have significant methodological flaws. Conclusions. At present there is no evidence showing that gastric lavage should be used routinely in the management of poisonings. Further, the evidence supporting gastric lavage as a beneficial treatment in special situations is weak, as is the evidence to exclude benefit in all cases. Gastric lavage should not be performed routinely, if at all, for the treatment of poisoned patients. In the rare instances in which gastric lavage is indicated, it should only be performed by individuals with proper training and expertise.

Bertolote, J. M., A. Fleischmann, et al. (2006). "Deaths from pesticide poisoning: a global response." Br J Psychiatry **189**: 201-203.

Self-poisoning with pesticides accounts for about a third of all suicides worldwide. To tackle this problem, the World Health Organization announced a global public health initiative in the second half of 2005. Planned approaches were to range from government regulatory action to the development of new treatments for pesticide poisoning. With broad-based support, this strategy should have a major impact on the global burden of suicide.

Bleakley, C., E. Ferrie, et al. (2008). "Self-poisoning with metaldehyde." Emerg Med J **25**(6): 381-382.

Metaldehyde poisoning is rare. This case report details the largest toxic dose of self-poisoning with metaldehyde ever recorded in the literature to the authors' knowledge, the aim being to emphasise the features of metaldehyde toxicity and the potential for good clinical outcome. The patient was admitted unconscious with features consistent with poisoning. Appropriate critical care was instituted early with correction of his acid-base disorder, ventilatory support, correction of haemodynamic instability, anticonvulsant therapy and early admission to the critical care unit. An almost complete recovery was seen over the following weeks, the only lasting deficit being to short-term memory, a finding common to other reported incidents of metaldehyde

toxicity. This case is notable in that the patient took more than one and a half times what is considered to be a lethal dose of metaldehyde (the largest reported), but has had a remarkably good clinical outcome that is proposed to be due to methodical and timely interventions delivered according to basic principles irrespective of the absence of the early identification of the poison. The case demonstrates several of the key features of metaldehyde toxicity and the emergency management of such a situation. The published literature pertaining to metaldehyde overdose is reviewed.

Bogle, R. G., P. Theron, et al. (2006). "Aluminium phosphide poisoning." Emerg Med J **23**(1): e3.

We describe a lethal poisoning in a healthy woman caused by deliberate ingestion of aluminium phosphide (AlP), a pesticide used to kill rodents and insects. Toxicity of AlP and review of cases reported to the National Poisons Information Service (London) 1997-2003 are discussed.

Bradberry, S. M., A. T. Proudfoot, et al. (2004). "Glyphosate poisoning." Toxicol Rev **23**(3): 159-167.

Glyphosate is used extensively as a non-selective herbicide by both professional applicators and consumers and its use is likely to increase further as it is one of the first herbicides against which crops have been genetically modified to increase their tolerance. Commercial glyphosate-based formulations most commonly range from concentrates containing 41% or more glyphosate to 1% glyphosate formulations marketed for domestic use. They generally consist of an aqueous mixture of the isopropylamine (IPA) salt of glyphosate, a surfactant, and various minor components including anti-foaming and colour agents, biocides and inorganic ions to produce pH adjustment. The mechanisms of toxicity of glyphosate formulations are complicated. Not only is glyphosate used as five different salts but commercial formulations of it contain surfactants, which vary in nature and concentration. As a result, human poisoning with this herbicide is not with the active ingredient alone but with complex and variable mixtures. Therefore, It is difficult to separate the toxicity of glyphosate from that of the formulation as a whole or to determine the contribution of surfactants to overall toxicity. Experimental studies suggest that the toxicity of the surfactant, polyoxyethyleneamine (POEA), is greater than the toxicity of glyphosate alone and commercial formulations alone. There is insufficient evidence to conclude that glyphosate preparations containing POEA are more toxic than those containing alternative surfactants. Although surfactants probably contribute to the acute toxicity of glyphosate formulations, the weight of evidence is against surfactants potentiating the toxicity of glyphosate. Accidental ingestion of glyphosate formulations is generally associated with only mild, transient, gastrointestinal features. Most reported cases have followed the deliberate ingestion of the concentrated formulation of Roundup (The use of trade names is for product identification purposes only and does not imply endorsement.) (41% glyphosate as the IPA salt and 15% POEA). There is a reasonable correlation between the amount ingested and the likelihood of serious systemic sequelae or death. Advancing age is also associated with a less favourable prognosis. Ingestion of >85 mL of the concentrated formulation is likely to cause significant toxicity in adults.

Gastrointestinal corrosive effects, with mouth, throat and epigastric pain and dysphagia are common. Renal and hepatic impairment are also frequent and usually reflect reduced organ perfusion. Respiratory distress, impaired consciousness, pulmonary oedema, infiltration on chest x-ray, shock, arrythmias, renal failure requiring haemodialysis, metabolic acidosis and hyperkalaemia may supervene in severe cases. Bradycardia and ventricular arrhythmias are often present pre-terminally. Dermal exposure to ready-to-use glyphosate formulations can cause irritation and photo-contact dermatitis has been reported occasionally; these effects are probably due to the preservative Proxel (benzisothiazolin-3-one). Severe skin burns are very rare. Inhalation is a minor route of exposure but spray mist may cause oral or nasal discomfort, an unpleasant taste in the mouth, tingling and throat irritation. Eye exposure may lead to mild conjunctivitis, and superficial corneal injury is possible if irrigation is delayed or inadequate. Management is symptomatic and supportive, and skin decontamination with soap and water after removal of contaminated clothing should be undertaken in cases of dermal exposure.

Brvar, M., R. Okrajsek, et al. (2008). "Metabolic acidosis in prometryn (triazine herbicide) self-poisoning." Clin Toxicol (Phila) **46**(3): 270-273.

INTRODUCTION: Prometryn is a triazine herbicide, which is one of the most extensively used groups of herbicides. The mechanism of acute triazine herbicide toxicity in humans is not known. We report a first case of acute prometryn poisoning. CASE REPORT: A 62-year-old male ingested 50 g of prometryn and ethanol in a suicide attempt. On arrival two hours after ingestion, he was somnolent and vomited. Seven hours after ingestion laboratory tests showed metabolic acidosis with a calculated anion gap of 47.5 mmol/L and lactate of 23.4 mmol/L. Gas chromatography/mass spectrometry revealed serum prometryn concentrations of 48.1 mg/L. Hemodialysis corrected metabolic acidosis, but the serum prometryn concentration increased to 67.7 mg/L. The lactate level after hemodialysis was 11.7 mmol/L and returned within normal limits 47 hours after ingestion. The patient was discharged without any sequelae after psychiatric evaluation. CONCLUSION: In high anion gap metabolic acidosis we should consider poisoning with prometryn and other triazine herbicides. Hemodialysis corrects metabolic derangements, but it does not lower serum prometryn concentration.

Buckley, N. A., M. Eddleston, et al. (2005). "The need for translational research on antidotes for pesticide poisoning." Clin Exp Pharmacol Physiol **32**(11): 999-1005.

1. Pesticide poisoning kills hundreds of thousands of people in the Asia-Pacific region each year. The majority of deaths are from deliberate self-poisoning with organophosphorus pesticides (OP), aluminium phosphide and paraquat. The current response from a public health, medical and research perspective is inadequate. 2. There are few proven or effective treatments; in addition, very little clinical research has been performed to transfer antidotes shown to work in animal studies into clinical practice. 3. The human toxicity of pesticides is poorly studied and better information may inform a more sustained and appropriate regulatory response. Further understanding may also lead to improvements in diagnosis and treatment. 4.

The few effective treatments are not being recommended or delivered in an optimal and timely fashion to poisoned patients. A regional approach to facilitate appropriate pricing, packaging and delivery of antidotes is required.

Buckley, N. A., L. Karalliedde, et al. (2004). "Where Is the Evidence for Treatments Used in Pesticide Poisoning? Is Clinical Toxicology Fiddling while the Developing World Burns?" Journal of Toxicology - Clinical Toxicology **42 (1)**: 113-116.

Caravati, E. M., A. R. Erdman, et al. (2007). "Long-acting anticoagulant rodenticide poisoning: an evidence-based consensus guideline for out-of-hospital management." Clin Toxicol (Phila) **45**(1): 1-22.

The objective of this guideline is to assist poison center personnel in the out-of-hospital triage and initial management of patients with suspected exposure to long-acting anticoagulant rodenticides (LAAR). An evidence-based expert consensus process was used to create this guideline. It is based on an assessment of current scientific and clinical information. The panel recognizes that specific patient care decisions may be at variance with this guideline and are the prerogative of the patient and health professionals providing care. The grade of recommendation is in parentheses. 1) Patients with exposure due to suspected self-harm, abuse, misuse, or potentially malicious administration should be referred to an emergency department immediately regardless of the doses reported (Grade D). 2) Patients with symptoms of LAAR poisoning (e.g., bleeding, bruising) should be referred immediately to an emergency department for evaluation regardless of the doses reported (Grade C). 3) Patients with chronic ingestion of LAAR should be referred immediately to an emergency department for evaluation of intent and potential coagulopathy (Grade B). 4) Patients taking anticoagulants therapeutically and who ingest any dose of a LAAR should have a baseline prothrombin time measured and then again at 48-72 hours after ingestion (Grade D). 5) Patients with unintentional ingestion of less than 1 mg of LAAR active ingredient can be safely observed at home without laboratory monitoring. This includes practically all unintentional ingestions in children less than 6 years of age (Grade C). 6) Pregnant patients with unintentional exposure to less than 1 mg of LAAR active ingredient should be evaluated by their obstetrician or primary care provider as an outpatient. Immediate referral to an ED or clinic is not required (Grade D). 7) Patients with unintentional ingestion of 1 mg or more of active ingredient and are asymptomatic should be evaluated for coagulopathy at 48-72 hours after exposure (Grade B). 8) Physicians' offices or outpatient clinics must be able to obtain coagulation study results in a timely manner, preferably in less than 24 hours, for patients who require outpatient monitoring (Grade D). 9) Gastrointestinal decontamination with ipecac syrup or gastric lavage is not recommended (Grade D). 10) Transportation to an emergency department should not be delayed for administration of activated charcoal (Grade D). 11) Patients with dermal exposures should be decontaminated by washing the skin with mild soap and water (Grade D). 12) The administration of vitamin K is not recommended prior to evaluation for coagulopathy (Grade D).

Cherin, P., E. Voronska, et al. (2012). "Acute toxicity of pesticides in human. [French]." Medecine et Longevite **4 (2)**: 68-74.

Pesticides constitute a very heterogeneous group of chemical substances adapted to the wrestling against plants and unwanted animals: weed-killers, fungicides, insecticides, acaricides, nematicides and rodenticides mainly. These phytosanitary products possess all a toxicity, of variable intensity, for the human. The acute toxicity of pesticides results from a misuse, from an accidental use of pesticides (accidents in the home) or from an often very serious voluntary poisoning. Organophosphate pesticides and carbamates are at the origin of the cases of poisonings by the most frequent pesticides. The exposure is essentially made by cutaneo-mucous and respiratory way, oral exposure would concern more the general population by accidental or deliberate ingestion of pesticides. According to the World Health Organization (WHO), there is every year in the world one million grave poisonings by pesticides, at the origin of approximately 220,000 deaths a year. 2012.

Chesneau, P., M. Knibiehly, et al. (2009). "Suicide attempt by ingestion of rotenone-containing plant extracts: one case report in French Guiana." Clin Toxicol (Phila) **47**(8): 830-833.

INTRODUCTION: Several species of plants in the Fabaceae family are traditionally used for poison fishing because they contain ichthyotoxic rotenoids. In French Guiana two species of Fabaceae belonging to Lonchocarpus genus with a toxic rotenone effect are used for such ancestral practices. Rotenone is of low toxicity for humans when it is diluted, but its neurotoxicity at higher concentrations is well known to users. CASE REPORT: The purpose of this article is to describe a case of self-poisoning by an 86-year-old woman who ingested a bowl of mashed ichthyotoxic plants. Despite early onset of severe symptoms, the patient regained consciousness and resumed normal breathing within a few hours with only symptomatic treatment. CONCLUSION: The clinical pattern observed in this patient (onset of digestive manifestations followed quickly by loss of conscience and respiratory insufficiency) is in agreement with the few poisonings reported in the literature involving other Fabaceae species containing rotenoids in Asia or involving concentrated rotenone used in insecticides. In patients, who survive the initial phase, symptoms usually regress quickly.

Chiu, H. F., S. S. Chan, et al. (2012). "Suicide prevention in the Asia-Pacific region." Asia-Pacific Psychiatry **4 (1)**: 3-4.

Chomchai, C. and A. Tiawilai (2007). "Fetal poisoning after maternal paraquat ingestion during third trimester of pregnancy: case report and literature review." J Med Toxicol **3**(4): 182-186.

INTRODUCTION: Paraquat remains one of the common substances involved in intentional ingestions in Thailand. However, data on outcomes of paraquat ingestion during pregnancy is rarely available and the management is controversial. CASE REPORT: A 17-year-old female in 36 weeks of gestation attempted suicide by ingesting 1/2 a glass of Gramozonetrade mark (paraquat 27.6 % w/v) 5 hours prior to arrival to the hospital. Gastric

aspiration and lavage was performed and she was given 50 g of activated charcoal and 150 g of Fuller's Earth suspension. A male infant, weighing 2,390 g with an Apgar score of 71 1010, was delivered via emergency caesarean section 7 hours after ingestion. Due to presence of paraquat in the gastric lavage fluid, the mother was placed on dexamethasone cyclophosphamide therapy. She developed mild renal insufficiency 63 hours after the ingestion. The infant developed tachypnea immediately after birth that self-resolved. The infant developed tachypnea again on day 6 of life. A chest x-ray revealed right lower lobe infiltration that progressed to diffuse interstitial pattern; subsequent chest x-rays showed evidence of fibrosis. Both mother and infant survived and the infant was discharged and sent home with oxygen 0.5 LPM. Upon follow up at 10 months of age, he still had evidence of chronic lung disease clinically and on chest x-ray. CONCLUSION: Paraquat ingestion during the third trimester of pregnancy usually carries a very poor prognosis. Review of reported literature suggests that this case report represents only the second survival of mother and child.

Connors, N. J., R. Biary, et al. (2013). "Comments on 'Spectrum of toxic hepatitis following intentional paraquat ingestion'." Liver Int **33**(3): 494.

Dadpour, B., M. Forooghian, et al. (2013). "A case report of deep coma in a pregnant women with amitraz poisoning." Iranian Journal of Obstetrics, Gynecology and Infertility **16 (45)**: 9-12.

Introduction: Pesticide poisoning is common in Iran especially in rural communities. Amitraz is a formamidine compound that the prevalence of its poisoning is less common than organophosphate poisoning. In this study a case of pregnant women with brain edema due to amitraz poisoning is reported. Case Presentation: A 15 years old female in 18th week of pregnancy was referred to Imam Reza hospital with history of deliberate consumption of about half a glass of liquid pesticide of amitraz, 5 hours before hospitalization. At first, she had nausea and vomiting then became confused in about an hour. Initial vital sign on arrival were: blood pressure: 90/60 mmHg, pulse rate 70, with Glasgow Coma Scale scores of 3/15. Both pupils were dilated and unresponsive to light. There was no evidence of trauma and no focal neurologic deficit signs. According to deep coma and moist mucous membranes, atropine and pralidoxime were prescribed assuming severe poisoning. Atropine and pralidoxime were discontinued when it became clear that was amitraz poisoning and treatment of cerebral edema was started due to cerebral edema was detected in brain CT-scan. Her consciousness gradually improved 3 days after admission. The patient was discharged after 3 days and 21 weeks later a healthy neonate was born by vaginal delivery. Conclusion: Amitraz poisoning has no known antidote and the symptoms improve with treatment in most of cases. 2013 All Rights Reserved.

Dally, S. (2000). "[Non-accidental criminal poisonings]." Rev Prat **50**(4): 407-409.

Among the different types of chemical aggressions, murder is very rare. Most cases are less straight forward: "jokes", ill-wills, impulsive acts.... Pesticides, metals, household products and illicit drugs are most often in cause, in addition to self-defence sprays. Intoxication may be suspected by the victim,

in which case paranoia should be eliminated. In other cases, unusual circumstances or symptoms are suspected by the physician. The toxicological analysis must be guided by the clinical context.

Davanzo, F., P. Vignally, et al. (2009). "Suicide attempt by poisoning in Italy: A preliminary characterization." Clinical Toxicology **Conference: 29th International Congress of the European Association of Poison Centres and Clinical Toxicologists Stockholm Sweden. Conference Start: 20090512 Conference End: 20090515. Conference Publication: (var.pagings). 47 (5)**: 477-478.

Objective: The availability of toxic chemicals and of selected pharmaceuticals tends to facilitate suicide acts by poisoning.¹ Therefore, accurate information about chemicals used and mode of exposure are important in order to devise national strategies and programmes for suicide and suicide attempt prevention. In the present study a preliminary characterization of suicide attempts by poisoning in Italy is provided. Methods: The Poison Control Centre of Milan (PCCM) handles about 60% of all cases referred to the PCCs active in Italy. For each patient examined, the PCCM collects the following information: demographic characteristics; exposure characteristics; clinical effects; therapy; outcomes. The PCCM database was searched to identify all cases with intentional exposure due to suicide attempts occurring in Italy in 2005. Results: In the period under study, the PCCM handled 42,483 new cases of human exposure and about 19% of them (n = 6699) were classified as due to suicide attempts. Among these patients there was an over representation of females (70 vs. 30%). The median age was 35 years (range: 8-95). About 83% of cases were exposed to pharmaceuticals, 14% to non pharmaceuticals, and 8% to both pharmaceuticals and non pharmaceuticals in combination. The route of exposure was mainly ingestion (97%), inhalation (1%) and parenteral (1%). The categories of agents most frequently reported were: sedative/hypnotics antipsychotics (43%), antidepressants (23%), analgesics (13%), anticonvulsants (11%), cardiovascular drugs (7%), and alcohol (7%). The group exposed to agricultural pesticides (1% of cases) was the only one with a higher percentage of men (65 vs. 35%). More than one agent was reported for about 45% of cases. Most of these were exposed to sedative/hypnotics antipsychotics in combination with other drugs (30%), mainly antidepressants (12%) and anticonvulsants (5%). Combined exposure to drugs and alcohol was reported in 6% of cases. Among these, about half were exposed to sedative/hypnotics/antipsychotics. Poisoning severity was low for 46% of cases, moderate for 48%, elevated for 6%. Death was reported in 5 cases. Conclusion: The observations reported here should be considered as a starting point for further analyses focused on specific chemicals and commercial products.

David, D., I. A. George, et al. (2007). "Toxicology of the newer neonicotinoid insecticides: imidacloprid poisoning in a human." Clin Toxicol (Phila) **45**(5): 485-486.

Imidacloprid, a potent neonicotinoid insecticide, is currently one of the best selling insecticides. We report a patient with clinical toxicity due to the ingestion of imidacloprid in a deliberate suicide attempt. The structure and mode of action of imidacloprid are discussed.

Davies, J., D. Roberts, et al. (2008). "Hypotension in severe dimethoate self-poisoning." Clin Toxicol (Phila) **46**(9): 880-884.

INTRODUCTION: Acute self-poisoning with the organophosphorus (OP) pesticide dimethoate has a human case fatality three-fold higher than poisoning with chlorpyrifos despite similar animal toxicity. The typical clinical presentation of severe dimethoate poisoning is quite distinct from that of chlorpyrifos and other OP pesticides: many patients present with hypotension that progresses to shock and death within 12-48 h post-ingestion. The pathophysiology of this syndrome is not clear. CASE REPORTS: We present here three patients with proven severe dimethoate poisoning. Clinically, all had inappropriate peripheral vasodilatation and profound hypotension on presentation, which progressed despite treatment with atropine, i.v. fluids, pralidoxime chloride, and inotropes. All died 2.5-32 h post-admission. Continuous cardiac monitoring and quantification of troponin T provided little evidence for a primary cardiotoxic effect of dimethoate. CONCLUSION: Severe dimethoate self-poisoning causes a syndrome characterized by marked hypotension with progression to distributive shock and death despite standard treatments. A lack of cardiotoxicity until just before death suggests that the mechanism is of OP-induced low systemic vascular resistance (SVR). Further invasive studies of cardiac function and SVR, and post-mortem histology, are required to better describe this syndrome and to establish the role of vasopressors and high-dose atropine in therapy.

Dawson, A. (2010). "Practical approaches to toxicosurveillance in Asia." Toxicology Letters **Conference: 12th International Congress of Toxicology Barcelona Spain. Conference Start: 20100719 Conference End: 20100723. Conference Publication: (var.pagings). 196**: S1.

Toxico-surveillance in Asia operates in an environment of variable quality non-harmonised regulatory systems, a large exposed populations, difficulties in communication and analytical capacity. It encompasses risk from deliberate, accidental, environmental and occupational exposure. As a major global supplier of many goods and medicines successful toxicosurveillance has both local and global importance. Thus any practical approach in Asia must involve current global toxicosurveillance mechanisms. Within Asia approaches fall into two broad areas most commonly spontaneous reporting and less commonly systematic data collection. The most widespread system is poison information centres, they have the advantage of relatively similar information structures and existing regional links. They are based on spontaneous reporting generally of acute events. There is evidence that these systems give comparable results to prospective studies for death. Also they have been able to pick up new sporadic events. There is considerable variation in the standard of poisons information centres and their ability to be effective. Prospective studies are expensive but have the capacity to collect more detailed information about exposure and clinical outcomes. In some areas such as pesticide toxicity acute exposures occur in populations who have high occupational/environmental exposure in these populations negative studies are very informative regarding chronic health effects. Proposed sentinel prospective monitoring sites could add greater depth to spontaneous reporting but are not likely to detect regional sporadic events. Systems based on repeated analytical testing are unlikely to ever be able to

have the capacity to address the large volume of sources of potential toxicological threat for example from adulterated traditional medicines. The most practical approach is to continue to improve networking between various monitoring services in the region and globally to detect early signals, then to provide appropriate capacity to investigate these signals. Ultimately toxicosurveillance must be linked to some capacity for response.

Dawson, A. H. and N. A. Buckley (2011). "Toxicologists in public health - Following the path of Louis Roche (based on the Louis Roche lecture "an accidental toxicologist in public health", Bordeaux, 2010)." Clinical Toxicology **49 (2)**: 94-101.

Background. The global burden of clinical toxicology suggests a natural partnership with public health. This article reflects the content of a Louis Roche lecture given in 2010. Historical context. Our practice and research in clinical toxicology has evolved from clinical cases to toxico-epidemiology to public health. This evolution in practice was initially unplanned but gained momentum and impact as we placed it more formally in a public health framework. This perspective is implicit in Louis Roche's call to "examine all aspects of the poisoning problem" and still provides a valuable starting point for any clinical toxicologist. Discussion. Clinical toxicology has always had a patient centered focus but its greatest successes have been related to public health interventions. Our early failures and later success in pubic health toxicology correlated with our understanding of the importance of partnerships outside our field. The most rapid dissemination and implementation of information derived from research occur through apriori partnerships with other agencies and international partners. Conclusion. Addressing both local and global need has a number of bilateral synergies. Repositioning clinical toxicology into a public health framework increases access to strategic partnerships, research funds, and policy implementation while still addressing questions that are important to clinical practice. 2011 Informa Healthcare USA, Inc.

De Wilde, V., D. Vogelaers, et al. (1991). "Postsynaptic neuromuscular dysfunction in organophosphate induced intermediate syndrome." Klinische Wochenschrift **69 (4)**: 177-183.

A 65-year-old Caucasian female developed an intermediate syndrome seven days after an acute cholinergic crisis, caused by the ingestion of fenthion. Cholinesterase activity in the blood, plasma and red cells was monitored daily by the method according to Nenner and serial serum fenthion levels were measured by capillary gas chromatography. Electromyographic studies showed fade on tetanic stimulation by means of surface electrodes at 20 Hz of the left M. abductor digiti quinti at day 7, which could no longer be observed at day 19. Fade on low-frequency stimulation and post-tetanic facilitation were both absent. A biopsy of the N. suralis was normal. A biopsy of the M. tibialis anterior revealed a limited rhabdomyolysis with a very weak staining for cholinesterase. It is hypothesized that the pathophysiologic process underlying the syndrome is the result of a time-confined phenomenon, which includes both changes in the postsynaptic structures by a desensitization process and a gradually restoring ratio of acetylcholine to acetylcholinesterase. This hypothesis is suggested by the similarity in the

EMG-findings of this patient and those in myasthenia gravis, which is known to be characterized by a postsynaptic transmission defect.

Dillard, M. and J. Webb (1999). "Administration of succinylcholine for electroconvulsive therapy after organophosphate poisoning: a case study." AANA J **67**(6): 513-517.

A 53-year-old man was admitted to the hospital psychiatric unit for evaluation and treatment following a recent suicide attempt, which involved ingestion of an unknown amount of Dursban (DowElanco, Indianapolis, Ind) and a self-inflicted knife wound to the abdomen. Dursban is a commercially prepared organophosphate insecticide in which the active ingredient is chlorpyrifos in a petroleum distillate solvent. The patient received 7 electroconvulsive therapy treatments during a 2-week hospital stay. The anesthetic regimen included methohexital for induction and succinylcholine for neuromuscular relaxation. Cholinesterase levels were low on admission at 5,780 IU (reference range, 11,000-15,000), yet succinylcholine was used successfully at low doses.

Dinis-Oliveira, R. J., P. G. de Pinho, et al. (2009). "Postmortem analyses unveil the poor efficacy of decontamination, anti-inflammatory and immunosuppressive therapies in paraquat human intoxications." PLoS One **4**(9): e7149.

BACKGROUND: Fatalities resulting from paraquat (PQ) self-poisonings represent a major burden of this herbicide. Specific therapeutic approaches have been followed to interrupt its toxic pathway, namely decontamination measures to prevent PQ absorption and to increase its excretion from organism, as well as the administration of anti-inflammatory and immunosuppressive drugs. Until now, none of the postmortem studies resulting from human PQ poisonings have assessed the relationship of these therapeutic measures with PQ toxicokinetics and related histopathological lesions, these being the aims of the present study. METHODOLOGY PRINCIPAL FINDINGS: For that purpose, during 2008, we collected human fluids and tissues from five forensic autopsies following fatal PQ poisonings. PQ levels were measured by gas chromatography-ion trap mass spectrometry. Structural inflammatory lesions were evaluated by histological and immunohistochemistry analysis. The samples of cardiac blood, urine, gastric and duodenal wall, liver, lung, kidney, heart and diaphragm, showed quantifiable levels of PQ even at 6 days post-intoxication. Structural analysis showed diffused necrotic areas, intense macrophage activation and leukocyte infiltration in all analyzed tissues. By immunohistochemistry it was possible to observe a strong nuclear factor kappa-B (NF-kappaB) activation and excessive collagen deposition. CONCLUSIONS/SIGNIFICANCE: Considering the observed PQ levels in all analyzed tissues and the expressive inflammatory reaction that ultimately leads to fibrosis, we conclude that the therapeutic protocol usually performed needs to be reviewed, in order to increase the efficacy of PQ elimination from the body as well as to diminish the inflammatory process.

Dinis-Oliveira, R. J., A. Sarmento, et al. (2006). "Acute paraquat poisoning: report of a survival case following intake of a potential lethal dose." Pediatr Emerg Care **22**(7): 537-540.

When properly used, paraquat (PQ) is a widely used bipyridil herbicide with a good safety record. Most cases of PQ poisoning result from intentional ingestion, with death resulting from hypoxemia secondary to lung fibrosis in moderate to severe poisonings. With high ingestion volumes (>50 mL of a 20% wt/vol formulation), death results from multiple organ failure and cardiovascular collapse within 1 week after intoxication. The present report describes a successful clinical case regarding the intoxication of a 15-year-old girl by a presumed lethal dose of PQ. The adolescent ingested approximately 50 mL of a commercialized concentrate (20% wt/vol of dichloride salt) formulation of PQ. High serum and urinary levels of PQ confirmed the bad prognosis. However, the therapeutic protocol followed in the present clinical case led to a positive outcome. Besides the measures for decreasing PQ absorption and increasing its elimination, other protective procedures were applied in aiming to reduce the production of reactive oxygen species (ROS), to scavenge ROS, to repair ROS-induced lesions, and to reduce inflammation. The status-of-the-art concerning the biochemical and toxicological aspects of PQ poisoning and the pharmacologic basis of the respective treatment is also presented.

Dive, A., P. Mahieu, et al. (1994). "Unusual manifestations after malathion poisoning." Human and Experimental Toxicology **13 (4)**: 271-274.

We report a case of organophosphate poisoning with a commercial preparation of malathion (deliberate ingestion of Malathane Garden Spray: malathion 15% in isopropyl alcohol) in which the initial cholinergic crisis was followed by cardiac, pulmonary, neurological and renal manifestations. They occurred when erythrocyte and plasma cholinesterases were reactivating. A chemical analysis of the pesticide preparation revealed, apart from malathion itself, the presence of isopropylmalathion and O,O,S-trimethylphosphorothioate. Although pure malathion is regarded as one of the safest organophosphate insecticides, this observation underlines the possibility of severe complications after exposure to a preparation which has been stored for a long period of time.

Drault, J. N., E. Baelen, et al. (1999). "[Massive paraquat poisoning. Favorable course after treatment with n-acetylcysteine and early hemodialysis]." Ann Fr Anesth Reanim **18**(5): 534-537.

Case report of a 30-year-old patient, admitted one hour after an intentional ingestion of paraquat (60 g). The initial treatment included gastric washing, parenteral n-acetylcysteine and forced diuresis. Considering the severity of the intoxication, conventional haemodialysis was started four hours after the ingestion. Plasma concentrations of paraquat, in the lethal range at admission, decreased rapidly and significantly after haemodialysis. This case raises the question of the part played by n-acetylcysteine and haemodialysis respectively in a favourable outcome. As the determination of paraquat blood concentrations requires some delay, these data are of no help for therapeutic decisions. Therefore, in cases of massive poisoning or uncertainty of the ingested dose, a technique of blood purification in indicated. Charcoal haemoperfusion is the most efficient, however conventional haemodialysis, which is more widespread, should be considered if the former is not available.

Eddleston, M. (2000). "Patterns and problems of deliberate self-poisoning in the developing world." QJM **93**(11): 715-731.

Deliberate self-harm is a major problem in the developing world, responsible for around 600 000 deaths in 1990. The toxicity of available poisons and paucity of medical services ensure that mortality from self-poisoning is far greater in the tropics than in the industrialized world. Few data are available on the poisons most commonly used for self-harm in different parts of the world. This paper reviews the literature on poisoning, to identify the important poisons used for self-harm in these regions. Pesticides are the most important poison throughout the tropics, being both common and associated with a high mortality rate. In some regions, particular pesticides have become the most popular method of self-harm, gaining a notoriety amongst both health-care workers and public. Self-poisoning with medicines such as benzodiazepines and antidepressants is common in urban areas, but associated with few deaths. The antimalarial chloroquine appears the most significant medicine, self-poisoning being common in both Africa and the Pacific region, and often fatal. Paracetamol (acetaminophen) is used in many countries but in few has it reached the popularity typical of the UK. Domestic and industrial chemicals are responsible for significant numbers of deaths and long-term disabilities world-wide. Self-poisoning with plant parts, although uncommon globally, is locally popular in some regions. Few of these poisons have specific antidotes. This emphasizes the importance of determining whether interventions aimed at reducing poison absorption actually produce a clinical benefit, reducing death and complication rates. Future research to improve medical management and find effective ways of reducing the incidence of self-harm, together with more widespread provision of interventions proven to be effective, could rapidly reduce the number of deaths from self-poisoning in the developing world.

Eddleston, M. (2008). "The pathophysiology of organophosphorus pesticide self-poisoning is not so simple." Neth J Med **66**(4): 146-148.

Eddleston, M. (2010). "Response to Peter and colleagues." Regulatory Toxicology and Pharmacology **57 (2-3)**: 338.

Eddleston, M. (2013). "Applied clinical pharmacology and public health in rural Asia--preventing deaths from organophosphorus pesticide and yellow oleander poisoning." Br J Clin Pharmacol **75**(5): 1175-1188.

Self-poisoning with pesticides or plants is a major clinical problem in rural Asia, killing several hundred thousand people every year. Over the last 17 years, our clinical toxicology and pharmacology group has carried out clinical studies in the North Central Province of Sri Lanka to improve treatment and reduce deaths. Studies have looked at the effectiveness of anti-digoxin Fab in cardiac glycoside plant poisoning, multiple dose activated charcoal in all poisoning, and pralidoxime in moderate toxicity organophosphorus insecticide poisoning. More recently, using a Haddon matrix as a guide, we have started conducting public health and animal studies to find strategies that may work outside of the hospital. Based on the 2009 GSK Research in Clinical Pharmacology prize lecture, this review shows the evolution of the group's research from a clinical pharmacology approach to one that studies

possible interventions at multiple levels, including the patient, the community and government legislation.

Eddleston, M. and D. N. Bateman (2007). "Pesticides." Medicine **35 (12)**: 646-648.
300,000 people die each year from pesticide self-poisoning in the rural developing world where pesticides are widely used in smallholder agricultural practice. Significant acute poisoning is much less common in industrialized countries and it is the long-term effects of low-dose chronic exposure that most concern the population. Organophosphorus and carbamate insecticides cause most acute fatalities; severe poisoning requires urgent resuscitation and administration of oxygen, atropine and oximes. The incidence of organochlorine poisoning will decrease as more of this environmentally persistent class are banned. Paraquat and aluminium phosphide are major problems in particular countries with extremely high fatality ratios of over 60%. No effective treatments are available. Chlorphenoxyacetate herbicides and superwarfarin rodenticides cause fewer deaths; other pesticides are generally less toxic and require only supportive care. 2007 Elsevier Ltd. All rights reserved.

Eddleston, M. and D. N. Bateman (2012). "Pesticides." Medicine **40 (3)**: 147-150.
300,000 people die each year from pesticide self-poisoning in the rural developing world where pesticides are widely used in smallholder agricultural practice. Significant acute poisoning is much less common in industrialized countries and it is the long-term effects of low-dose chronic exposure that most concern the population. Organophosphorus and carbamate insecticides cause most acute fatalities; severe poisoning requires urgent resuscitation and administration of oxygen, atropine and oximes. Paraquat and aluminium phosphide are major problems in some countries with extremely high fatality rates of over 60%. No effective treatments are available. Newer pesticides that are becoming more widely used are the herbicide, glyphosate, and neo-nicotinoid insecticides. Chlorphenoxyacetate herbicides and superwarfarin rodenticides cause fewer deaths; other pesticides are generally less toxic and require only supportive care. Most UK exposures are accidental and of low toxicity. 2011 Published by Elsevier Ltd.

Eddleston, M., N. A. Buckley, et al. (2008). "Management of acute organophosphorus pesticide poisoning." Lancet **371**(9612): 597-607.
Organophosphorus pesticide self-poisoning is an important clinical problem in rural regions of the developing world, and kills an estimated 200,000 people every year. Unintentional poisoning kills far fewer people but is a problem in places where highly toxic organophosphorus pesticides are available. Medical management is difficult, with case fatality generally more than 15%. We describe the limited evidence that can guide therapy and the factors that should be considered when designing further clinical studies. 50 years after first use, we still do not know how the core treatments--atropine, oximes, and diazepam--should best be given. Important constraints in the collection of useful data have included the late recognition of great variability in activity and action of the individual pesticides, and the care needed cholinesterase assays for results to be comparable between studies. However, consensus suggests that early resuscitation with atropine, oxygen,

respiratory support, and fluids is needed to improve oxygen delivery to tissues. The role of oximes is not completely clear; they might benefit only patients poisoned by specific pesticides or patients with moderate poisoning. Small studies suggest benefit from new treatments such as magnesium sulphate, but much larger trials are needed. Gastric lavage could have a role but should only be undertaken once the patient is stable. Randomised controlled trials are underway in rural Asia to assess the effectiveness of these therapies. However, some organophosphorus pesticides might prove very difficult to treat with current therapies, such that bans on particular pesticides could be the only method to substantially reduce the case fatality after poisoning. Improved medical management of organophosphorus poisoning should result in a reduction in worldwide deaths from suicide.

Eddleston, M., N. A. Buckley, et al. (2006). "Identification of strategies to prevent death after pesticide self-poisoning using a Haddon matrix." Inj Prev **12**(5): 333-337.

Despite pesticide self-poisoning causing around 300 000 deaths each year in the rural Asia Pacific region, no comprehensive public health response has yet been formulated. The authors have developed a Haddon matrix to identify factors that increase the risk of fatal rather than non-fatal pesticide self-poisoning in Sri Lanka. Many important host factors such as age, gender, and genetics are not alterable; factors that could be changed-alcohol use and mental health-have previously proved difficult to change. Interventions affecting agent or environmental factors may be easier to implement and more effective, in particular those limiting the human toxicity and accessibility of the pesticides, and the quality, affordability, and accessibility of health care in the community. Controlled studies are required to identify effective strategies for prevention and harm minimization and to garner political support for making the changes necessary to reduce this waste of life. Lessons learnt from Sri Lanka are likely to be highly relevant for much of rural Asia.

Eddleston, M., A. Dawson, et al. (2004). "Early management after self-poisoning with an organophosphorus or carbamate pesticide - a treatment protocol for junior doctors." Crit Care **8**(6): R391-397.

Severe organophosphorus or carbamate pesticide poisoning is an important clinical problem in many countries of the world. Unfortunately, little clinical research has been performed and little evidence exists with which to determine best therapy. A cohort study of acute pesticide poisoned patients was established in Sri Lanka during 2002; so far, more than 2000 pesticide poisoned patients have been treated. A protocol for the early management of severely ill, unconscious organophosphorus/carbamate-poisoned patients was developed for use by newly qualified doctors. It concentrates on the early stabilisation of patients and the individualised administration of atropine. We present it here as a guide for junior doctors in rural parts of the developing world who see the majority of such patients and as a working model around which to base research to improve patient outcome. Improved management of pesticide poisoning will result in a reduced number of suicides globally.

Eddleston, M. and A. H. Dawson (2012). "Triage and clinical management of patients with acute pesticide self-poisoning presenting to small rural hospitals." Clin Toxicol (Phila) **50**(6): 455-457.

Acute pesticide self-poisoning is the single most important cause of fatal self-harm worldwide, killing at least 250,000 people every year, the vast majority in rural Asia. However, for many years the problem was little studied and no systematic approach taken to reduce harm and prevent deaths. Eight years ago this changed when the World Health Organization (WHO) proposed an inter-sectoral public health campaign to improve patient management, prevention, knowledge of its epidemiology, and information dissemination. One aim was to improve the triage and acute care of pesticide self-poisoned patients presenting to small rural hospitals with few resources. To this end, a WHO meeting was held in Bangkok at the end of 2007 that developed a protocol for triage and early care that was published online. Unfortunately, this approach has not resulted in dissemination or uptake and, 4 years later, the guidance has not been widely read, critiqued, or used. In this commentary, we describe the basis for the guidance that was produced. We hope it will bring the work to a wider clinical toxicology audience, to ultimately improve management of pesticide poisoned patients, and to encourage clinicians to take part in this important campaign. Future attempts to improve clinical care in rural Asia will need to better understand and utilise methods for influencing policy makers and clinicians in target areas if practice is to be changed.

Eddleston, M. and D. Gunnell (2006). "Why suicide rates are high in China [3]." Science **311 (5768)**: 1711-1713.

Eddleston, M., L. Karalliedde, et al. (2002). "Pesticide poisoning in the developing world--a minimum pesticides list." Lancet **360**(9340): 1163-1167.

In parts of the developing world, pesticide poisoning causes more deaths than infectious diseases. Use of pesticides is poorly regulated and often dangerous; their easy availability also makes them a popular method of self-harm. In 1985, the UN Food and Agriculture Organisation (FAO) produced a voluntary code of conduct for the pesticide industry in an attempt to limit the harmful effects of pesticides. Unfortunately, a lack of adequate government resources in the developing world makes this code ineffective, and thousands of deaths continue today. WHO has recommended that access to highly toxic pesticides be restricted--where this has been done, suicide rates have fallen. Since an Essential Drugs List was established in 1977, use of a few essential drugs has rationalised drug use in many regions. An analogous Minimum Pesticides List would identify a restricted number of less dangerous pesticides to do specific tasks within an integrated pest management system. Use of safer pesticides should result in fewer deaths, just as the change from barbiturates to benzodiazepines has reduced the number of deaths from pharmaceutical self-poisoning.

Eddleston, M. and M. R. Phillips (2004). "Self poisoning with pesticides." BMJ **328**(7430): 42-44.

Eddleston, M., M. H. Rezvi Sheriff, et al. (1998). "Deliberate self harm in Sri Lanka: An overlooked tragedy in the developing world." British Medical Journal **317 (7151)**: 133-135.

Eddleston, M., J. M. Street, et al. (2012). "A role for solvents in the toxicity of agricultural organophosphorus pesticides." Toxicology **294**(2-3): 94-103.

Organophosphorus (OP) insecticide self-poisoning is responsible for about one-quarter of global suicides. Treatment focuses on the fact that OP compounds inhibit acetylcholinesterase (AChE); however, AChE-reactivating drugs do not benefit poisoned humans. We therefore studied the role of solvent coformulants in OP toxicity in a novel minipig model of agricultural OP poisoning. Gottingen minipigs were orally poisoned with clinically relevant doses of agricultural emulsifiable concentrate (EC) dimethoate, dimethoate active ingredient (AI) alone, or solvents. Cardiorespiratory physiology and neuromuscular (NMJ) function, blood AChE activity, and arterial lactate concentration were monitored for 12h to assess poisoning severity. Poisoning with agricultural dimethoate EC40, but not saline, caused respiratory arrest within 30 min, severe distributive shock and NMJ dysfunction, that was similar to human poisoning. Mean arterial lactate rose to 15.6 [SD 2.8] mM in poisoned pigs compared to 1.4 [0.4] in controls. Moderate toxicity resulted from poisoning with dimethoate AI alone, or the major solvent cyclohexanone. Combining dimethoate with cyclohexanone reproduced severe poisoning characteristic of agricultural dimethoate EC poisoning. A formulation without cyclohexanone showed less mammalian toxicity. These results indicate that solvents play a crucial role in dimethoate toxicity. Regulatory assessment of pesticide toxicity should include solvents as well as the AIs which currently dominate the assessment. Reformulation of OP insecticides to ensure that the agricultural product has lower mammalian toxicity could result in fewer deaths after suicidal ingestion and rapidly reduce global suicide rates.

Ergun, S. S., K. Ozturk, et al. (2009). "Delayed neuropathy due to organophosphate insecticide injection in an attempt to commit suicide." Hand (N Y) **4**(1): 84-87.

Organophosphates (OPs) are commonly used as pesticides throughout the world. Exposures to OPs cause a significant number of poisonings and deaths every year. Organophosphate-induced delayed polyneuropathy is a sensory-motor distal axonopathy which usually occurs after exposure of certain OP insecticides. Neuropathies due to ingestion of OPs have rarely been reported in the literature. Moreover, until now, there is no report of a patient developing organophosphorus injection-induced delayed neuropathy in the literature. We report a patient with serious organophosphorus-induced delayed neuropathy due to malathion injection. The patient was a 32-year-old female who self-injected undetermined amounts of malathion over the median nerve trace on the forearm crease in a suicide attempt which resulted in peripheral neuropathy.

Erickson, T., K. M. Brown, et al. (1997). "A case of paraquat poisoning and subsequent fatality presenting to an emergency department." J Emerg Med **15**(5): 649-652.

Paraquat (1,1'-dimethyl-4,4'-dipyridylium) is an herbicide associated with both accidental and intentional ingestion, leading to severe and often fatal toxicity. Prognosis is largely dependent on the amount of paraquat absorbed. Rapid identification of the symptoms of paraquat toxicity (burns or ulceration at the site of ingestion or injection, acute respiratory distress, and renal failure) can facilitate early treatment intervention to limit absorption. We report a case of a 71-year-old man with a suicidal ingestion of paraquat 2 days prior to presentation. Serum paraquat levels, time elapsed since ingestion, and clinical symptoms all indicated poor prognosis. The patient developed severe respiratory distress and progressive renal failure, and died 6 days after admission to the hospital.

Ernouf, D., N. Boussa, et al. (1998). "Acute paraquat poisoning: increased toxicity in one case with high alcohol intake." Hum Exp Toxicol **17**(3): 182-184.

Human paraquat poisoning from accidental or intentional ingestion is very often fatal. According to the amount of paraquat involved, death can occur within hours or weeks following ingestion. The inefficacy of the various treatments undertaken have led to determine prognostic factors based upon the evolution of plasma and urine paraquat concentrations or of usual biochemical parameters. We report one case of acute poisoning which, although the ingested dose of paraquat was not massive (< 50 mg/kg-1) and the severity indices were in favour of a delayed fatal outcome, has ended in an early death. The high blood alcohol level of the patient (3.34 g l-1) seems to be the main cause of the precocity of this death (86th hour).

Eroglu, A., U. Kucuktulu, et al. (2003). "Multiple dose-activated charcoal as a cause of acute appendicitis." J Toxicol Clin Toxicol **41**(1): 71-73.

We presented a case of a 55-year-old woman who intentionally ingested an unknown amount of carbosulfan, a carbamate insecticide. On admission, her clinical findings were coma, pinpoint pupils, hypersalivation, respiratory failure, bradycardia, and hypotension. Hertrachea was intubated after suction of secretions, and atropine was administered intravenously. After gastric lavage, multiple doses of activated charcoal were instilled through the nasogastric tube over five days (total doses of 840 g). On the fourteenth day, she developed right-lower quadrant abdominal pain, anorexia, nausea, and vomiting, and she underwent an appendectomy. On pathologic examination of the specimen, particles of activated charcoal were seen within the dilated part of the appendiculer lumen. The patient was discharged from the hospital after antidepressant therapy at the psychiatry clinic. This case documents that multiple doses of activated charcoal may be associated with acute appendicitis.

Eyer, F., N. Felgenhauer, et al. (2004). "Acute endosulfan poisoning with cerebral edema and cardiac failure." J Toxicol Clin Toxicol **42**(6): 927-932.

BACKGROUND: Organochlorine insecticides are highly toxic compounds that are responsible for a number of severe intoxications worldwide with several deaths. Despite their widespread use in agriculture during the 1940s to 1960s and the well-known signs and symptoms of intoxication, the clinical picture in case of poisoning varies. We report two cases of acute intentional endosulfan intoxication with cerebral edema and cardiac failure. CASE

REPORTS: Both cases developed life-threatening signs like epileptic state, respiratory insufficiency and hemodynamic instability soon after ingestion. The survivor developed severe myocardial insufficiency and pulmonary edema documented by echocardiography and x-ray of the chest. The deceased patient developed severe cerebral edema and multiorgan failure ten days after ingestion of Thiodan 35. The peak serum concentration of endosulfan in the survivor was 0.12 mg/L approximately 23 hours after ingestion, whereas the peak blood concentration in the fatal case was 0.86 mg/L approximately 25 hours post-ingestion. Post-mortem endosulfan levels in different organs were determined. CONCLUSION: Endosulfan is a highly toxic organochlorine insecticide that produces well-known neurological symptoms of tonic-clonic convulsions, headache, dizziness and ataxia but also can cause gastrointestinal symptoms and metabolic disturbances. Life-threatening cerebral edema and hemodynamic instability may occur. Treatment is symptomatic and supportive.

Eyer, F., D. M. Roberts, et al. (2009). "Extreme variability in the formation of chlorpyrifos oxon (CPO) in patients poisoned by chlorpyrifos (CPF)." Biochem Pharmacol **78**(5): 531-537.

Chlorpyrifos (CPF) is a pesticide that causes tens of thousands of deaths per year worldwide. Chlorpyrifos oxon (CPO) is the active metabolite of CPF that inhibits acetylcholinesterase. However, this presumed metabolite has escaped detection in human samples by conventional methods (HPLC, GC-MS, LC-MS) until now. A recently developed enzyme-based assay allowed the determination of CPO in the nanomolar range and was successfully employed to detect this metabolite. CPO and CPF were analysed in consecutive plasma samples of 74 patients with intentional CPF poisoning. A wide concentration range of CPO and CPF was observed and the ratio of CPO/CPF varied considerably between individuals and over time. The ratio increased during the course of poisoning from a mean of 0.005 in the first few hours after ingestion up to an apparent steady-state mean of 0.03 between 30 and 72h. There was a hundred-fold variation in the ratio between samples and the interquartile range (between individuals) indicated over half the samples had a 5-fold or greater variation from the mean. The ratio was independent of the CPF concentration and the pralidoxime regimen. CPO was present in sufficient quantities to explain any observed acetylcholinesterase inhibitory activity. The effectiveness of pralidoxime in reactivating the inhibited acetylcholinesterase is strongly dependent on the CPO concentration. Differences in clinical outcomes and the response to antidotes in patients with acute poisoning may occur due to inter-individual variability in metabolism.

Eyer, P., M. Radtke, et al. (2008). "Reactions of isodimethoate with human red cell acetylcholinesterase." Biochem Pharmacol **75**(10): 2045-2053.

Isodimethoate is a thermal decomposition product that is present in usual pesticide formulations of dimethoate. Owing to its PO structure the compound is a direct anticholinesterase agent whose properties, to the best of our knowledge, are presented here for the first time. Isodimethoate shows an inhibition rate constant towards human red blood cell acetylcholinesterase (AChE) of 2.3x10(3) M(-1) min(-1) (pH 7.4, 37 degrees C), indicating a

somewhat higher potency than found with omethoate, the CYP450-mediated active metabolite of pure dimethoate. Isodimethoate-inhibited AChE shows fast spontaneous reactivation and aging kinetics (half-life 2.3 and 25 min, respectively). The inhibited, non-aged enzyme is readily reactivated by obidoxime (k(r)=9 min(-1); K(D)=0.1 mM) but hardly by pralidoxime at therapeutic concentrations. Interestingly, isodimethoate hydrolyzes readily in buffered solutions at pH 7.4 and 37 degrees C with liberation of methylmercaptan (half-life 16 min). Liberation of N-(methyl)mercaptoacetamide, the expected leaving group, was not observed. These properties make isodimethoate a hit-and-run agent that renders part of AChE non-reactivatable within a short period of time. The clinical consequences of exposure to or intentional ingestion of isodimethoate-containing dimethoate formulations are a partly untractable AChE shortly after incorporation. In fact, aging of AChE in dimethoate-poisoned patients on admission was much more advanced than expected from the reaction with omethoate. Manufacturers, researching scientists and clinical toxicologists should be aware of this problem.

Fonseka, M. M., K. Medagoda, et al. (2003). "Self-limiting cerebellar ataxia following organophosphate poisoning." Hum Exp Toxicol **22**(2): 107-109.

Deliberate self-harm by ingestion of organophosphate insecticides is a common health problem in Sri Lanka. The poisoning results in an initial life-threatening cholinergic crisis and several intermediate and late neurological and psychiatric manifestations. A patient who developed self-limiting cerebellar signs 8 days after ingestion of dimethoate, an organophosphorous insecticide, is reported on.

Gaar, G. G. (1994). "Gastrointestinal decontamination for acute poisoning by ingestion. Prevention of absorption of toxic compounds." Journal of the Florida Medical Association **81 (11)**: 747-749.

Gastrointestinal decontamination therapy in the patient with accidental or intentional ingestion of toxic substances has been standard therapy for several decades, although based on theory of presumed action and benefit. As scientific knowledge accumulates in this area of clinical toxicology, old assumptions are being challenged by scientific evidence relating to gastric emptying, efficacy of activated charcoal, and usefulness of whole-bowel irrigation with polyethylene glycol electrolyte lavage solutions. An overview is presented of the scientific data now available. Although realizing the still unresolved controversies, a logical plan is described for gastrointestinal decontaminaticn following acute overdose.

Gawarammana, I. B. and A. H. Dawson (2010). "Peripheral burning sensation: a novel clinical marker of poor prognosis and higher plasma-paraquat concentrations in paraquat poisoning." Clin Toxicol (Phila) **48**(4): 347-349.

INTRODUCTION: Self-poisoning with paraquat has a case fatality ratio (CFR) over 65% in Sri Lanka. Plasma-paraquat concentration is the best prognostic indicator for patient outcome but is not readily available. Alternative surrogate clinical markers could be useful in management and determining prognosis. Anecdotal reports by medical and research staff suggested that patients who complained of burning sensation of the body

had a poor prognosis and a prospective study was initiated. METHODS: This was a prospective observational study in three hospitals in Sri Lanka. We collected demographic data, presence or absence of burning sensation, and major outcome, and determined the plasma-paraquat concentration within 24 h post-ingestion. RESULTS: There were 179 patients with deliberate self-ingestion of paraquat over 30 months. Burning sensation was reported in 84 patients (48%), which was initiated at a median of 1 day (range 1-3 days) post-ingestion. Of the patients who had burning, 61 died [CFR = 72.62%; 95% confidence interval (CI) = 62-81]. Of the 91 patients who had no peripheral burning, 23 died (CFR = 25.27%, 95% CI = 18.15-35.9). Presence of peripheral burning sensation was associated with a significantly higher risk of death (odds ratio = 7.8, 95% CI = 3.9-15, $p < 0.0001$). Patients who complained of peripheral burning died at a median of 36 h (interquartile range = 30.5-88) following ingestion whereas those who had no peripheral burning died at a median of 50.5 h (interquartile range = 16.75-80). The difference was not significant ($p > 0.05$). Median admission plasma-paraquat concentration in patients with peripheral burning (2.67 microg/mL, 95% CI = 0.84-14.2) was significantly higher than in the patients with no peripheral burning (0.022 microg/mL, 95% CI = 0.005-0.78; $p < 0.001$). Peripheral burning has a sensitivity of 0.72 (95% CI = 0.6-8) and specificity of 0.74 (95% CI = 0.64-0.08) and a positive predictive value of 0.73 (95% CI = 0.6-0.8). DISCUSSION: It is possible that this symptom may help discriminate between patients who have poor chance of survival and those who may potentially benefit from interventions. The mechanism is not clear but could either include a direct concentration-related effect or be a marker of oxidative stress. CONCLUSION: Presence of burning sensation is associated with high plasma-paraquat concentrations and is strongly predictive of death.

George, T., A. I. Shaikh, et al. (2014). "Severe methemoglobinemia due to insecticide poisoning." Indian J Crit Care Med **18**(2): 113-114.

Methemoglobinemia is an altered state of hemoglobin resulting in impaired oxygen delivery to the tissues. Deliberate ingestion of certain insecticides and pesticides may result in this condition. We report a case of severe methemoglobinemia after deliberate ingestion of an insecticide marketed to be safe and containing only biological extracts and fillers. Methemoglobinemia should be suspected with low oxygen saturation on pulse oxymetry and the presence of chocolate colored blood. The methemoglobin level of 91% in our patient is the highest level reported among methemoglobinemia survivors.

Gil, H., S. Seok, et al. (2012). "A case of acute prochloraz-manganese complex intoxication treated with extracorporeal elimination." Blood Purif **34**(3-4): 344-348.

BACKGROUND/AIM: We treated a patient with critical manganese intoxication with vigorous extracorporeal elimination. In this article, we describe the clinical characteristics and treatment modalities of the patient. PATIENT: A 65-year-old man was brought to the emergency room (ER) 5.5 h after ingesting prochloraz-manganese complex. He experienced circulatory collapse and went into a coma without self-breathing on arrival at the ER. Mechanical ventilation was initiated and hemoperfusion, hemodialysis and continuous venovenous hemodiafiltration were performed with the help of

norepinephrine. MEASUREMENT AND RESULT: The manganese levels on the first, second and fourth hospital days were 34.1, 23.6 and 12.5 microg/l, respectively. He recuperated from the shock state within 7 hospital days. After 4 critical weeks, the patient regained full consciousness. CONCLUSION: Rigorous extracorporeal elimination by hemoperfusion, hemodialysis and continuous venovenous hemodiafiltration was an effective treatment modality for patients with acute manganese intoxication.

Gray, J. P., D. E. Heck, et al. (2007). "Paraquat increases cyanide-insensitive respiration in murine lung epithelial cells by activating an NAD(P)H:paraquat oxidoreductase: identification of the enzyme as thioredoxin reductase." J Biol Chem **282**(11): 7939-7949.

Pulmonary fibrosis is one of the most severe consequences of exposure to paraquat, an herbicide that causes rapid alveolar inflammation and epithelial cell damage. Paraquat is known to induce toxicity in cells by stimulating oxygen utilization via redox cycling and the generation of reactive oxygen intermediates. However, the enzymatic activity mediating this reaction in lung cells is not completely understood. Using self-referencing microsensors, we measured the effects of paraquat on oxygen flux into murine lung epithelial cells. Paraquat (10-100 microm) was found to cause a 2-4-fold increase in cellular oxygen flux. The mitochondrial poisons cyanide, rotenone, and antimycin A prevented mitochondrial- but not paraquat-mediated oxygen flux into cells. In contrast, diphenyleneiodonium (10 microm), an NADPH oxidase inhibitor, blocked the effects of paraquat without altering mitochondrial respiration. NADPH oxidases, enzymes that are highly expressed in lung epithelial cells, utilize molecular oxygen to generate superoxide anion. We discovered that lung epithelial cells possess a distinct cytoplasmic diphenyleneiodonium-sensitive NAD(P)H:paraquat oxidoreductase. This enzyme utilizes oxygen, requires NADH or NADPH, and readily generates the reduced paraquat radical. Purification and sequence analysis identified this enzyme activity as thioredoxin reductase. Purified paraquat reductase from the cells contained thioredoxin reductase activity, and purified rat liver thioredoxin reductase or recombinant enzyme possessed paraquat reductase activity. Reactive oxygen intermediates and subsequent oxidative stress generated from this enzyme are likely to contribute to paraquat-induced lung toxicity.

Guadarrama-Naveda, M., L. C. de Cabrera, et al. (2001). "Intermediate syndrome secondary to ingestion of chlorpiriphos." Vet Hum Toxicol **43**(1): 34.

A rural-area resident male patient deliberately ingested chlorpiriphos, an organophosphate insecticide. Although presented with cholinergic symptoms initially, he suffered general condition deterioration after 4 d characterized by muscular weakness, hypotonia, arreflexia and recumbent dyspnea requiring ventilatory support. These clinical manifestations occur from liposoluble organophosphates or metabolites with long-lasting half time, causeing delayed inhibition of acetylcholinesterase and subsequent burn out of the neuromuscular junction from acetylcholine overstimulation.

Gunnell, D. and G. Lewis (2005). "Studying suicide from the life course perspective: Implications for prevention." British Journal of Psychiatry **187 (SEPT.)**: 206-208.

Suicide is an important contributor to premature mortality accounting for over 800 000 deaths worldwide every year. Environmental and genetic factors acting from before birth to old age affect an individual's risk of suicide. Risk is influenced not only by psychiatric illness and impulsive behaviour but also by factors such as the cultural acceptability of suicide, the ease of availability of lethal suicide methods, help-seeking behaviours in times of crisis and access to effective treatments following self-harm. Suicide prevention programmes might usefully focus on two discrete areas: the prevention of the psychiatric illnesses that precede suicide and tackling those risk factors particular to suicide such as media influences, help-seeking, the availability of methods and the medical management of self-harm.

Hong, S. Y., D. H. Yang, et al. (2000). "Associations between laboratory parameters and outcome of paraquat poisoning." Toxicology Letters **118 (1-2)**: 53-59.

Paraquat, a non-selective herbicide, is a known fatal substance in humans, and intentional ingestion of paraquat is increasing among Korean suicides. In 1999, 147 subjects admitted to the Institute of Pesticide Poisoning, Soonchunhyang Chunan Hospital, Korea ingested paraquat. Initial routine laboratory tests were conducted and the outcome of paraquat poisoning was categorized as survivor and fatality. Mean amount (S.D.) of ingestion was 54.5 (104.9) ml, and the overall fatality rate was 44.2%. Abnormal liver function (GOT and GPT), renal dysfunction (BUN and creatinine), metabolic acidosis (pH and PaCO₂), and abnormal urine analysis (RBC, WBC, and protein) had significant odds ratios (ORs) for paraquat fatality ($P < 0.05$). In multiple logistic regression, subjects with liver or renal dysfunction or metabolic acidosis had significant risks of the fatality. Our results determined that initial routine laboratory parameters could be used to predict the outcome of paraquat poisoning and recommended that evaluation of acid-base status and renal and liver function should be conducted and evaluated before intensive therapy. 2000 Elsevier Science Ireland Ltd.

Hu, Y. H., C. C. Yang, et al. (2010). "Methomyl-alphamethrin poisoning presented with cholinergic crisis, cortical blindness, and delayed peripheral neuropathy." Clin Toxicol (Phila) **48**(8): 859-862.

OBJECTIVE: Methomyl-alphamethrin is a mixture of carbamate and pyrethroid insecticides. Carbamate insecticides function as reversible cholinesterase inhibitors, which may produce life-threatening cholinergic syndrome. Cortical blindness and delayed neuropathy were rarely reported complications of carbamate insecticide exposures. Here we reported a case of intentional methomyl-alphamethrin ingestion. CASE REPORT: A 41-year-old woman attempted suicide by drinking 200 mL of methomyl-alphamethrin insecticide and soon presented with unconsciousness, hypothermia, and shock. She developed pulseless electrical activity and regained spontaneous circulation after resuscitation. Diagnosis of carbamate poisoning was made by her clinical features, decreased levels of cholinesterases and the presence of methomyl in her urine. She complained of blurred vision and blindness 4 days post-exposure. Visual evoked potential and brain magnetic resonance imaging study confirmed the diagnosis of cortical blindness. On day 21, she had low limbs numbness, progressive weakness, and right foot drop. Electophysiological

tests performed on day 27 revealed neuropathy of bilateral peroneal nerves. CONCLUSION: We reported a patient who manifested severe carbamate insecticide poisoning and developed cortical blindness and delayed neuropathy. Physicians should be aware of these rare toxicities among patients with severe carbamate insecticide poisoning.

Huan, W. M., C. H. Cheng, et al. (2013). "Carbamate poisoning mixed with methanol intoxication - Misfortunes never come singly: Case report." Clinical Toxicology **Conference: 33rd International Congress of the European Association of Poisons Centres and Clinical Toxicologists, EAPCCT 2013 Copenhagen Denmark. Conference Start: 20130528 Conference End: 20130531. Conference Publication: (var.pagings). 51 (4)**: 356-357.

Objective: Pesticide poisoning is a common occurrence in Taiwan, due to agriculture being one of the main occupations. Carbamate is the fifth cause of pesticide poisoning according to epidemiology in Taiwan, but is third in mortality. Intentional ingestion is the most common reason for carbamate intoxication. Symptoms of carbamate intoxication are similar to organophosphate intoxication, including muscarinic and nicotinic toxidromes. Metabolic acidosis can be seen in cases of carbamate intoxication, but not very frequently. Case series: Here we report two cases of carbamate intoxication with severe metabolic acidosis, which was proven to result from methanol intoxication. Although hemodialysis was arranged immediately, both patients died in 3-5 days. One case, a 59-yearold woman, was sent to the emergency department (ED) due to collapse on the road, and was found to be in cardiac arrest when the emergency medical technician (EMT) arrived. Cardiopulmonary resuscitation (CPCR) was carried out successfully in ED, and pinpoint pupils, bronchorrhea, sweating and bradycardia were noted. Organophosphate or carbamate intoxication was highly suspected. Blood tests disclosed low cholinesterase level, mixed respiratory and metabolic acidosis and elevated anion gap. Elevated methanol level was confirmed later by laboratory examination. Her family mentioned that she took a bottle of pesticide in a suicide attempt and the pesticide contained 30% methomyl (carbamate), 26% methanol and 16% ethylene glycol as emulsifiable concentrate. Hemodialysis was performed immediately, but the patient died 5 days later. The other, an 85-year-old woman, drank a bottle of carbamate (methomyl and alpha-cypermethrin mix) to commit suicide. Cardiac arrest was found in ED, and there was return of spontaneous circulation after CPCR. Like the first case, blood tests revealed severe metabolic acidosis, elevated anion gap and elevated methanol level. The patient died 3 days later although hemodialysis was arranged. Conclusion: For patients with pesticide poisoning, most clinicians may put emphasis on the main component of the intoxication such as the organophosphate or carbamate. However, hidden toxic solvents such as methanol can be the cause of death for these patients.

Huang, C. J., M. C. Yang, et al. (2005). "Subacute pulmonary manifestation in a survivor of severe paraquat intoxication." Am J Med Sci **330**(5): 254-256.

Paraquat has been widely used as a nonselective contact herbicide since 1962. It is highly toxic for humans, and many cases of acute poisoning, especially intentional self-poisoning, have been reported over the past few

decades in developing countries. Ingestion of a threshold volume results in multiple organ failure and death after a longer period of time, but aggressive clinical studies are rarely done when the diagnosis is clear. We report the case of a patient who survived severe paraquat intoxication; he presented with subacute pulmonary manifestations including physiologic dysfunction and abnormalities on radiographs.

Ignjatovic, I. and J. Stosic (2012). "Self-poisoning by injection of dimethoate: Case report." Clinical Toxicology **Conference: 2012 International Congress of the European Association of Poisons Centres and Clinical Toxicologists, EAPCCT 2012 London United Kingdom. Conference Start: 20120525 Conference End: 20120601. Conference Publication: (var.pagings). 50 (4)**: 357.

Objective: Dimethoate toxicity in humans is recorded after ingestion, inhalation and dermal absorption. This unique case of poisoning by intravenous/partially paravenous application of dimethoate is presented. Case report: A 56-year old man attempted suicide by injecting about 40 - 50 mL of insecticide containing 40% of dimethoate into the left cubital area. At admission reddening of the skin and bullous changes were noticed due to the injection and applied dose. Six to eight hours after the attempt, the patient was somnolent. Vital signs included a pulse of 120 beats/min, blood pressure 110/70 mmHg, and respiratory rate of 18 breaths/min. Pupils were miotic, lung auscultation revealed normal breath sounds. The patient's condition rapidly deteriorated with the development of cholinergic syndrome, so atropine was administered according to the symptoms. Despite the intravenous atropine the patient developed respiratory failure and hypotensive shock. Five hours post-admission he was intubated and mechanically ventilated. At reception serum cholinesterase activity was 341 ij L (reference value is 4620 - 11,500 ij/L). Oximes were not available in the hospital, so he was treated with large doses of atropine by infusion. He needed dopamine stimulation for one day. The patient was on mechanical ventilation for 13 days, and received a total dose of 3082 mg of atropine. Because of the insecticide application in the cubital area there was a small necrosis. This wound was surgically treated after reception. Bullous changes were removed and it was covered with Vaseline gauze. With further treatment of this wound it improved greatly. Conclusion: Severe dimethoate poisoning was successfully treated with high doses of atropine. As atropine is ineffective at the nicotine receptors, and there was no possibility for oxime treatment, the patient needed prolonged mechanical ventilation. Mortality in dimethoatepoisoned patients may be greater than in those ingesting other pesticides due to hypotensive shock. In our case, the patient responded well to the treatment with dopamine and high doses of atropine.

Inoue, S., T. Saito, et al. (2008). "Prognostic factors and toxicokinetics in acute fenitrothion self-poisoning requiring intensive care." Clin Toxicol (Phila) **46**(6): 528-533.

OBJECTIVE: We aimed to evaluate prognostic factors and toxicokinetics in acute fenitrothion self-poisoning. METHODS: We reviewed 12 patients with fenitrothion self-poisoning admitted to the intensive care unit between 2003 and 2006. We compared the characteristics, initial vital signs, physiological scores, corrected QT interval on electrocardiogram and laboratory data

(serum fenitrothion concentration and cholinesterase activity) of non-survivors and survivors. Furthermore, we evaluated the correlation between the prognostic factors and severity of poisoning (lengths of intensive care unit and hospital stays), and the toxicokinetics of the patients. RESULTS: In the 2 non-survivors, the estimated fenitrothion ingestion dose and the serum fenitrothion concentration at the emergency department and at 24 h after ingestion were significantly higher than those in the 10 survivors. (P = 0.008, 0.003, and 0.04, respectively). In the 10 survivors, the serum fenitrothion concentration at 24 h after ingestion was significantly correlated with the lengths of intensive care unit and hospital stays (P = 0.004 and 0.04, respectively); however, the initial vital signs, physiological scores, corrected QT interval on electrocardiogram at the emergency department, and serum cholinesterase activity did not show any correlation. In five patients successfully fitted to a two-compartment model, the distribution and elimination half-lives were 2.5 and 49.8 h, respectively, which is compatible with the slow and prolonged clinical course of fenitrothion poisoning. CONCLUSION. Estimated fenitrothion ingestion dose and serum fenitrothion concentration at the emergency department and at 24 h after ingestion may be useful prognostic factors in acute fenitrothion self-poisoning. Furthermore, we should take care for the patients whose serum fenitrothion concentration is high.

Iyyadurai, R., V. Surekha, et al. (2010). "Azadirachtin poisoning: a case report." Clin Toxicol (Phila) **48**(8): 857-858.

The use of neem-based products is widespread in the Indian Subcontinent. Neem-based pesticides obtained from neem kernels are considered natural and safe. The toxic effects of ingestion and overdose of this pesticide in adults have not been described in this literature. We report the case of a 35-year-old lady who had consumed Azadirachtin in an attempt of deliberate self-harm. The patient had features of neurotoxicity because of Azadirachtin requiring intensive medical care with mechanical ventilation. The patient survived the overdose with no long-lasting side effects of the toxin.

Jacob, J. and A. F. Tarabar (2012). "A rare case of combined strychnine and propoxur toxicity from a single preparation." Clinical Toxicology **50 (3)**: 224.

Jin, K. (2012). "Rhabdomyolysis, methemoglobinemia and acute kidney injury after indoxacarb poisoning." Clinical Toxicology **50 (3)**: 227.

Jin, M. C., M. Q. Cai, et al. (2009). "Simultaneous measurement of indandione-type rodenticides in human serum by liquid chromatography-electrospray ionization-tandem mass spectrometry." J Anal Toxicol **33**(6): 294-300.

Measurement of indandione rodenticides is important in the diagnosis and treatment of accidental rodenticide ingestion. Current assays lack effective measurements for simultaneous analysis of the indandiones, especially the isomers. The intent of this study was to establish a novel and selective method for the simultaneous determination of indandione-type rodenticides (diphacinone, chlorophacinone, valone, and pindone) in human serum by liquid chromatography-electrospray ionization-tandem mass spectrometry. After addition of internal standard, the sample was extracted with 10%

methanol in acetonitrile and cleaned by solid-phase extraction (SPE). The analytes were separated on a C(18) rapid column and infused into an ion trap mass spectrometer in the negative electrospray ionization mode. The multiple-reaction monitoring ion pairs were m/z 339 --> 167, m/z 373 --> 201, m/z 229 --> 145, m/z 229 --> 172, and m/z 307 --> 161 for diphacinone, chlorophacinone, valone, pindone, and IS, respectively. Recoveries were between 81.5 and 94.6%, and the limits of quantification were 0.2 to 0.5 ng mL. Intra- and interday RSDs were less than 7.9 and 11.5%, respectively. The assay was linear in the range of 0.5-100.0 ng/mL with coefficients of determination (r(2) > 0.99) for all analytes. The proposed method enables the unambiguous confirmation and quantification of the indandiones in both clinical and forensic specimens.

Kallel, H., A. Charfeddine, et al. (2007). "Curious fatal intentional poisoning case with organophosphate pesticide." Med Sci Monit **13**(1): CS1-3.

BACKGROUND: A case of organophosphorus intoxication with rebounding symptoms is reported. CASE REPORT: Case report of a 24-year-old man who poisoned himself with organophosphorus pesticide and was hospitalized in a 22-bed adult medical surgical intensive care unit at a tertiary care hospital. The patient had ingested organophosphorus pesticide after an argument and fight with his family and had presented typical clinical and biological manifestations of intoxication by this chemical. He was treated by mechanical ventilation, large fluid infusion, gastric lavage, as well as atropine and pralidoxime. After 48 hours of intensive care, the patient improved considerably, but shortly after this improvement, mental, hemodynamic, and respiratory status altered again. Gastric fibroscopy showed a small plastic bag containing powder in the stomach which was responsible for the rebounding symptoms of the intoxication. CONCLUSIONS: Gastric fibroscopy can be helpful in case of organophosphorus intoxication with persistent or rebounding symptoms.

Kervegant, M., C. Schmitt, et al. (2013). "Self poisonings with paraquat in French Guiana: Persistent use during suicidal behavior in French overseas territories. [French]." Annales de Toxicologie Analytique **25 (2)**: 71-73.

Objective: Paraquat is a pesticide widely used around the world as herbicide. The toxicity of this molecule on human beings is high as it induces after ingestion liver and renal failure with possible delayed pulmonary fibrosis. After numerous reports about this major toxicity the European authorities decided to withdraw this herbicide of the market in July 2007. The authors report a collective case of poisoning with paraquat in French Guiana in 2011. Method: A teenager boy and his mother ingested paraquat deliberately. Hepatic and renal failures were observed for the young male who was treated with the immunosuppressive protocol treatment in order to prevent the pulmonary complications. His mother rapidly developed multi-organic failure. Results: The young boy's hepatic and renal failure evolved quickly favorably. No respiratory disturbances were reported with him allowing a discharge after 16 days of hospitalization. His mother who ingested higher quantities of paraquat died in 2 days. Conclusion: This collective case proves that 4 years after the prohibition of paraquat in French Guiana it is still

possible to observe life-threatening poisonings induced by such a dangerous herbicide. 2013 Societe Francaise de Toxicologie Analytique.

Kim, J. M. and B. S. Jeon (2009). "Survivors from beta-fluoroethyl acetate poisoning show a selective cerebellar syndrome." J Neurol Neurosurg Psychiatry **80**(5): 528-532.

AIM/ BACKGROUND: beta-Fluoroethyl acetate (FEA), a derivative of sodium fluoroacetate (Compound 1080, FA), is one of the high-potency toxic chemicals, and it has been used against rats and wild animals. Human casualties from FA or FEA poisoning, accidental or suicidal, have been reported. Survivors of the poisoning are extremely rare. The objective of this study is to present survivors of FEA poisoning. METHOD: Data on the survivors were collected at the Department of Neurology over the past 20 years. Reviews of the medical record and brain imaging were performed. RESULTS: A total of 10 survivors of FEA poisoning were found. All of the cases were suicide attempts. The amount of FEA ingested varied from 600 to 1800 mg with a mean of 1200 mg, which is close to the lethal dose of FEA. Immediately after ingestion, all of the patients had an altered mental status. On awakening, all of the patients had severe cerebellar dysfunction, such as ataxic gait, dysarthria and intention tremor. The cerebellar dysfunction usually improved gradually over the years after the event, but this improvement eventually plateaued, resulting in residual and persistent cerebellar dysfunction. Serial imaging showed swelling in the posterior fossa during the acute phase and progressive cerebellar atrophy on follow-up. CONCLUSION: In summary, FEA poisoning causes a selective cerebellar syndrome in its survivors. The pathomechanism underlying the selective cerebellar toxicity of FEA remains to be elucidated. The selective involvement of the cerebellum might provide a useful model for cerebellar degeneration.

Konradsen, F. (2007). "Acute pesticide poisoning - A global public health problem." Danish Medical Bulletin **54 (1)**: 58-59.

Acute pesticide poisoning has become a major public health problem worldwide, following the intensification of agriculture and the promotion of agro-chemicals in low and middle income countries, with more than 300.000 deaths each year. The easy availability of highly toxic pesticides in the homes of farming communities has made pesticides the preferred means of suicide with an extremely high case fatality. Similarly, the extensive use of pesticides exposes the community to both long-term and acute occupational health problems. A concerted effort is urgently needed to address the situation.

Konradsen, F., A. H. Dawson, et al. (2007). "Pesticide self-poisoning: thinking outside the box." Lancet **369**(9557): 169-170.

Konradsen, F., W. van der Hoek, et al. (2003). "Reducing acute poisoning in developing countries--options for restricting the availability of pesticides." Toxicology **192**(2-3): 249-261.

Hundreds of thousands of people are dying around the world each year from the effects of the use, or misuse, of pesticides. This paper reviews the

different options to reduce availability of the most hazardous chemicals, focusing on issues in developing countries. Emphasis is placed on the fatal poisoning cases and hence the focus on self-harm cases. Overall, it is argued here that restricting access to the most hazardous pesticides would be of paramount importance to reduce the number of severe acute poisoning cases and case-fatalities and would provide greater opportunities for preventive programmes to act effectively. The aim should be to achieve an almost immediate phasing out of the WHO Classes I and II pesticides through national policies and enforcement. These short-term aims will have to be supported by medium- and long-term objectives focusing on the substitution of pesticides with safe and cost-effective alternatives, possibly guided by the establishment of a Minimum Pesticide List, and the development of future agricultural practices where pesticide usage is reduced to an absolute minimum. Underlying factors that make individuals at risk for self-harm include domestic problems, alcohol or drug addiction, emotional distress, depression, physical illness, social isolation or financial hardship. These should be addressed through preventive health programmes and community development efforts.

Konradsen, F., W. van der Hoek, et al. (2005). "Missing deaths from pesticide self-poisoning at the IFCS Forum IV." Bull World Health Organ **83**(2): 157-158.

Kucuker, H., O. Sahin, et al. (2009). "Fatal acute endosulfan toxicity: a case report." Basic Clin Pharmacol Toxicol **104**(1): 49-51.

Endosulfan is an organochlorine pesticide. It is banned in the USA and Europe, but use is unrestricted for insect control. Endosulfan causes many intentional and unintentional toxicities in developing countries and in Turkey. Acute exposure to endosulfan has rarely been reported in deaths due to ingestion. Here, a fatality of 61-year-old woman of a family who was poisoned due to ingestion of endosulfan has been reported. Based on autopsy findings, patient history and toxicological results, the cause of death was determined to be acute intoxication of endosulfan and the manner, unintentional toxicities. Endosulfan has histopathological toxic effects on many organs and this toxic effect occurs within a short period after ingestion. To prevent endosulfan poisoning, the usage of it must be restricted and even prohibited. To prevent death and to accelerate improvement, the organs that have more apparent histopathological injury should be considered and early and intensive supportive treatment be initiated.

Lalloo, U. G. and A. Ambaram (2008). "Survival after massive intentional overdose of paraquat." S Afr Med J **98**(5): 370-372.

Lawson, R. and E. Estrade-Chapellaz (1999). "[Self-induced poisoning with glufosinate (Basta)]." Ann Fr Anesth Reanim **18**(9): 1025-1026.

Lee, J. C., K. L. Lin, et al. (2010). "Non-accidental chlorpyrifos poisoning-an unusual cause of profound unconsciousness." Eur J Pediatr **169**(4): 509-511.

Chlorpyrifos is an organophosphorus anticholinesterase insecticide, and organophosphate intoxication can induce symptoms such as miosis, urination, diarrhea, diaphoresis, lacrimation, excitation of central nervous

system, salivation, and consciousness disturbance (MUDDLES). Although accidental poisoning of children with drugs and chemicals is a common cause for consciousness disturbance in children, the possibility of deliberate poisoning is rarely considered. We report on a healthy 5-year 6-month-old boy with recurrent organophosphate intoxication. Reports of chlorpyrifos intoxication in children are quite rare. This case report demonstrates decision-making process and how to disclose deliberate chlorpyrifos poisoning of the toddler by the stepmother, another example of Munchausen syndrome by proxy.

Li, B., P. Eyer, et al. (2013). "Protein tyrosine adduct in humans self-poisoned by chlorpyrifos." Toxicol Appl Pharmacol **269**(3): 215-225.

Studies of human cases of self-inflicted poisoning suggest that chlorpyrifos oxon reacts not only with acetylcholinesterase and butyrylcholinesterase but also with other blood proteins. A favored candidate is albumin because in vitro and animal studies have identified tyrosine 411 of albumin as a site covalently modified by organophosphorus poisons. Our goal was to test this proposal in humans by determining whether plasma from humans poisoned by chlorpyrifos has adducts on tyrosine. Plasma samples from 5 self-poisoned humans were drawn at various time intervals after ingestion of chlorpyrifos for a total of 34 samples. All 34 samples were analyzed for plasma levels of chlorpyrifos and chlorpyrifos oxon (CPO) as a function of time post-ingestion. Eleven samples were analyzed for the presence of diethoxyphosphorylated tyrosine by mass spectrometry. Six samples yielded diethoxyphosphorylated tyrosine in pronase digests. Blood collected as late as 5days after chlorpyrifos ingestion was positive for CPO-tyrosine, consistent with the 20-day half-life of albumin. High plasma CPO levels did not predict detectable levels of CPO-tyrosine. CPO-tyrosine was identified in pralidoxime treated patients as well as in patients not treated with pralidoxime, indicating that pralidoxime does not reverse CPO binding to tyrosine in humans. Plasma butyrylcholinesterase was a more sensitive biomarker of exposure than adducts on tyrosine. In conclusion, chlorpyrifos oxon makes a stable covalent adduct on the tyrosine residue of blood proteins in humans who ingested chlorpyrifos.

Li, B., I. Ricordel, et al. (2010). "Dichlorvos, chlorpyrifos oxon and Aldicarb adducts of butyrylcholinesterase, detected by mass spectrometry in human plasma following deliberate overdose." J Appl Toxicol **30**(6): 559-565.

The goal of this study was to develop a method to detect pesticide adducts in tryptic digests of butyrylcholinesterase in human plasma from patients poisoned by pesticides. Adducts to butyrylcholinesterase in human serum may serve as biomarkers of pesticide exposure because organophosphorus and carbamate pesticides make a covalent bond with the active site serine of butyrylcholinesterase. Serum samples from five attempted suicides (with dichlorvos, Aldicarb, Baygon and an unknown pesticide) and from one patient who accidentally inhaled dichlorvos were analyzed. Butyrylcholinesterase was purified from 2 ml serum by ion exchange chromatography at pH 4, followed by procainamide affinity chromatography at pH 7. The purified butyrylcholinesterase was denatured, digested with trypsin and the modified peptide isolated by HPLC. The purified peptide was

analyzed by multiple reaction monitoring in a QTRAP 4000 mass spectrometer. This method successfully identified the pesticide-adducted butyrylcholinesterase peptide in four patients whose butyrylcholinesterase was inhibited 60-84%, but not in two patients whose inhibition levels were 8 and 22%. It is expected that low inhibition levels will require analysis of larger serum plasma volumes. In conclusion, a mass spectrometry method for identification of exposure to live toxic pesticides has been developed, based on identification of pesticide adducts on the active site serine of human butyrylcholinesterase.

Li, L. R., E. Sydenham, et al. (2010). "Glucocorticoid with cyclophosphamide for paraquat-induced lung fibrosis." Cochrane Database Syst Rev(6): CD008084.

BACKGROUND: Paraquat is an effective and widely used herbicide but is also a lethal poison. In many developing countries paraquat is widely available and inexpensive, making poisoning prevention difficult. However most of the people who become poisoned from paraquat have taken it as a means of suicide.Standard treatment for paraquat poisoning both prevents further absorption and reduces the load of paraquat in the blood through haemoperfusion or haemodialysis. The effectiveness of standard treatments is extremely limited.The immune system plays an important role in exacerbating paraquat-induced lung fibrosis. Immunosuppressive treatment using glucocorticoid and cyclophosphamide in combination is being developed and studied. OBJECTIVES: To assess the effects of glucocorticoid with cyclophosphamide on mortality in patients with paraquat-induced lung fibrosis. SEARCH STRATEGY: To identify randomised controlled trials on this topic, we searched the Cochrane Injuries Group's Specialised Register (searched 15 Sept 2009), CENTRAL (The Cochrane Library 2009, Issue 3), MEDLINE (Ovid SP) (1950 September Week 1 2009), EMBASE (Ovid SP) (1980 to 2009 Week 37), ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to Sept 2009), ISI Web of Science: Conference Proceedings Citation Index - Science (CPCI-S) (1990 to Sept 2009), Chinese bio-medical literature & retrieval system (CBM) (1978 to Sept 2009), Chinese medical current contents (CMCC) (1995 to Sept 2009), and Chinese medical academic conference (CMAC) (1994-Sept 2009). The searches were completed in September 2009. SELECTION CRITERIA: Randomised controlled trials (RCTs) were included in this review. All patients were to receive standard care, plus the intervention or control. The intervention was glucocorticoid with cyclophosphamide in combination versus a control of a placebo, standard care alone, or any other therapy in addition to standard care. DATA COLLECTION AND ANALYSIS: The mortality risk ratio (RR) and 95% confidence interval (CI) was calculated for each study on an intention-to-treat basis. Data for all-cause mortality at final follow-up were summarised in a meta-analysis using a fixed-effects model. MAIN RESULTS: This systematic review includes three trials with a combined total of 164 participants who had moderate to severe paraquat poisoning. Patients who received glucocorticoid with cyclophosphamide in addition to standard care had a lower risk of death at final follow-up than those receiving standard care only (RR 0.72 (95% CI 0.59 to 0.89)). AUTHORS' CONCLUSIONS: Based on the findings of three small RCTs of moderate to severely poisoned patients, glucocorticoid with

cyclophosphamide in addition to standard care may be a beneficial treatment for patients with paraquat-induced lung fibrosis. To enable further study of the effects of glucocorticoid with cyclophosphamide for patients with moderate to severe paraquat poisoning, hospitals may provide this treatment as part of an RCT with allocation concealment.

Lluis, M., S. Nogue, et al. (2008). "Severe acute poisoning due to a glufosinate containing preparation without mitochondrial involvement." Hum Exp Toxicol **27**(6): 519-524.

Glufosinate is a non-selective herbicide widely used in domestic gardens and agriculture. Few cases of glufosinate poisoning have been reported although there has been an increase in recent years, particularly in Japan. Glufosinate toxicity is related to its capacity to inhibit glutamine synthetase and glutamate decarboxylase, which may lead to a potentially fatal multiorgan failure. We report the case of a 41-year-old woman who ingested between 30 and 50 mL of a herbicide (Finale) containing glufosinate (14%) in a suicide attempt. One hour after ingestion, the patient attended the Emergency Department of her own volition. Her overall status was good, and the physical examination was unremarkable. Gastric lavage was carried out, 25 g of activated charcoal was administered, and the patient was admitted for observation. Seventeen hours later, the patient presented drowsiness and a sinus bradycardia of 40 bpm. Thirty-two hours after ingestion, the Glasgow Coma Score was 8, and orotracheal intubation and mechanical ventilation were begun. At 3 days, the patient presented a self-limiting episode of ventricular tachycardia. She recovered consciousness progressively and was extubated without complications. The evolution was favorable, but the sinus bradycardia persisted up to 8 days after the ingestion. A study of lymphocyte mitochondrial function showed no alteration in mitochondrial oxidative capacity or the enzymatic activity of the complexes of the electron transport chain. A small ingestion of glufosinate can cause severe poisoning, whose manifestations predominantly involve the central nervous system and heart rhythm. Signs and symptoms may not appear for several hours and may persist for several days. In spite of these multi-organ manifestations, no alteration in lymphocyte mitochondrial function has been reported.

Lo, Y. C., C. C. Yang, et al. (2008). "Acute alachlor and butachlor herbicide poisoning." Clin Toxicol (Phila) **46**(8): 716-721.

BACKGROUND: Alachlor and butachlor are commonly used herbicides. However, data on acute human poisonings are scarce. We retrospectively analyzed the data of human alachlor/butachlor poisoning in Taiwan. METHODS: The study period ran from October 1986 through February 2007. Sixty-three alachlor and 70 butachlor poisoning cases were reported to the Taiwan National Poison Center during the study period. Clinical data were reviewed and analyzed. RESULTS: Most patients intentionally ingested the herbicides. The toxicities of alachlor and butachlor were largely similar. Twenty-eight out of 102 patients with oral exposure were asymptomatic, while the others developed vomiting, central nervous system depression, and other outcomes. Among patients using other exposure pathways, gastrointestinal effects were the main manifestation. Three patients died after manifesting profound hypotension and/or coma following alachlor ingestion.

CONCLUSION: Alachlor and butachlor poisonings are usually of low toxicity. However, severe neurological and cardiovascular outcomes may develop rarely, especially following oral ingestion. Medical management of such poisonings is primarily supportive.

Louriz, M., T. Dendane, et al. (2009). "Prognostic factors of acute aluminum phosphide poisoning." Indian J Med Sci **63**(6): 227-234.

BACKGROUND: In Morocco, acute aluminum phosphide poisoning (AAlPP) is a serious health care problem. It results in high mortality rate despite the progress of critical care. AIMS: The present paper aims at determining the characteristics of AAlPP and evaluating its severity factors. SETTING AND DESIGN: We studied consecutive patients of AAlPP admitted to the medical intensive care unit (ICU) (Ibn Sina Hospital, Rabat, Morocco) between January 1992 and December 2007. MATERIALS AND METHODS: Around 50 parameters were collected, and a comparison was made between survivor and nonsurvivor groups. STATISTICAL ANALYSIS: Data were analyzed using Fisher exact test, Mann-Whitney U test and Cox regression model. RESULTS: Forty-nine patients were enrolled: 31 females and 18 males; their average age was 26+/-11 years. The ingested dose of aluminum phosphide was 1.2+/-0.7 g. Self-poisoning was observed in 47 cases, and the median of delay before admission to the hospital was 5.3 hours (range, 2.9-10 hours). Glasgow coma scale was 14+/-2. Shock was reported in 42.6% of the patients. pH was 7.1+/-0.4, and bicarbonate concentration was 16.3+/-8.8 mmol/L. Electrocardiogram abnormalities were noted in 28 (57%) cases. The mortality rate was 49% (24 cases). The prognostic factors were APACHE II (P=0.01), low Glasgow coma scale (P=0.022), shock (P=0.0003), electrocardiogram abnormalities (P=0.015), acute renal failure (P=0.026), low prothrombin rate (P=0.020), hyperleukocytosis (P=0.004), use of vasoactive drugs (P<0.001), use of mechanical ventilation (P=0.003). Multivariate analysis by logistic regression revealed that mortality in AAlPP correlated with shock (RR=3.82; 95% CI=1.12-13.38; P=0.036) and altered consciousness (RR=3.26; 95% CI=1.18-8.99; P=0.022). CONCLUSION: AAlPP is responsible for a high mortality, which is primarily due to hemodynamic failure.

Lund, C. M. and G. Iversen (2005). "[Parathion poisoning still occurs]." Ugeskr Laeger **167**(34): 3195-3196.

A case of lethal ethyl-parathion poisoning following intentional ingestion is reported. The patient presented with classical symptoms of the cholinergic hyperstimulation syndrome. Although ethyl-parathion is now prohibited in the EU, cases of this serious poisoning are still seen. The symptomatology and treatment are described.

Malla, G., B. Basnet, et al. (2013). "Parenteral organophosphorus poisoning in a rural emergency department: a case report." BMC Res Notes **6**: 524.

BACKGROUND: Poisoning is a common presentation in the emergency department. Oral exposures to organophosphorus compounds are especially frequent in rural and agricultural regions of South Asia and throughout the developing world. CASE PRESENTATION: Here we report a case of deliberate self-harm with an organophosphorus pesticide via the relatively

uncommon parenteral route. A young woman injected herself with chlorpyriphos. Although the cholinergic effects were mild, cellulitis and abscess development were noted as a result. CONCLUSION: Resource limited agricultural countries like Nepal present health care workers with numerous challenges in poisoning management. This case represents a rare but potentially morbid method of agrochemical poison exposure.

Mao, Y. C., J. D. Wang, et al. (2011). "Hyperammonemia following glufosinate-containing herbicide poisoning: a potential marker of severe neurotoxicity." Clin Toxicol (Phila) **49**(1): 48-52.

Glufosinate-ammonium (GLA) is the active ingredient of certain widely used non-selective contact herbicides ("e.g.," Basta). Although it is thought to be much less toxic to humans than to plants, deliberate ingestion of GLA could still lead to serious effects ("e.g.," neurotoxicity) or even death. Three cases presented with delayed-onset neurotoxicity including stupor, delirium, seizures, coma, and amnesia after ingesting large amount of Basta. Considering that GLA could irreversibly inhibit glutamine synthetase (GS) in plants, we performed serial measurements of serum ammonia in those patients and revealed marked hyperammonemia in all of them. All patients recovered with the sequelae of persistent amnesia after receiving intensive care and hemodialysis. We speculated that the occurrence of hyperammonemia might at least be partially related to GS inhibition in humans. Moreover, hyperammonemia could serve as a potential marker of severe neurotoxicity, especially prolonged amnesia, following massive ingestion of GLA-containing herbicides. The possible dose-response relation between GLA exposure and serum ammonia level, however, needs more investigations.

Markowitz, J. S., E. M. Gutterman, et al. (1986). "Self-reported physical and psychological effects following a malathion pesticide incident." Journal of Occupational Medicine **28 (5)**: 377-383.

To assess effects attributed to malathion which escaped from an overheated tank at a chemical plant in Linden, New Jersey, researchers surveyed seamen subjects (n=22) on board a nearby tanker and seamen control subjects (n=21). Self-report measurement strategies included a medical review of body systems, the 'demoralization' scale reflecting psychological symptoms of distress, demographics, and factors that may buffer stress, specifically, social support and knowledge regarding toxic chemicals. Self-reported postincident physical health differences between the two groups of seamen were noted. There were no differences between subjects and control subjects on demoralization levels. Further analysis indicated higher levels of demoralization among less knowledgeable seamen subjects.

Martinez, M. A., S. Ballesteros, et al. (2004). "Attempted suicide by ingestion of chlorpyrifos: identification in serum and gastric content by GC-FID/GC-MS." J Anal Toxicol **28**(7): 609-615.

A mild case of self-poisoning with a chlorpyrifos formulation following oral ingestion is reported. A 15-year-old female went to the emergency room after the ingestion of a product from a bottle marked with a label "Poison". On admission, she was obtunded, with normal vital signs and a strong smell of

solvent. Therapeutic measures included the application of decontamination procedures, oxygen, and gastric protectors. She had a good outcome with mild CNS depression and bradycardia. Two hours after ingestion, biological samples were collected in the emergency room and sent for analysis to our laboratory with instructions to investigate the presence of solvents. The serum and gastric content contained 5.3 and 9.4 microg/mL of unmetabolized chlorpyrifos, 4.6 and 6.9 microg/mL of toluene, and 2.5 and 7.9 microg/mL of butyl acetate, respectively. Small traces of other solvents and tetradifon were also detected. Toxicological analyses were negative for ethanol, other volatile solvents, and common drugs of abuse. The simultaneous determination of chlorpyrifos, toluene, and butyl acetate was performed using the combination of gas chromatography (GC)-flame ionization detection for screening analysis and GC-mass spectrometry for confirmation of the obtained results. The method provides an excellent and rapid tool for use in cases of pesticide poisonings, allowing the simultaneous detection of the pesticide and distillates in the performance of systematic toxicological analysis in forensic and clinical laboratories.

Mehrpour, O., S. Alfred, et al. (2008). "Hyperglycemia in acute aluminum phosphide poisoning as a potential prognostic factor." Hum Exp Toxicol **27**(7): 591-595.

Aluminum phosphide (AlP) is a solid fumigant widely used in Iran as a grain preservative. When reacted with water or acids, AlP produces phosphine gas, a mitochondrial poison that interferes with oxidative phosphorylation and protein synthesis. Poisoning by AlP is one of the most important causes of fatal chemical toxicity in Iran. There are few studies in the medical literature addressing prognostic factors associated with AlP poisoning. In this prospective study conducted across a 14-month period commencing on 21st March 2006, we enrolled all patients admitted to the ICU of Loghman-Hakim Hospital Poison Center (Tehran, Iran) with AlP poisoning, no history of diabetes mellitus diagnosed before hospitalization, and normal body mass index. We recorded patient-specific demographic information, blood glucose level on presentation (before treatment), arterial blood gas (ABG) analysis, time elapsed between ingestion and presentation, ingested dose, duration of intensive care admission, and outcome data related to each presentation. We enrolled the group of patients who survived the intoxication as a control group and compared their blood glucose levels with those who died because of AlP poisoning. Data were analyzed by Statistical Product and Service Solutions (SPSS) software (Version 12; Chicago, Ilinois, USA) using logistic regression, Pearson correlation coefficient and Student's t-test. P values of 0.05 or less were considered as the statistical significant levels. Forty-five patients (21 women and 24 men) with acute AlP poisoning were included in the study. The mean age was 27.3 +/- 11.5 years (range: 14-62 years). Thirteen patients survived (29%) and 32 expired (71%). AlP poisoning followed deliberate ingestion in all patients. The time elapsed between ingestion and arrival at the hospital was 3.2 +/- 0.4 h. There was no significant difference between survived and non-survived groups according to age, gender, and time to treatment. However, the difference between mean blood glucose levels in survived (143.4 +/- 13.7 mg/dL) and non-survived (222.6 +/- 20 mg/dL) cases was statistically significant (P = 0.021). There was no significant correlation between blood glucose level and time to

treatment, age, gender, pH, HCO3 concentration, and ingested dose. Twenty-three (71.9%) of non-survived and four (30.8%) of survived patients had a blood glucose level greater than 140 mg/dL. After adjusting according to age, gender, ingested dose, pH and HCO3 concentration The odds ratio for hyperglycemia as a risk factor for death was 5.7 (CI of 1.4-23.4). In our study, patients who succumbed to AIP poisoning had significantly higher mean blood glucose levels than those who survived. This correlation of hyperglycemic effect and mortality suggests that it may be useful in guiding risk assessment and treatment of AIP poisoning. Management of hyperglycemia may have a useful role in treatment of these patients by allowing increased entrance of glucose into cells and reducing oxygen consumption.

Mehrpour, O., A. Amouzeshi, et al. (2014). "Successful treatment of cardiogenic shock with an intraaortic balloon pump following aluminium phosphide poisoning." Arh Hig Rada Toksikol **65**(1): 121-126.

Aluminium phosphide (AlP) is a highly toxic pesticide that inhibits cytochrome oxidase c and causes oxidative stress. Death results from refractory cardiogenic shock due to myocardial dysfunction. There is very little information regarding extracorporeal life support in severe AlP poisoning. Although several therapies are available, none are curative. We report on the use of an intra-aortic balloon pump (IABP) in a 24-year-old woman brought to our hospital after an intentional ingestion of a tablet of AlP (3 g), which caused refractory AlP-induced cardiogenic shock and acute respiratory distress syndrome (ARDS). The patient underwent gastric lavage with potassium permanganate, received sodium bicarbonate intravenously, and was admitted to the intensive care unit. Echocardiography at 36 h post ingestion showed a left ventricular ejection fraction (LVEF) of <20 %. An IABP was inserted and the patient's vital signs stabilised. After eight days, the IABP was removed and on day 20, the patient's LVEF increased to 50 %. IABP was successfully used and may improve future prognoses for severely poisoned AlP patients with refractory cardiogenic shock. We encourage clinical toxicologists to examine this new treatment.

Miller, M. and K. Bhalla (2010). "An urgent need to restrict access to pesticides based on human lethality." PLoS Medicine **7 (10)**(e1000358).

Miranda, J., R. McConnell, et al. (2002). "Tactile vibration thresholds after acute poisonings with organophosphate insecticides." Int J Occup Environ Health **8**(3): 212-219.

This study evaluated the association between acute poisoning with organophosphate pesticides (OPs) and quantitative tactile vibration thresholds. Thresholds of the dominant index fingers and big toes of 56 men hospitalized for acute poisoning with OPs were measured at hospital discharge (1-24 days after poisoning) and around seven weeks later (24-176 days after poisoning), and compared with those of controls. Thresholds of the big toes of men with severe intentional poisonings due to neuropathic OPs (metamidophos and chlorpyrifos) increased between the first and second examinations. Threshold impairment was not detected in the index finger regardless of poisoning agent or severity. The development of

threshold impairment as a consequence of severe intentional poisonings with neuropathic OPs is consistent with other reports indicating that only severe OP poisonings produce sensory peripheral nerve effects.

Mishara, B. L. (2007). "Prevention of deaths from intentional pesticide poisoning." Crisis-the Journal of Crisis Intervention and Suicide Prevention **28**: 10-20.

Ingestion of pesticides is the most common suicide method worldwide, accounting for one third of all suicides, predominantly in Asia, Africa, Central and South America. Case fatalities are high, particularly in rural areas. This high case fatality may explain the similar numbers of male and female suicides in Asia, since more women die from their attempts. In Asia, pesticide suicides are mostly impulsive acts with little advance planning and they are less often associated with mental illness than in Western countries. Pesticides are generally chosen for their easy access. Prevention strategies include treating the problems leading to suicidal behaviors involving pesticides; changing attitudes, knowledge, and beliefs about pesticides; controlling access to dangerous pesticides, including developing secure storage practices (which are currently being evaluated); and improving the medical treatment of poisonings. More research is needed to better understand suicides involving pesticides in their cultural contexts and to evaluate the effectiveness of intervention programs, including assessment of possible substitution of methods. Also, more knowledge about protective factors may help suggest innovative prevention strategies.

Mishra, A., H. V. Pandya, et al. (2013). "Multi-organ Dysfunction Syndrome with Dual Organophosphate Pesticides Poisoning." Toxicol Int **20**(3): 275-277.

Organophosphate (OP) pesticide self-poisoning is common in developing countries. Poisoning with dual OP compounds is rare. Multi-organ dysfunction after OP poisoning has a high mortality rate. We report the case of a 27-year-old man who developed multi-organ dysfunction syndrome with fatal outcome after intentional ingestion of 50:50 mixture of two OP compounds, dichlorvos and profenofos.

Moon, H. J. and J. W. Lee (2013). "Availability of intravenous lipid emulsion therapy on endosulfan-induced cardiovascular collapse." Am J Emerg Med **31**(5): 886 e881-882.

Acute Endosulfan poisoning is associated with a high mortality rate in humans, and can exceed 30% [Moon JM, Chun BJ. Acute endosulfan poisoning: a retrospective study. Hum Exp Toxicol 2009;28:309-16]. Prophylactic anticonvulsant therapy for symptomatic patients and aggressive treatment for seizures may limit morbidity, but, no effective antidote is available [Moses V, Peter JV. Acute intentional toxicity: endosulfan and other organochlorines. Clin Toxicol (Phila) 2010;48:539-44]. However, endosulfan poisoning is often completely reversible with the appropriate management [Karatas AD, Aygun D, Baydin A. Characteristics of endosulfan poisoning: a study of 23 cases. Singapore Med J 2006;47:1030-2]. Intravenous lipid emulsion (ILE) may be a useful in treatment of lipophilic medication overdoses as an adjunct to antidotal therapy [Rothschild L, Berns S, Oswald S, et al. Intravenous lipid emulsion in clinical toxicology. Scand J Trauma

Resusc Emerg Med 2010;18:51]. We believe that this is its first reported use in endosulfan toxicity.

Moon, J. M. and B. J. Chun (2012). "Acute intoxication with the adjuvant itself for Gramoxone INTEON." Hum Exp Toxicol **31**(1): 18-23.

The adjuvant for Gramoxone INTEON is composed of 20% methanol, 20% sodium lingo sulphonate, 10% alkylaryl polyoxyethylene ether, and 50% water. Although the adjuvant is a potential source of intoxication due to the widespread use of Gramoxone INTEON, there has been no prior report characterizing the acute toxicity of this adjuvant. This study evaluated the acute toxicity of adjuvant ingestion. Seven patients presenting with acute adjuvant intoxication at Chonnam National University Hospital were enrolled in this retrospective study. The patients had intentionally or accidentally ingested 20-150 mL of adjuvant. Gastrointestinal symptoms such as nausea and vomiting were most common, and no ocular symptoms were reported. Cardiovascular symptoms were limited to electrocardiogram changes such as corrected QT interval (QTc) prolongation (71.4%) and sinus tachycardia (28.6%). All patients had an elevated serum osmolar gap and lactate levels. One patient had metabolic acidosis with a high anion gap that required administration of sodium bicarbonate. These clinical symptoms were resolved within 3 days with supportive treatment without any sequelae. There were no life-threatening symptoms and no deaths. However, the physician should keep in mind the possibility of methanol intoxication in patients poisoned with this adjuvant.

Moon, J. M., Y. I. Min, et al. (2006). "Can early hemodialysis affect the outcome of the ingestion of glyphosate herbicide?" Clin Toxicol (Phila) **44**(3): 329-332.

The ingestion of small amounts of glyphosate herbicide usually causes only mild symptoms. However, when large volumes of concentrates are ingested intentionally, it can generate potentially fatal symptoms that are refractory to treatment. It also is well known that the treatment for glyphosate poisoning is primarily of a supportive nature. We report two patients who intentionally ingested glyphosate herbicide, and both exhibited cardiovascular collapse and complicated renal failure despite the use of aggressive supportive therapy. Hemodialysis was conducted and the results were satisfactory; both patients were discharged without any sequelae. After analyzing these cases, we suggest that hemodialysis might have contributed to the favorable outcomes of our patients, and that there are several mechanisms that might justify the use of hemodialysis in these patients. In conclusion, physicians may wish to consider the early use of hemodialysis to improve the prognosis of patients exhibiting refractory hypotension and oliguria, despite vigorous supportive treatment in glyphosate herbicide intoxication.

Mori, H., T. Sato, et al. (1998). "A method for rapid analysis of pesticides causing acute poisoning in patients and application of this method to clinical treatment." Japanese Journal of Toxicology and Environmental Health **44 (6)**: 413-427.

Pesticide concentration in serum must be measured in order to determine the proper treatment for patients with pesticide poisoning. We previously investigated the effectiveness of a screening method for fat-soluble pesticides by HPLC equipped with photo-diode-array detection (HPLC-DAD)

and found that the method was effective in emergency medical units. In the present study, we investigated the effectiveness of a method for quantitative analysis for these fat-soluble pesticides. The concentrations of all pesticides were proportional to the peak area up to 100 mug/ml (injection amount: 1 mug), and the recovery ratio was excellent. This method was applied to three actual cases of acute poisoning, and we were able to give important advice to the doctor according to the concentration of the pesticides in the serum. The screening of pesticides by HPLC-DAD was confirmed by GC-MS.

Moses, V. and J. V. Peter (2010). "Acute intentional toxicity: endosulfan and other organochlorines." Clin Toxicol (Phila) **48**(6): 539-544.

INTRODUCTION: Organochlorine pesticides continue to be used in several developing countries despite concerns regarding their toxicity profile. Endosulfan is an organochlorine recognized as an important agent of acute toxicity. METHODS: In this retrospective study, the clinical features, course, and outcomes among patients with acute endosulfan poisoning requiring admission to the hospital during an 8-year period (1999-2007) were reviewed. RESULTS: Among 34 patients hospitalized during this study period for alleged organochlorine poisoning, 16 patients with endosulfan poisoning were identified. The majority (75%) received initial treatment at a primary or secondary center. Neurological toxicity predominated, particularly low sensorium (81%) and generalized seizures (75%), including status epilepticus (33%). Other features observed included hepatic transaminase elevation, azotemia, metabolic acidosis, and leukocytosis. Mechanical ventilation was required in 69% and vasoactive agents in 19%. In-hospital mortality was 19%. There were no gross neurological sequelae at discharge. In three other patients who presented with organochlorine poisoning, the compounds ingested were lindane, endrin, and dicofol (n = 1 each). The course and outcomes in these patients were unremarkable and all three patients survived. CONCLUSIONS: Endosulfan is capable of high lethality and significant morbidity. The commonest manifestations are neurological although other organ dysfunction also occurs. In the absence of effective antidotes, restriction of its availability, along with prompt treatment of toxicity, including preemptive anticonvulsant therapy are suggested.

Mostafa, A., G. Medley, et al. (2011). "Simultaneous quantification of carbamate insecticides in human plasma by liquid chromatography/tandem mass spectrometry." J Chromatogr B Analyt Technol Biomed Life Sci **879**(23): 2234-2238.

Carbofuran (CFN), carbosulfan (CSN) and fenobucarb (FBC) are carbamate pesticides that are widely used in gardening and agriculture for the control of insects. Human poisoning due to occupational or self-poisoning exposures is also reported, so assays are required to quantify the plasma concentration of these insecticides. An LC-MS/MS method was developed and validated for the simultaneous quantification of these three carbamate insecticides in the plasma of patients with acute intentional self-poisoning. Plasma samples were pretreated by acetonitrile for protein precipitation. Chromatography was carried out on a Luna C18(2) analytical column with gradient elution using a mobile phase containing acetonitrile and water with 10mM ammonium acetate. Mass spectrometric analysis was performed by an Applied Biosystems MDS Sciex API 2000 triple quadrupole mass spectrometer

coupled with electrospray ionization (ESI) source in the positive ion mode. The total run time was 7 min. The assay was validated over a concentration range from 10 to 1000 ng/ml for CSN and FBC and 20-2000 ng/ml for CFN. The precision and accuracy for both intra- and inter-day determination of all analytes were acceptable (<15%). No significant matrix effect was observed. Stability of compounds was established for short term bench and autosampler storage as well as freeze/thaw cycles. The method was effectively applied to 270 clinical samples from patients with a history of acute intentional carbamate self-poisoning.

Muller, I. B., H. Willads Petersen, et al. (2003). "Fatal overdose of the herbicide bentazone." Forensic Sci Int **135**(3): 235-236.

A 59-year-old woman who intentionally ingested 100-200 ml Basagran was taken to the hospital with a cardiac arrest 2 days after she had consumed the herbicide. During this period she suffered vomiting, urination and diarrhoea and she was drowsy with a muddled speech. Biological samples obtained at the autopsy were analysed and presence of bentazone, alcohol and an active metabolite of citalopram were detected. Blood concentrations of bentazone, alcohol and desmethyl-citalopram were 625 mg/kg, 0.62 g/l and 0.03 mg/kg, respectively.

Neguin, C., A. Beuchee, et al. (1999). "[Voluntary poisoning with a rodenticide in an adolescent]." Arch Pediatr **6**(8): 855-858.

Suicide attempts are frequent during adolescence. Intentional ingestion of rat poison is not well known in France. The complications of this are prolonged and may be serious. CASE REPORT: An adolescent, 15 years old, with clinical hemorrhagic syndrome, had coagulation deficiency. Rat poison had been found in serum. The young girl recognized later that the ingestion of these toxins was intentional. CONCLUSION: Suicide attempt with rat poison is exceptional, but we have to mention it when vitamin K-dependent factors failed without any other explication.

Nurulain, S. M. (2012). "Different approaches to acute organophosphorus poison treatment." J Pak Med Assoc **62**(7): 712-717.

Organophosphorus compounds (OPCs) have a wide variety of applications and are a serious threat for self-poisoning, unintentional misuse, terrorist attack, occupational hazard and warfare attack. The present standard treatment has been reported to be unsatisfactory. Many novel approaches are being used and tested for acute organophosphorus (OP) poison treatment. The bioscavenger concept captured high attention among the scientific community during the last few decades. Other approaches like alkalinisation of blood plasma/serum and use of weak inhibitors against strong inhibitors, though it showed promising results, did not get such wide attention. The introduction of a novel broad-spectrum oxime has also been in focus. In this mini-review, an update of the overview of four different approaches has been discussed. The standard therapy that is atropine+oxime+benzodiazepine along with supportive measures will continue to be the best option with only the replacement of a single oxime to improve its broad-spectrum efficacy.

Ohta, H., M. Mori, et al. (2006). "A case of suicide by ingestion of completely decomposed pesticide diazinon." Journal of the Canadian Society of Forensic Science **39 (3)**: 141-151.

Diazinon is an organophosphorus insecticide with a long history, that is widely used throughout the world. It is involved in many cases of suicide or accidental intoxication. Diazinon is considered to be relatively stable under normal conditions, but often undergoes self-decomposition during storage for unknown reasons. We report a case of suicide by ingestion of completely decomposed diazinon. The victim's stomach contents and the liquid that the victim drank underwent forensic examinations. The constituents of the liquid sample were detected from the stomach contents by conventional forensic analytical methods such as thin-layer chromatography and gas chromatography - mass spectrometry. Diazinon itself was not detected in either sample, but several decomposition products of diazinon were detected. In particular, monothiono-TEPP, which is much more toxic than diazinon itself, was detected as a major component. Therefore, in this case, the cause of death was thought to be poisoning by monothiono-TEPP and/or other ingredients such as xylenes. The most abundant components in the samples were 6,6'-thiobis (2-isopropyl-4- methylpyrimidine) and 2-isopropyl-4-ethylthio-6-methylpyrimidine, which are known to be characteristic degradation products of diazinon. These compounds were easily detected, thus providing persuasive evidence that the liquid the victim drank was decomposed diazinon.

Olson, D. P., J. A. Diaz, et al. (2010). "A fatal case of paraquat ingestion: clinical course and review of pathophysiology." Med Sci Monit **16**(12): CS153-156.

BACKGROUND: Exposure to the dipyridyl herbicide paraquat can cause many manifestations of toxicity, and is a common method of suicide in developing countries. CASE REPORT: We present a case of a 20 year old healthy gentleman who intentionally overdosed on paraquat in a suicide attempt. He presented to the hospital within 4 hours of ingestion. Despite standard supportive measures, the patient's clinical condition worsened. He developed ulceration of his oral mucosa. He also developed acute non-oliguric renal failure and acute liver injury. After his mental status began to deteriorate, the patient expired. CONCLUSIONS: There are several therapies that may have helped this patient's condition. An explanation about the pathophysiology of toxicity and updated information on treatment is provided for this common condition with poor prognosis.

Oom, P., P. Pereira, et al. (2002). "Poisoning with methanol and carbamates. [Portuguese]." Acta Medica Portuguesa **15 (1)**: 45-48.

We describe the case of a eleven years old boy with a simultaneous intentional poisoning with methanol and carbamates. The symptomatology was biphasic due to the addition of the symptomatology of both intoxications. Therapeutic measures included gastrointestinal decontamination, sodium bicarbonate, atropine, ethanol administration and hemodialysis.

Pasquale-Styles, M. A., M. A. Sochaski, et al. (2006). "Fatal bromethalin poisoning." J Forensic Sci **51**(5): 1154-1157.

Bromethalin is a neurotoxin found in some rodenticides. A delusional 21-year-old male presented to a hospital with altered mental status the day after ingesting a bromethalin-based rodenticide. He died 7 days after his self-reported exposure to c. 17 mg bromethalin (equivalent to 0.33 mg bromethalin/kg). His clinicopathologic course was characterized by altered mental status, obtundation, increased cerebrospinal fluid pressure, cerebral edema, death, and diffuse histologic vacuolization of the white matter in the central nervous system seen on microscopic examination at autopsy. The presence of a demethylated form of bromethalin in the patient's liver and brain was confirmed by gas chromatography with mass spectrometry. Clinical signs and lesions observed in this patient are similar to those seen in animals poisoned with bromethalin. This case illustrates the potential for bromethalin ingestion to result in fatal human poisoning.

Patel, V. (2007). "Commentary: Preventing suicide: Need for a life course approach." International Journal of Epidemiology **36 (6)**: 1242-1243.

Pattnaik, R. B., S. K. Satpathy, et al. (2001). "Self injection of organophosphorous insecticide." J Assoc Physicians India **49**: 770.

Paudyal, B. P. (2008). "Organophosphorus poisoning." JNMA J Nepal Med Assoc **47**(172): 251-258.

Acute poisoning by organophosphorus (OP) compounds is a major global clinical problem, with thousands of deaths occurring every year. Most of these pesticide poisoning and subsequent deaths occur in developing countries following a deliberate self ingestion of the poison. Metacid (Methyl parathion) and Nuvan (Dichlorovos) are commonly ingested OP pesticides; Dimethoate, Profenofos, and Chlorpyrifos are other less frequently ingested compounds in Nepal. The toxicity of these OP pesticides is due to the irreversible inhibition of acetylcholinesterase (AChE) enzyme leading to accumulation of acetylcholine and subsequent over-activation of cholinergic receptors in various parts of the body. Acutely, these patients present with cholinergic crisis; intermediate syndrome and delayed polyneuropathy are other sequel of this form of poisoning. The diagnosis depends on the history of exposure to these pesticides, characteristic manifestations of toxicity and improvements of the signs and symptoms after administration of atropine. The supportive treatment of OP poisoning includes the same basic principles of management of any acutely poisoned patient i.e., rapid initial management of airways, breathing, and circulation. Gastric lavage and activated charcoal are routinely used decontamination procedures, but their value has not been conclusively proven in this poisoning. Atropine is the mainstay of therapy, and can reverse the life threatening features of this acute poisoning. However, there are no clear cut guidelines on the dose and duration of atropine therapy in OP poisoning. Cholinesterase reactivators, by regenerating AChE, can reverse both the nicotinic and muscarinic effects; however, this benefit has not been translated well in clinical trials. All these facts highlight that there are many unanswered questions and controversies in the management of OP poisoning and there is an urgent need for research on this aspect of this common and deadly poisoning.

Peoples, S. and K. Maddy (1979). "Poisoning due to ingestion of the rodent poison, Vacor." Veterinary and Human Toxicology **21 (SUPPL.)**: 216-218.

The chemical 1-(3-pyridyl-methyl)-3-(4 nitro-phenyl) urea is the active ingredient used in a rodent poison sold under the trade name of Vacor. It is usually sold with 2% of active ingredient in 39 gram bait packets of grain with a peanut flavor. The LD(50) of the active ingredient in rats is 4.5 mg per kg, in mice it is 80 mg per kg, and in monkeys it is more than 2,000 mg per kg. It now appears that the LD(50) in man is close to that of the rat. In California there have been nine serious adult human poisonings with two of them fatal; there have also been 12 reported accidental exposures of children. These nine adult cases ingested up to a full packet or more each of Vacor, probably all with suicidal intent. Two of the nine cases died. All developed severe hypotension and diabetes mellitus. The seven serious cases who are still living are under intensive treatment for hypotension and diabetes. For the 12 ingestions by children that have been observed, emetics were given and no symptoms of poisoning have been reported. There is no way of knowing how many children may have ingested toxic amounts of this pesticide without observations of the events and developed symptoms of poisoning. The manufacturer has withdrawn all current formulations of this product from the market and will market a new formulation containing 1/8 the amount of active ingredient per bait. Label changes which indicate more specifically the toxic effects and treatment have been made.

Premaratna, R., Y. Tilakarathna, et al. (2001). "Parasuicide by self-injection of an organophosphate insecticide." Hum Exp Toxicol **20**(7): 377-378.

Parasuicide by ingestion of organophosphate (OP) insecticides is common in Sri Lanka, but the use of the parateral route to self administer the poison is extremely rare. We report a patient who deliberately injected herself intramuscularly with an OP compound with suicidal intent. The clinical manifestations of OP poisoning were unpredictable and posed a therapeutic problem.

Proenca, P., E. Pinho Marques, et al. (2003). "A fatal forensic intoxication with fenarimol: analysis by HPLC/DAD/MSD." Forensic Sci Int **133**(1-2): 95-100.

Fenarimol (Rubigan) is a pyrimidine ergosterol biosynthesis inhibitor used as a systemic fungicide. The authors present a fatal fenarimol intoxication case analysed in the Forensic Toxicology Service of the National Institute of Legal Medicine. The results were used to compare two different HPLC techniques, regarding selectivity and sensitivity: an HPLC system with a diode array detector (DAD) and an HPLC system with a DAD and a mass spectrometry detector (MSD) with an electrospray interface. All biological samples were submitted to a solid-phase extraction procedure. The detection and quantification limits of fenarimol, linearity, precision and accuracy were evaluated. The fenarimol concentration levels determined were of 89.0 mg ml in gastric contents, 1.9 mg/g in liver and 0.4 mg/g in kidney. Blood was not available at autopsy. No published data related to fenarimol self-poisoning were found, so it was not possible to interpret the results obtained by comparison with toxic/lethal levels.

Radhakrishnan, R. and C. Andrade (2012). "Suicide: An Indian perspective." Indian Journal of Psychiatry **54 (4)**: 304-319.

Suicide is the third leading cause of death among young adults worldwide. There is a growing recognition that prevention strategies need to be tailored to the region-specific demographics of a country and to be implemented in a culturally-sensitive manner. This review explores the historical, epidemiological and demographic factors of suicide in India and examines the strategies aimed at the prevention of suicide. There has been an increase in the rates of suicide in India over the years, although trends of both increases and decline in suicide rates have been present. Distinct from global demographic risk factors, In India, marital status is not necessarily protective and the female: male ratio in the rate of suicide is higher. The motives and modes of suicide are also distinct from western countries. Preventive strategies implemented at a community level and identifying vulnerable individuals maybe more effective than global strategies.

Rao Ch, S., V. Venkateswarlu, et al. (2005). "Pesticide poisoning in south India: Opportunities for prevention and improved medical management." Tropical Medicine and International Health **10 (6)**: 581-588.

OBJECTIVE: Warangal district in Andhra Pradesh, southern India, records >1000 pesticide poisoning cases each year and hundreds of deaths. We aimed to describe their frequency and distribution, and to assess quality of management and subsequent outcomes from pesticide poisoning in one large hospital in the district. METHODS: We reviewed data on all patients admitted with pesticide poisoning to a district government hospital for the years 1997 to 2002. For 2002, details of the particular pesticide ingested and management were abstracted from the medical files. FINDINGS: During these 6 years, 8040 patients were admitted to the hospital with pesticide poisoning. The overall case fatality ratio was 22.6%. More detailed data from 2002 revealed that two-thirds of the patients were <30 years old, 57% were male and 96% had intentionally poisoned themselves. Two compounds, monocrotophos and endosulfan, accounted for the majority of deaths with known pesticides in 2002. Low fixed-dose regimens were used in the majority of cases for the most commonly used antidotes (atropine and pralidoxime). Inappropriate antidotes were also used in some patients. CONCLUSIONS: It is likely that these findings reflect the situation in many rural hospitals of the Asia Pacific region. Even without an increase in resources, there appear to be significant opportunities for reducing mortality by better medical management and further restrictions on the most toxic pesticides. 2005 Blackwell Publishing Ltd.

Ratnayake, R. (2008). "Building capacity to address emerging problems in developing countries: intentional self-poisoning and pesticides." Open Med **2**(2): e51-53.

Riyaz, R., S. L. Pandalai, et al. (2013). "A fatal case of thallium toxicity: challenges in management." J Med Toxicol **9**(1): 75-78.

BACKGROUND: Thallium is a highly toxic compound and is occasionally involved in intentional overdoses or criminal poisonings. Accidental poisonings also occur, but are increasingly rare owing to restricted use and

availability of thallium. We report a fatal suicidal ingestion of thallium sulfate rodenticide in which multi-dose activated charcoal (MDAC) and Prussian Blue (PB) were both used without changing the outcome. CASE REPORT: A 36 year old man ingested an unknown amount of thallium sulfate grains from an old rodenticide bottle. He presented to an emergency department (ED) 45 minutes later with abdominal pain and vomiting. On examination he was agitated with a blood pressure of 141/60 mmHg and a heart rate of 146 beats per minute (bpm). He received MDAC during his initial ED management and was started on PB 18 hours post arrival; he was intubated on the following day for airway protection. The patient continued to be tachycardic and hypertensive and subsequently developed renal failure. On hospital day three, the patient developed hypotension that did not respond to fluids. The patient required vasopressors and was transferred to a tertiary care center to undergo continuous renal replacement therapy (CRRT). The patient died shortly after his transfer. His last blood thallium concentration was 5369 mcg L, a spot urine thallium >2000 mcg/L, and a 24- hour urine thallium was >2000 mcg/L. CONCLUSION: Though extremely rare, thallium intoxication can be lethal despite early administration of MDAC and use of Prussian blue therapy. Rapid initiation of hemodialysis can be considered in cases of severe thallium poisoning, to remove additional thallium, to correct acid-base disturbance, or to improve renal function.

Roberts, D. M., W. Dissanayake, et al. (2004). "Refractory status epilepticus following self-poisoning with the organochlorine pesticide endosulfan." J Clin Neurosci **11**(7): 760-762.

We describe a case of refractory status epilepticus presenting to a rural general hospital in Sri Lanka. This patient's condition was precipitated by intentional self-poisoning with the organochlorine insecticide endosulfan. Although rarely seen in developed countries, pesticide poisoning particularly with endosulfan is an important cause of difficult-to-manage seizures in Asian countries. In this case report, we discuss the management of status epilepticus and refractory status epilepticus. Further, we specifically discuss the clinical pharmacology and toxicology of endosulfan.

Roberts, D. M., R. Seneviratne, et al. (2005). "Intentional self-poisoning with the chlorophenoxy herbicide 4-chloro-2-methylphenoxyacetic acid (MCPA)." Ann Emerg Med **46**(3): 275-284.

STUDY OBJECTIVE: Data on poisoning with MCPA (4-chloro-2-methyl-phenoxyacetic acid) are limited to 6 case reports. Our objective is to describe outcomes from intentional self-poisoning with MCPA in a prospective case series of 181 patients presenting to hospitals in Sri Lanka. METHODS: Patient information was collected by on-site study physicians as part of an ongoing prospective cohort study of poisoned patients. Medical history, clinical details, and blood samples were obtained prospectively. RESULTS: Overall clinical toxicity was minimal in 85% of patients, including mild gastrointestinal symptoms in 44% of patients. More severe clinical signs of chlorophenoxy poisoning reported previously, such as rhabdomyolysis, renal dysfunction, and coma, also occurred but were uncommon. Eight patients died (4.4%). Most deaths occurred suddenly from cardiorespiratory arrest within 48 hours of poisoning; the pathophysiological

mechanism of death was not apparent. The correlation between admission plasma MCPA concentration and clinical markers of severity of toxicity (physical signs, symptoms, and increased creatine kinase level) was poor. CONCLUSION: Intentional self-poisoning with MCPA generally causes mild toxicity, but cardiorespiratory arrest and death may occur. All patients should receive routine resuscitation and supportive care. It seems reasonable to correct acidosis and maintain an adequate urine output, but there is insufficient evidence to support other specific interventions. Our data do not support a clinical role for measurement of plasma MCPA in the acute management of poisoning, and insufficient data were available to fully examine the utility of measured electrolytes and creatine kinase levels.

Roberts, D. M., M. F. Wilks, et al. (2011). "Changes in the concentrations of creatinine, cystatin C and NGAL in patients with acute paraquat self-poisoning." Toxicol Lett **202**(1): 69-74.

An increase in creatinine > 3 mumol/L/h has been suggested to predict death in patients with paraquat self-poisoning and the value of other plasma biomarkers of acute kidney injury has not been assessed. The aim of this study was to validate the predictive value of serial creatinine concentrations and to study the utility of cystatin C and neutrophil gelatinase-associated lipocalin (NGAL) as predictors of outcome in patients with acute paraquat poisoning. The rate of change of creatinine (dCr/dt) and cystatin C (dCyC/dt) concentrations were compared between survivors and deaths. Receiver-operating characteristic (ROC) curves were constructed to determine the best threshold for predicting death. Paraquat was detected in 20 patients and 7 of these died between 18 h and 20 days post-ingestion. The dCr/dt ROC curve had an area of 0.93 and the cut-off was > 4.3 mumol L/h (sensitivity 100%, specificity 85%, likelihood ratio 7). The dCyC/dt ROC curve had an area of 0.97 and the cutoff was > 0.009 mg/L/h (sensitivity 100%, specificity 91%, likelihood ratio 11). NGAL did not separate survivors from deaths. Death due to acute paraquat poisoning is associated with changes in creatinine and cystatin concentrations. Further validation of these measurements is needed before they can be adopted in guiding intensive treatments.

Robinson, R. F., J. R. Griffith, et al. (2002). "Intoxication with sodium monofluoroacetate (compound 1080)." Vet Hum Toxicol **44**(2): 93-95.

The highly toxic sodium monofluoroacetate (SMFA) was banned as a rodenticide in the U.S. in 1972. We report the first case of intentional ingestion in this country in over 15y. A 47-y-old male was brought to the emergency room status post tonic clonic seizure. At 34 h post ingestion, he responded ony to noxious stimuli and at 48 h, he was unresponsive to painful stimuli, was intubated and placed on a ventilator. Over the following 3 d, he was became minimally responsive to external stimuli with bouts of agitation and hypertension. Two days later he was discharged with no evidence of neurologic sequelae. We report this patient to increase awareness of SMFA toxicity, and its ability to cause anion gap metabolic acidosis.

Roeyen, G., T. Chapelle, et al. (2008). "Necrotizing pancreatitis due to poisoning with organophosphate pesticides." Acta Gastroenterol Belg **71**(1): 27-29.

Several complications have been reported in relation to organophosphate poisoning. Pancreatitis due to cholinergic hypersecretion related to this type of poisoning, is however rare and has usually a subclinical course. Necrotizing pancreatitis has only been reported in 3 patients. We present a case of a young man who deliberately ingested the organophosphate dichlorvos and developed a necrotizing pancreatitis. A distal spleen and vessel preserving pancreatectomy was performed already 36 hours after ingestion. We believe that due to this very early surgery, this patient could be discharged as early as 12 days after surgery.

Romeo, K., M. Bikramjit, et al. (2005). "Organophosphorus pesticides poisoning via intravenous route: (Case reports)." International Journal of Medical Toxicology and Legal Medicine **8 (1)**: 20-21.

Two rare cases of a self injectdd intravenous poisoning with an organo phosphorus compound namely Monocrotophos and Hildane are being presented. First patient was an ex-intravenous drugs user (IDU) and second one is a farmer. Both of them attempted to commit suicide by injecting organophosphorous compound through I.V. route. Both of them improved on treatment with injection atropine and pralidoxime.

Salm, P., P. J. Taylor, et al. (2009). "Liquid chromatography-tandem mass spectrometry method for the simultaneous quantitative determination of the organophosphorus pesticides dimethoate, fenthion, diazinon and chlorpyrifos in human blood." Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences **877 (5-6)**: 568-574.

Simultaneous determination of the organophosphorus pesticides dimethoate, fenthion, diazinon and chlorpyrifos in human blood by HPLC-tandem mass spectrometry was developed and validated. The pesticides were extracted by a simple one-step protein precipitation procedure. Chromatography was performed on a Luna C₁₈ (30 mm x 2.0 mm, 3 mum) column, using a step-gradient at a flow rate of 0.4 ml/min. The assay was linear from 0.5 to 100 ng/ml ($r^2 > 0.992$, n = 24) for all pesticides. The inter- and intra-day accuracy and precision for the method was 96.6-106.1% and <10%, respectively. The lower limit of quantification was 0.5 ng/ml. In conclusion, the method described displays analytical performance characteristics that are suitable for the quantification of these pesticides in cases of acute poisoning.

Sam, K. G., K. Kondabolu, et al. (2009). "Poisoning severity score, APACHE II and GCS: effective clinical indices for estimating severity and predicting outcome of acute organophosphorus and carbamate poisoning." J Forensic Leg Med **16**(5): 239-247.

Self-poisoning with organophosphorus (OP) compounds is a major cause of morbidity and mortality across South Asian countries. To develop uniform and effective management guidelines, the severity of acute OP poisoning should be assessed through scientific methods and a clinical database should be maintained. A prospective descriptive survey was carried out to assess the utility of severity scales in predicting the outcome of 71 organophosphate (OP) and carbamate poisoning patients admitted during a one year period at the Kasturba Hospital, Manipal, India. The Glasgow coma

scale (GCS) scores, acute physiology and chronic health evaluation II (APACHE II) scores, predicted mortality rate (PMR) and Poisoning severity score (PSS) were estimated within 24h of admission. Significant correlation (P<0.05) between PSS and GCS and APACHE II and PMR scores were observed with the PSS scores predicting mortality significantly (P< or =0.001). A total of 84.5% patients improved after treatment while 8.5% of the patients were discharged with severe morbidity. The mortality rate was 7.0%. Suicidal poisoning was observed to be the major cause (80.2%), while other reasons attributed were occupational (9.1%), accidental (6.6%), homicidal (1.6%) and unknown (2.5%) reasons. This study highlights the application of clinical indices like GCS, APACHE, PMR and severity scores in predicting mortality and may be considered for planning standard treatment guidelines.

Sampogna, R. V. and R. Cunard (2007). "Roundup intoxication and a rationale for treatment." Clin Nephrol **68**(3): 190-196.

A 51-year-old man with no history ofrenal disease was admitted to our hospital after an intentional ingestion of Roundup, a glyphosate-based herbicide. His course was significant for the development of acute renal failure with oliguria and severe hypoxia. Although efficacy data are sparse and controversial, we proceeded with hemodialysis in an effort to correct his worsening volume status and to potentially clear toxins that are normally excreted by the kidney. His condition improved immediately and his renal function returned to normal over the course of several weeks. We argue that hemodialysis in the setting of such herbicide ingestions may facilitate significant intoxicant clearance, especially in the setting of impaired glomerular filtration. We also make recommendations regarding possible toxin-related sequelae that may warrant initiation of hemodialysis therapy.

Sarchiapone, M., L. Mandelli, et al. (2011). "Controlling access to suicide means." International Journal of Environmental Research and Public Health **8 (12)**: 4550-4562.

Background: Restricting access to common means of suicide, such as firearms, toxic gas, pesticides and other, has been shown to be effective in reducing rates of death in suicide. In the present review we aimed to summarize the empirical and clinical literature on controlling the access to means of suicide. Methods: This review made use of both MEDLINE, ISI Web of Science and the Cochrane library databases, identifying all English articles with the keywords "suicide means", "suicide method", "suicide prediction" or "suicide prevention" and other relevant keywords. Results: A number of factors may influence an individual's decision regarding method in a suicide act, but there is substantial support that easy access influences the choice of method. In many countries, restrictions of access to common means of suicide has lead to lower overall suicide rates, particularly regarding suicide by firearms in USA, detoxification of domestic and motor vehicle gas in England and other countries, toxic pesticides in rural areas, barriers at jumping sites and hanging, by introducing "safe rooms" in prisons and hospitals. Moreover, decline in prescription of barbiturates and tricyclic antidepressants (TCAs), as well as limitation of drugs pack size for paracetamol and salicylate has reduced suicides by overdose, while increased prescription of SSRIs seems to have lowered suicidal rates.

Conclusions: Restriction to means of suicide may be particularly effective in contexts where the method is popular, highly lethal, widely available, and/or not easily substituted by other similar methods. However, since there is some risk of means substitution, restriction of access should be implemented in conjunction with other suicide prevention strategies. 2011 by the authors; licensee MDPI, Basel, Switzerland.

Savin, S., B. Cartigny, et al. (2003). "1H NMR spectroscopy and GC-MS analysis of alpha-chloralose. Application to two poisoning cases." J Anal Toxicol **27**(3): 156-161.

Alpha-chloralose, a compound widely used as a rodenticide and in the control of bird pests, is readily available. Two cases of intentional poisoning are reported. Both patients became comatose and presented hypersialorrhea and myoclonal crises in the legs. They were discharged from hospital after several days. As clinical signs of alpha-chloralose poisoning lack specificity, anamnesis might be difficult, particularly in the case of delayed diagnosis. Toxicological analysis is therefore critical, and this article reports the investigation of serum and urine samples by gas chromatography-mass spectrometry (GC-MS) in the electron-impact mode, and by 1H nuclear magnetic resonance (1H NMR) spectroscopy. Non-hydrolyzed urinary samples and those hydrolyzed by beta-glucuronidase were taken into consideration. After acetylation, GC-MS analysis was based on characteristic mass-to-charge ratio values of 272 for alpha-chloralose and 206 for beta-hydroxyethyltheophylline, which was used as internal standard. Characterization of alpha-chloralose species by 1H NMR spectroscopy was performed taking two parameters into account: chemical shift and coupling-constant values. Without any pretreatment, 1H NMR spectroscopy revealed the presence of free (5.50 and 6.15 ppm) and conjugated forms of alpha-chloralose by characteristic resonances of H1 and chloral-type protons, respectively. Quantitative analysis was performed by relative integration of peak areas. Serum alpha-chloralose showed concentrations below the quantitation limit of both methods. In urine samples, the free chemical species rapidly decreased. GC-MS analysis revealed the predominence of conjugation after a beta-glucuronidase hydrolysis step. 1H NMR analysis directly showed that on admission of the first patient, average urinary concentrations were 1.73 mmol/L (535 mg/L) for the free form and 13.72 and 6.25 mmol/L for the two conjugated forms. A later enzymatic treatment confirmed the total concentration of alpha-chloralose chemical species. Analysis of alpha-chloralose in urine by either GC-MS or 1H NMR spectroscopy methods proved to be comparable.

Senthilkumaran, S., N. Balamurgan, et al. (2011). "An unusual case of attempted suicide by rectal administration of parathion." J Forensic Leg Med **18**(8): 383-384.

Although organophosphate (OP) poisoning is well known, unusual routes of administration of OP compounds are reported occasionally. Herein, a case of self administration of parathion, an OP compound, into the rectum using a six inches (15 cm) nozzle of a sprayer in a 35-year-old man is highlighted along with probable mechanisms for rapid absorption and severe systemic toxicity.

Shadnia, S., M. Rahimi, et al. (2005). "Successful treatment of acute aluminium phosphide poisoning: possible benefit of coconut oil." Hum Exp Toxicol **24**(4): 215-218.

Aluminium phosphide is used to control rodents and pests in grain storage facilities. It produces phosphine gas, which is a mitochondrial poison. Unfortunately, there is no known antidote for aluminium phosphide intoxication, but our recent experience with a case showed that rapid prevention of absorption by coconut oil might be helpful. In the present case, we used the same protocol in a 28-year-old man who had ingested a lethal amount (12 g) of aluminium phosphide with suicidal intent and was admitted to hospital approximately 6 hours postingestion. The patient had signs and symptoms of severe toxicity, and his clinical course included metabolic acidosis and liver dysfunction. Treatment consisted of gastric lavage with potassium permanganate solution, oral administration of charcoal and sorbitol suspension, intravenous administration of sodium bicarbonate, magnesium sulphate and calcium gluconate, and oral administration of sodium bicarbonate and coconut oil. Conservative and supportive therapy in the Intensive Care Unit was also provided. The patient survived following rapid treatment and supportive care. It is concluded that coconut oil has a positive clinical significance and can be added to the treatment protocol of acute aluminium phosphide poisoning in humans.

Shadnia, S. and K. Soltaninejad (2011). "Spontaneous ignition due to intentional acute aluminum phosphide poisoning." J Emerg Med **40**(2): 179-181.

BACKGROUND: Acute aluminum phosphide (AlP) poisoning is one of the most common cause of acute pesticide poisoning in Iran. Spontaneous ignition is a rare finding in AlP poisoning. OBJECTIVE: To present two cases of fatal AlP poisoning that involved spontaneous ignition. CASE REPORT: Two patients presented with suicidal ingestion of AlP tablets. In the Emergency Department (ED), they received gastric lavage. During insertion of a nasogastric tube, both patients experienced spontaneous ignition, and flames were witnessed by the medical personnel. Unfortunately, both patients died due to systemic effects of AlP poisoning. CONCLUSION: Patients who present with acute aluminum phosphide poisoning may experience spontaneous ignition in the ED.

Siegal, D., M. A. Kotowycz, et al. (2009). "Complete heart block following intentional carbamate ingestion." Can J Cardiol **25**(8): e288-290.

Organophosphates and carbamate compounds are acetylcholinesterase inhibitors used as agricultural insecticides and represent a common cause of cholinergic toxicity. Cardiac manifestations of organophosphate and carbamate toxicity are described primarily from reports of organophosphate exposure and include sinus bradycardia, prolonged PR interval, sinus tachycardia, prolonged corrected QT interval and ventricular arrhythmias. Complete atrioventricular block has rarely been reported with insecticide poisonings. A case of complete heart block following carbamate ingestion is described and the importance of extended cardiac monitoring in these patients is emphasized.

Singh, S., S. Yadav, et al. (2003). "Fatal 2,4-D (ethyl ester) ingestion." J Assoc Physicians India **51**: 609-610.

2,4-D (2,4-dichlorphenoxyacetic acid) is widely used in agriculture and forestry to destroy broad leaved weeds (herbicide). It has a moderate mammalian toxicity and human poisoning has rarely been reported except following ingestion with suicidal intent. We report two young adults who ingested it with suicidal intent, developed neurological, cardiac, hepatic and renal toxicity and died.

Sorensen, F. W. and M. Gregersen (1999). "Rapid lethal intoxication caused by the herbicide glyphosate-trimesium (Touchdown)." Hum Exp Toxicol **18**(12): 735-737.

Two cases of rapid lethal intoxication with the herbicide glyphosate-trimesium (Touchdown) are presented. A 6-year-old boy who accidentally ingested a mouthful of glyphosate-trimesium died within minutes. The same happened to a 34-year-old woman who intentionally ingested approximately 150 ml of glyphosate-trimesium. The post-mortem examination revealed gastric content and oedema of the mucus membranes of the airways, erosion of the mucus membranes of the gastrointestinal tract, pulmonary oedema, cerebral oedema, and dilated right atrium and ventricle of the heart. The speed of which death occurs is much more rapid than lethal intoxications with the herbicide glyphosate (isoprophylamine), also known as 'Roundup'. It is suggested that the lethal mechanism between the two herbicides may be different. The component, trimethylsulfonium, of the glyphosate-trimesium may facilitate the absorption after oral ingestion. This difference can be crucial in the treatment of human intoxication. We propose that containers with glyphosate-trimesium must be labelled because of the apparent effect of lethal intoxication.

Soummer, A., B. Megarbane, et al. (2011). "Severe and prolonged neurologic toxicity following subcutaneous chlorpyrifos self-administration: a case report." Clin Toxicol (Phila) **49**(2): 124-127.

INTRODUCTION: Organophosphate poisoning by oral or inhalation routes is characterized by a typical time-course of clinical features. CASE PRESENTATION: We report a case of subcutaneous chlorpyrifos self-injection leading to a delayed cholinergic phase, prolonged coma, and severe permanent neurologic injury with electrophysiological patterns suggestive of overlapping intermediate syndrome and distal peripheral neuropathy. Time-course and severity of clinical features were not altered by either atropine or pralidoxime administration. Due to prolonged and severe alteration in consciousness, we used brain multimodal nuclear magnetic imaging and auditory cognitive event-related potentials to assess the patient's potential for awakening. Electrophysiological testing used to monitor muscle weakness showed the coexistence of 20 Hz-decremental responses in proximal muscles and severe denervation in distal muscles. Red blood cell acetylcholinesterase activity progressively normalized on day 60, while plasma butyrylcholinesterase activity remained low until day 100. Chlorpyrifos was detectable in serum until day 30 and urine metabolites for up to three months, supporting the hypothesis of a continuous chlorpyrifos release despite repeated surgical debridement. We suggest that adipose and muscle tissues acted as a chlorpyrifos reservoir. At one-year follow-up, the

patient exhibited significant neuromuscular sequelae. CONCLUSION: Subcutaneous chlorpyrifos self-injection may result in severe toxicity with prolonged neurologic injury, atypical overlapping electrophysiological patterns, and a poor final outcome.

Sribanditmongkol, P., P. Jutavijittum, et al. (2012). "Pathological and toxicological findings in glyphosate-surfactant herbicide fatality: a case report." Am J Forensic Med Pathol **33**(3): 234-237.

Glyphosate herbicide is promoted by the manufacturer as having no risks to human health, with acute toxicity being very low in normal use. In Thailand, however, poisoning from glyphosate agricultural herbicides has been increasing. A case of rapid lethal intoxication from glyphosate-surfactant herbicide involved a 37-year-old woman, who deliberately ingested approximately 500 mL of concentrated Roundup formulation (41% glyphosate as the isopropylamine salt and 15% polyoxyethylene amine; Mosanto Company). The postmortem examination revealed that the stomach contained 550 mL of yellow fluid. The gastric mucosa of anterior fundus revealed hemorrhage and the small intestines had marked dilatation and thin walls. We used the high-performance liquid chromatography method for determination of serum and gastric content levels of glyphosate. The glyphosate levels of serum and gastric content were 3.05 and 59.72 mg/mL, respectively. Toxic effects of polyoxyethylene amine and Roundup were caused by their ability to erode tissues including mucous membranes and linings of the gastrointestinal and respiratory tracts. A mild degree of pulmonary congestion and edema was observed in both lungs. We proposed that the characteristic picture of microvesicular steatosis of the hepatocytes, seen predominantly in centrilobular zones of the liver, resembled drug-induced hepatic toxicity or secondary hypoxic stress.

Sudakin, D. L., M. E. Mullins, et al. (2000). "Intermediate syndrome after malathion ingestion despite continuous infusion of pralidoxime." J Toxicol Clin Toxicol **38**(1): 47-50.

CASE REPORT: A 33-year-old female ingested an unknown quantity of malathion in a suicide attempt. Cholinergic signs consistent with severe organ, phosphate intoxication developed and were treated within 6 hours of ingestion. Intravenous atropine and a continuous infusion of pralidoxime (400 mg/h) were administered. Prolonged depression of plasma and red blood cell cholinesterases were documented. Despite an initial clinical improvement and the presence of plasma pralidoxime concentrations exceeding 4 microg mL, the patient developed profound motor paralysis consistent with the diagnosis of Intermediate Syndrome. In addition to the dose and frequency of pralidoxime administration, other factors including persistence of organophosphate in the body, the chemical structure of the ingested organophosphate, and the time elapsed between ingestion and treatment may limit the effectiveness of pralidoxime as an antidote in organophosphate ingestions. This case study suggests that these factors should be taken into account in assessing the risk of Intermediate Syndrome after intentional organophosphate ingestions.

Sundarka, M. K., H. L. Gupta, et al. (2000). "Self injection of insecticide." J Assoc Physicians India **48**(8): 856.

Thangjam, S. S., B. S. Thongam, et al. (2009). "Multiple system involvement in organophosphorous poisoning: Single case study." Journal of the Neurological Sciences **Conference: 19th World Congress of Neurology Bangkok Thailand. Conference Start: 20091024 Conference End: 20091030. Conference Publication: (var.pagings). 285**: S190-S191.

Purpose: To study a case of organophosphorous (OP) poisoning complicated by combination of transient hypergycaemia, transient extrapyramidal syndrome, acute inflammatory demyelinating polyradiculoneuropathy (AIDP), optic neuritis and auditory nerve involvement. Method: Patient was evaluated clinically, followed up closely and investigated with magnetic resonance imaging (MRI) brain, nerve conduction study (NCV), electromyography (EMG), visual evoked potentials (VEP) and brain-stem auditory evoked potential (BAEP). Result: Twenty-two years male admitted in unconscious and gasping state with history of self-deliberate ingestion of pesticide Monocrotophos 36% around 50 ml. He was ventilated followed by gastric lavage and given atropine plus pralidoxime. On 14th day of admission when he became fully conscious he developed choreoathetotic movement of the limbs and treated with trihexiphenedyl and levodopa. He was relieved of the symptoms completely in 3 days. During third week he developed flaccid asymmetrical paralysis with areflexia and difficult in seeing and hearing. The patient fulfilled the diagnosis of AIDP for her CSF showed albumino-cytological dissociation and EMG revealed peripheral neuropathy with polyradiculopathies. MRI brain showed patchy hyper intensities in bilateral fronto-temporal region. VEP showed prolonged P100 on right side confirming optic neuritis. BAEP showed prolonged inter peaked latencies I-III and I-V on right side. Conclusion: This case for the first time showed the occurrence of AIDP in OP poisoning, abnormal MRI signal changes in bilateral fronto-temporal region and abnormal VEP and BAEP study confirming diagnosis of auditory nerve involvement and optic neuritis in human OP poisoning. The association of these features in a single patient has not been reported in the literature. This report showing multiple systems involvement with severe OP poisoning supports the role of environmental toxins to cause various neurological syndromes.

Thundiyil, J. G., J. Stober, et al. (2008). "Acute pesticide poisoning: a proposed classification tool." Bull World Health Organ **86**(3): 205-209.

Cases of acute pesticide poisoning (APP) account for significant morbidity and mortality worldwide. Developing countries are particularly susceptible due to poorer regulation, lack of surveillance systems, less enforcement, lack of training and inadequate access to information systems. Previous research has demonstrated wide variability in incidence rates for APP. This is possibly due to inconsistent reporting methodology and exclusion of occupational and non-intentional poisonings. The purpose of this document is to create a standard case definition to facilitate the identification and diagnosis of all causes of APP, especially at the field level, rural clinics and primary health-care systems. This document is a synthesis of existing literature and case definitions that have been previously proposed by other authors around

the world. It provides a standardized case definition and classification scheme for APP into categories of probable, possible and unlikely/unknown cases. Its use is intended to be applicable worldwide to contribute to identification of the scope of existing problems and thus promote action for improved management and prevention. By enabling a field diagnosis for APP, this standardized case definition may facilitate immediate medical management of pesticide poisoning and aid in estimating its incidence.

Thunga, G., K. G. Sam, et al. (2009). "Profile of acute mixed organophosphorus poisoning." Am J Emerg Med **27**(5): 628 e621-623.

Organophosphorus (OP) pesticide self-poisoning is a major clinical and public health problem across much of rural Asia and responsible for two thirds of suicidal deaths. However, clinical reports or evidence for the management of mixed poisoning are lacking. Patients are often treated based on the type of symptoms they exhibit, and there are no specific guidelines available to treat mixed poisoning. In this case series, we report 3 acute OP poisoning cases with mixed poisons such as organochlorine, fungicide, copper sulfate, and kerosene. All 3 patients were treated successfully, with a greater focus on OP poisoning with pralidoxime and atropine infusion along with standard decontamination procedures. Because patients developed complications due to the concomitant poisons ingested, they were later treated symptomatically, and in one case, D-penicillamine was administered as antidote for copper poisoning. Mixed poisoning especially with OP compounds makes the diagnosis difficult because the clinical symptoms of OP predominate, whereas damage produced by other pesticides is late to develop and often neglected. Common treatment procedures are focused mainly on the OP poisoning ignoring the complications of other concomitant pesticides ingested. Treating physicians should be prepared and consider the possibility of mixed poisoning prevalent in that region before initiating therapy.

Tripathi, M., R. Pandey, et al. (2006). "A mixture of organophosphate and pyrethroid intoxication requiring intensive care unit admission: a diagnostic dilemma and therapeutic approach." Anesth Analg **103**(2): 410-412, table of contents.

The illegal mixing of organophosphates and pyrethroids in marketed agriculture insecticides is becoming prevalent in developing countries. Over a 12-mo period, 8 patients were admitted to the emergency department of a university hospital in Dharan, Nepal after ingestion of such a mixture with suicidal intent. All patients presented with a combination of miosis, bradycardia, tachypnea, and unconsciousness. The occurrence of both pupillary dilation after a small-dose infusion of atropine (0.08 to 0.2 mg/kg in 1-3 h) and seizures raised the possibility of pyrethroid poisoning. In each case, an examination of the insecticide container confirmed that it contained a mixture of organophosphate and pyrethroid. After seizure control, gastric lavage, respiratory support, hemodynamic stabilization and diuresis, seven of the patients recovered without neurological deficit. One patient suffered aspiration pneumonia and died. The early clinical picture after this mixed poisoning is based on the toxicity of organophosphates rather than pyrethroids. Because the patients responded to a small dose of atropine with

mydriasis and tachycardia, it suggested a mixed poisoning. Early suspicion of mixed poisoning may have a significant prognostic impact.

Tsamadou, A., K. Fountas, et al. (2009). "Intentional ingestion of diquat: A case report with fatal outcome." Clinical Toxicology **Conference: 29th International Congress of the European Association of Poison Centres and Clinical Toxicologists Stockholm Sweden. Conference Start: 20090512 Conference End: 20090515. Conference Publication: (var.pagings). 47 (5)**: 508.

Objective: Diquat is a pesticide chemically related to paraquat but with differentiated clinical picture. When ingested, the main difference between them is that diquat does not accumulate in the lung and does not cause pulmonary fibrosis. It is a strong poison. In human diquat poisonings, approximately 50% of patients have neurologic effects. The cause of these effects is not known. Some cases have involved progressive development of neurological effects within 72 to 96 hours. Hemorrhagic cerebral and brainstem infarctions may occur. Unlike the more frequent paraquat poisonings, diquat poisonings are rare. Below we describe the first case of intentional diquat ingestion which has been referred to our poison information centre for at least 5 years. Case report: A 30 year old man with a medical history of depression proceeded to the hospital after intentional ingestion 50 ml diquat. He was admitted to the Intensive Care Unit. Gastric decontamination was immediately performed and activated charcoal was administered in repeated doses. Hemofiltration was started within 4 hours post ingestion. The patient developed acute renal failure and hemodialysis continued after the first 24 hours. He showed moderate hepatic impairment (enzyme levels about 250-300, INR 1.4, bilirubin around 2). 72 hours post ingestion he developed neurological findings, GCS 3 and absence of brainstem reflexes. CT showed exaggerated cerebral swelling without response to aggressive therapy. The patient was intubated (he could not maintain his own breathing) with no evidence of pulmonary damage. MRI was not performed, therefore we do not know if there were brainstem infarctions. There was no improvement for the next 18 days and the patient died with evidence of multiple organ failure.

Tsukada, K., H. Azuhata, et al. (2009). "Acute gastroduodenal injury after ingestion of diluted herbicide pendimethalin." Singapore Med J **50**(3): e105-106.

The herbicide, pendimethalin, is used worldwide, but its acute toxicity is not yet widely known. There have been some reported acute pendimethalin poisoning cases in humans and most of them intentionally ingested the concentrated formulation. We describe a 73-year-old man who developed corrosive gastroduodenal injury after accidental ingestion of the diluted (300 times with water) pendimethalin formulation. He had a history of reflux oesophagitis and had been taking omeprazol (10 mg/day) for a year. He consumed alcohol two hours after the accidental ingestion and then had nausea and epigastric pain. Endoscopy performed three days post-exposure revealed gastroduodenal injury. As he had consumed alcohol every day for years and had no history of gastroduodenal ulcer, the accidental ingestion may be associated with this injury. He was successfully treated by increasing his dosage of omeprazol (20 mg/day) for two weeks. This case indicates that

ingestion of a small quantity of pendimethalin can provoke gastroduodenal injury.

Tunde-Ayinmode, M. F. and O. A. Adegunloye (2011). "Parenting style and conduct problems in children: A report of deliberate selfpoisoning in a Nigerian child." South African Journal of Psychiatry **17 (2)**: 60-63.

A correlation between unhealthy parenting styles and child psychopathology has been established. This case report describes how chronic harsh paternal parenting caused a young boy to deliberately poison himself with organophosphate chemicals (rat poison). This report is intended to stimulate the interest of physicians and psychiatrists in parenting style research and in how parenting style modification can be a therapeutic and preventive tool.

Upadhyaya, A. C., M. Nageshwar Rao, et al. (2014). "Diagnostic and therapeutic challenges in management of uncommon herbicide pesticide poisoning-Nims experience." Indian Journal of Critical Care Medicine **Conference: A Joint Meeting of 20th Annual Conference of the Indian Society of Critical Care Medicine, 18th Asia-Pacific Congress of Critical Care Medicine and 2nd Annual Conference of Critical Care Nurses Society, Criticare 2014 Jaipur India. Conference Start: 20140214 Conference End: 20140218. Conference Publication: (var.pagings). 18**: S23.

Introduction: Deliberate/accidental overdose and poisoning contributes to significant portion of acute medical workload in hospitals, dominated by organophosphate pesticides. Despite widespread availability, reports of herbicide pesticide poisoning from India are uncommon and highly under-reported. Diagnosis is often difficult in absence of proper history, nonspecific clinical features, lack of diagnostic tests besides lack of information concerning antidotes amongst clinicians/intensivists. Aim of Study: To study the clinical profile of patients admitted with "unknown poisoning" posing diagnostic and therapeutic challenges during management in the emergency room (ER)/medical intensive care unit (ICU) of our multi-specialty tertiary care university referral teaching hospital. We report a total of four cases admitted in the ER/medical ICU of NIMS, Hyderabad during the period from July to November 13, with male:female ratio of 3:1 in the age range of 18-38 years, mostly. Being referred from other hospitals with confused clinical picture. Clinical Profile and Results: The herbicides ingested included: (1) "Cartap hydrochloride", a commonly used low toxicity insecticide, the patient presented with vomiting and after decontamination was treated with conservative measures and with specific antidote - injection bronchoalveolar lavage with uneventful recovery and discharged. (2) "Green top" - a biopesticide with hydrolyzed yeast extract with fillers/ media; the patient presented with recurrent vomiting, altered sensorium and seizures, was intubated with ventilatory support along with methaemoglobinemia which was treated and discharged uneventfully. (3) "N-Kick" poisoning - patient presented with progressive cyanosis, jaundice slumped to fulminant hepatic failure/hepatic encephalopathy, methaemoglobinemia and renal failure and succumbed despite intensive care measures. (4) "Paraquat" poisoning - patient presented with recurrent vomitings with renal failure and respiratory distress, however had to be discharged on request (leave against medical advice). The presentation and clinical profile would be discussed highlighting

the diagnostic and therapeutic challenges calling for syndromic management. Conclusion: There is an urgent need for increased awareness amongst clinicians/intensivists of unusual poisonings in the ER/medical ICU settings besides establishing early diagnosis by meticulous history taking, to pursue aggressive decontamination and institute comprehensive intensive care supportive measures in salvaging lives.

Vale, J. A. (1992). "Treatment of acute organophosphorus insecticide poisoning." Human and Experimental Toxicology **11 (6)**: 558-559.

Vasilic, Z., V. Drevenkar, et al. (1992). "Urinary excretion of diethylphosphorus metabolites in persons poisoned by quinalphos or chlorpyrifos." Archives of Environmental Contamination and Toxicology **22 (4)**: 351-357.

The urinary excretion rates of diethyl phosphate and diethyl phosphorothioate and changes in blood cholinesterase activities were studied in fifteen persons self-poisoned either by the organophosphorus pesticide quinalphos (twelve persons) or by chlorpyrifos (three persons). The organophosphate poisoning was always indicated by a significant depression of serum and/or red blood cell cholinesterase activities. The return of serum cholinesterase activity in the range of referent values took more than 30 days and had a different course in different persons. The most rapid increase in red blood cell acetylcholinesterase activity was noted within 24 h after the first treatment with oximes Pralidoxime and/or HI-6. None of the spot urine samples, collected daily after admission of persons to hospital, contained measurable quantities of the parent pesticide. There was no correlation between the maximum concentration of total urinary diethylphosphorus metabolites normalized to creatinine and the initial inhibition of blood cholinesterase activities measured in samples collected on the day of admission to hospital. The excretion of metabolites followed the kinetics of a biphasic reaction. The half-time of urinary metabolites concentration decrease in the fast excretion phase in quinalphos poisoned persons was 5.5-14.2 h (eight persons) and 26.8-53.6 h (four persons) and in chlorpyrifos poisoned persons 3.5-5.5 h. The half-time for the slow excretion phase ranged from 66.5 to 127.9 h in all persons and for both compounds. For a given person, the rates of excretion of diethyl phosphate and diethyl phosphorothioate were about the same. However, in quinalphos poisoned persons the proportions of single metabolites in total diethylphosphorus metabolites varied with the initial maximum concentration of total metabolites. Simultaneous determination of both metabolites gave a more reliable and sensitive confirmation of absorption and retention of quinalphos and chlorpyrifos in the body.

Venkatesh, S., M. L. Kavitha, et al. (2006). "Progression of type I to type II paralysis in acute organophosphorous poisoning: is oxidative stress significant?" Arch Toxicol **80**(6): 354-361.

Organophosphorous poisoning is a common method of deliberate self-harm in countries where the pesticides are readily available and can result in type I, II and/or III paralysis. The in-hospital morbidity and mortality of the poisoning are mostly associated with type II paralysis (intermediate syndrome). The aim of this study was to determine the role of oxidative

stress in relation to the severity of poisoning and development of type II paralysis in patients suffering from acute organophosphate poisoning. This prospective study was carried out at the Christian Medical College Hospital. Thirty-two patients with acute organophosphorous poisoning, admitted in one medical unit over 17 months, were included in the study. They were clinically assessed for severity of poisoning and paralysis during the first 10 days of their hospitalisation. Temporal profiles of butyrylcholinesterase (BuChE) and oxidative stress parameters, for 4, 7 and 10 days of hospitalisation, were established in 25 of these patients. Type I and II paralysis were associated with severe poisoning. The majority of patients with type II paralysis had prior evidence of type I paralysis. The pattern of muscles that were paralysed in type I paralysis occurring alone and in type I paralysis proceeding to type II paralysis were similar. BuChE was significantly inhibited in all patients. Oxidative stress occurred in acute organophosphate poisoned patients and was greater in severe poisoning. The results suggest that type I paralysis may progress to type II paralysis in severely poisoned patients. They demonstrate early occurrence of oxidative stress in severe acute organophosphate poisoning. However, the development of type II paralysis is not associated with the level of oxidative stress. They suggest that mechanisms other than acetylcholine induced oxidative stress may be involved in the progression of type I to type II paralysis.

Venkatesh, S., A. Zachariah, et al. (2006). "Myofibril membranes in relation to the neuromuscular weakness of acute monocrotophos poisoning." Toxicol Mech Methods **16**(8): 419-426.

Organophosphate poisoning is a common method of deliberate self-harm in countries where the pesticides are readily available. The severity of neuroparalysis and myopathy occurring in acute organophosphate poisoned patients is determined by the severity of poisoning and is associated with morbidity and mortality. Molecular mechanisms that underlie severe paralysis are not well delineated but are essential to know to improve treatment. In this study rats were subjected to increasing doses (0.25 to 0.8 LD(50)) of monocrotophos, and cell membrane lipid profiles, particularly those of myofibril membranes, were examined in relation to neuromuscular weakness occurring in poisoning. Increasing doses of monocrotophos inhibited brain and RBC acetylcholinesterase >/=60% early in the poisoning. RBC acetylcholinesterase levels recovered to 70% to 80% of normal while brain acetylcholinesterase remained 44% to 67% inhibited 1 week after poisoning. Increasing severity of poisoning led to significant changes in myofibril membrane lipid composition with cholesterol to phospholipid ratios increasing from 0.029 +/- 0.008 in controls to 0.063 +/- 0.023 in severe poisoning ($p > 0.05$). These changes were associated with neuromuscular weakness in the first day of poisoning. Membrane changes were reversible and rats recovered muscle strength in 1 week with no treatment. Lipid compositions of the intestine, brain, and muscle mitochondrial membranes were not affected by monocrotophos. The study indicated that neuromuscular weakness was associated with muscle membrane disorganization early in the course of acute organophosphate poisoning and that subclinical neurotoxicity of long duration may be a consequence of acute organophosphate poisoning.

Controlling the severity of poisoning early in the course of acute organophosphate poisoning appears to be important for clinical recovery.

Viradiya, K. and A. Mishra (2011). "Imidacloprid poisoning." J Assoc Physicians India **59**: 594-595.

Imidacloprid is newer systemic insecticide, a nicotine analogue, acts on the nervous system. Patient can present with variable manifestations like irritability, labored breathing, emaciation, twitching and delirium. Here we report a case presented with sever neuropsychiatric symptoms with respiratory failure following self ingestion of poison. Patient recovered with supportive and symptomatic treatment.

Wahab, A., M. U. Rabbani, et al. (2009). "Spontaneous self-ignition in a case of acute aluminium phosphide poisoning." Am J Emerg Med **27**(6): 752 e755-756.

Walker, J. and F. X. Beach (2002). "Deliberate self-poisoning with rodenticide: a diagnostic dilemma." Int J Clin Pract **56**(3): 223-224.

A 71-year-old man presented with a recurrent bleeding diathesis requiring frequent blood transfusions, vitamin K and fresh frozen plasma. Extensive investigations revealed vitamin K deficiency. After repeated interviews the patient admitted to deliberately ingesting rat poison. Superwarfarins are an uncommon cause of deranged clotting and specialised tests are available to identify them. They can cause prolonged coagulation abnormalities and may require treatment with oral vitamin K for several months after just a single dose.

Watt, B. E., A. T. Proudfoot, et al. (2005). "Anticoagulant rodenticides." Toxicol Rev **24**(4): 259-269.

Anticoagulant pesticides are used widely in agricultural and urban rodent control. The emergence of warfarin-resistant strains of rats led to the introduction of a new group of anticoagulant rodenticides variously referred to as 'superwarfarins', 'single dose' or 'long-acting'. This group includes the second generation 4-hydroxycoumarins brodifacoum, bromadiolone, difenacoum, flocoumafen and the indanedione derivatives chlorophacinone and diphacinone. Most cases of anticoagulant rodenticide exposure involve young children and, as a consequence, the amounts ingested are almost invariably small. In contrast, intentional ingestion of large quantities of long-acting anticoagulant rodenticides may cause anticoagulation for several weeks or months. Occupational exposure has also been reported. Anticoagulant rodenticides inhibit vitamin K(1)-2,3 epoxide reductase and thus the synthesis of vitamin K and subsequently clotting factors II, VII, IX and X. The greater potency and duration of action of long-acting anticoagulant rodenticides is attributed to their: (i) greater affinity for vitamin K(1)-2,3-epoxide reductase; (ii) ability to disrupt the vitamin K(1)-epoxide cycle at more than one point; (iii) hepatic accumulation; and (iv) unusually long biological half-lives due to high lipid solubility and enterohepatic circulation. Substantial ingestion produces epistaxis, gingival bleeding, widespread bruising, haematomas, haematuria with flank pain, menorrhagia, gastrointestinal bleeding, rectal bleeding and haemorrhage into any internal organ; anaemia may result. Spontaneous haemoperitoneum has been

described. Severe blood loss may result in hypovolaemic shock, coma and death. The first clinical signs of bleeding may be delayed and patients may remain anticoagulated for several days (warfarin) or days, weeks or months (long-acting anticoagulants) after ingestion of large amounts. There are now sufficient data in young children exposed to anticoagulant rodenticides to conclude that routine measurement of the international normalised ratio (INR) is unnecessary. In all other cases, the INR should be measured 36-48 hours post exposure. If the INR is normal at this time, even in the case of long-acting formulations, no further action is required. If active bleeding occurs, prothrombin complex concentrate (which contains factors II, VII, IX and X) 50 units/kg, or recombinant activated factor VII 1.2-4.8 mg or fresh frozen plasma 15 mL/kg (if no concentrate is available) and phytomenadione 10mg intravenously (100 microg/kg bodyweight for a child) should be given. If there is no active bleeding and the INR is < or =4.0, no treatment is required; if the INR is > or =4.0 phytomenadione 10mg should be administered intravenously.

Weng, C. H., C. C. Hu, et al. (2012). "Sequential organ failure assessment score can predict mortality in patients with paraquat intoxication." PLoS One **7**(12): e51743.

INTRODUCTION: Paraquat poisoning is characterized by multi-organ failure and pulmonary fibrosis with respiratory failure, resulting in high mortality and morbidity. The objective of this study was to identify predictors of mortality in cases of paraquat poisoning. Furthermore, we sought to determine the association between these parameters. METHODS: A total of 187 patients were referred for management of intentional paraquat ingestion between January 2000 and December 2010. Demographic, clinical, and laboratory data were recorded. Sequential organ failure assessment (SOFA) and acute kidney injury network (AKIN) scores were collected, and predictors of mortality were analyzed. RESULTS: Overall hospital mortality for the entire population was 54% (101/187). Using a multivariate logistic regression model, it was found that age, time to hospitalization, blood paraquat level, estimated glomerular filtration rate at admission (eGFR(first day)), and the SOFA(48-h) score, but not the AKIN(48-h) score, were significant predictors of mortality. For predicting the in-hospital mortality, SOFA(48-h) scores displayed a good area under the receiver operating characteristic curve (AUROC) (0.795 +/- 0.033, P<0.001). The cumulative survival rate differed significantly between patients with SOFA(48-h) scores <3 and those >/= 3 (P<0.001). A modified SOFA (mSOFA) score was further developed by using the blood paraquat level, and this new score also demonstrated a better AUROC (0.848+/-0.029, P<0.001) than the original SOFA score. Finally, the cumulative survival rate also differed significantly between patients with mSOFA scores <4 and >/=4 (P<0.001). CONCLUSION: The analytical data demonstrate that SOFA and mSOFA scores, which are based on the extent of organ function or rate of organ failure, help to predict mortality after intentional paraquat poisoning.

Wilks, M. F. (2011). "Do laboratory studies help in the development of antidotes for pesticide poisoning?" Toxicology Letters **Conference: 47th Congress of the European Societies of Toxicology, EUROTOX 2011 Paris France. Conference**

Start: 20110828 Conference End: 20110831. Conference Publication: (var.pagings). 205: S30-S31.

Self-poisoning with organophosphorus (OP) insecticides is a significant public health problem in many developing countries. Much uncertainty still exists concerning the effectiveness of different treatment regimes, in particular with regard to the use of oximes. Experimental studies demonstrate clearly that oximes are able to reactivate OP-inhibited acetyl cholinesterase (AChE). However, data from well designed clinical trials are sparse and inconsistent. This is due to the different pharmacokinetics and -dynamics of both toxicants and therapeutic agents, leading to different clinical syndromes and responses to antidotal treatment. Experimental studies have provided important information which put the clinical findings into context and point towards promising modifications of treatment options. In aminipig model of dimethoate poisoning and oxime treatment there was a close agreement between calculated and in vivo AChE activities. Computer simulations also provided insight into the potential and limitations of oxime treatment in human poisoning (Worek, 2010). Human serum albumin nanoparticles have been shown to allow more effective transport of oximes across an in vitro blood-brain barriermodel(Wagner, 2010), raising the possibility of improved treatment options for CNS effects of OPs. Thus, in vivo, in vitro and in silico models have greatly improved our understanding of the possibilities and limitations of antidote therapy for OP poisoning. They can be used to guide future clinical trials with the aim to identify the most effective treatments forhumanOP poisoning.

Wille, T., L. Kaltenbach, et al. (2013). "Investigation of kinetic interactions between approved oximes and human acetylcholinesterase inhibited by pesticide carbamates." Chem Biol Interact **206**(3): 569-572.

Carbamates are widely used for pest control and act primarily by inhibition of insect and mammalian acetylcholinesterase (AChE). Accidental or intentional uptake of carbamates may result in typical signs and symptoms of cholinergic overstimulation which cannot be discriminated from those of organophosphorus pesticide poisoning. There is an ongoing debate whether standard treatment with atropine and oximes should be recommended for human carbamate poisoning as well, since in vitro and in vivo animal data indicate a deleterious effect of oximes when used in combination with the N-methyl carbamate carbaryl. Therefore, we performed an in vitro kinetic study to investigate the effect of clinically used oximes on carbamoylation and decarbamoylation of human AChE. It became evident that pralidoxime and obidoxime in therapeutic concentrations aggravate the inhibition of AChE by carbaryl and propoxur, with obidoxime being substantially more potent compared to 2-PAM. However, obidoxime had no impact on the decarbamoylation kinetics. Hence, the administration of 2-PAM and especially of obidoxime to severely propoxur and carbaryl poisoned humans cannot be recommended.

Wood, D. M., H. Alsahaf, et al. (2005). "Fatality after deliberate ingestion of the pesticide rotenone: a case report." Crit Care **9**(3): R280-284.

Rotenone is a pesticide derived from the roots of plants from the Leguminosae family. Poisoning following deliberate ingestion of these plant

roots has commonly been reported in Papua New Guinea. However, poisoning with commercially available rotenone in humans has been reported only once previously following accidental ingestion in a 3.5-year-old child. Therefore, the optimal management of rotenone poisoning is not known. After deliberate ingestion of up to 200 ml of a commercially available 0.8% rotenone solution, a 47-year-old female on regular metformin presented with a reduced level of consciousness, metabolic acidosis and respiratory compromise. Metformin was not detected in premortem blood samples obtained. Despite intensive supportive management, admission to an intensive care unit, and empirical use of N-acetylcysteine and antioxidant therapy, she did not survive. Poisoning with rotenone is uncommon but is potentially fatal because this agent inhibits the mitochondrial respiratory chain. In vitro cell studies have shown that rotenone-induced toxicity is reduced by the use of N-acetylcysteine, antioxidants and potassium channel openers. However, no animal studies have been reported that confirm these findings, and there are no previous reports of attempted use of these agents in patients with acute rotenone-induced toxicity.

Worek, F. and H. Thiermann (2013). "The value of novel oximes for treatment of poisoning by organophosphorus compounds." Pharmacol Ther **139**(2): 249-259.

Poisoning by organophosphorus compounds (OP) still is a major therapeutic problem. Intentional OP pesticide poisoning results in up to 300.000 deaths each year and highly toxic OP nerve agents pose a permanent threat for the civilian population and military forces. The therapeutic value of clinically used oximes, pralidoxime, obidoxime and TMB-4, in human OP pesticide poisoning is under debate. Moreover, these oximes lack efficacy in poisoning by various nerve agents. An innumerable number of novel oximes have been synthesized in the past five decades to provide more effective oximes and compounds with improved blood-brain-barrier penetration. Novel compounds were tested with largely different experimental protocols in vitro and in animals in vivo. The lack of comparable experimental conditions and the absence of human in vivo studies hamper a well-founded evaluation of the available data. At present, it appears that only a small number of (bispyridinium) oximes show superior potency and efficacy against individual OP. However, until now, no oxime with sufficient broad-spectrum activity against structurally different OP pesticides and nerve agents is available. An interim solution may be the combination of two oximes with overlapping reactivation spectrum. In conclusion, the unsatisfying situation calls for studies with standardized and comparable experimental conditions in order to allow a sound assessment of available and novel oximes.

Wu, K. C., Y. Y. Chen, et al. (2012). "Suicide methods in Asia: implications in suicide prevention." Int J Environ Res Public Health **9**(4): 1135-1158.

As the largest continent in the World, Asia accounts for about 60% of World suicides. Preventing suicide by restricting access to suicide methods is one of the few evidence-based suicide prevention strategies. However, there has been a lack of systematic exploration of suicide methods in Asian countries. To amend this shortage, the current review examines the leading suicide methods in different Asian countries, their trend, their age- and sex- specific characteristics, and their implications for suicide prevention. In total, 42

articles with leading suicide methods data in 17 Asian countries/regions were retrieved. The epidemiologic characteristics and recent trends of common suicide methods reflect specific socio-cultural, economic, and religious situations in the region. Common suicide methods shift with the introduction of technologies and constructions, and have specific age- or sex-characteristics that may render the restriction of suicide methods not equally effective for all sex and age sub-groups. Charcoal burning, pesticide poisoning, native plant poisoning, self-immolation, and jumping are all prominent examples. In the information society, suicide prevention that focuses on suicide methods must monitor and control the innovation and spread of knowledge and practices of suicide "technologies". It may be more cost-effective to design safety into technologies as a way of suicide prevention while there is no rash of suicides yet by the new technologies. Further research on suicide methods is important for public health approaches to suicide prevention with sensitivity to socio-cultural, economic, and religious factors in different countries.

Wunnapuk, K., X. Liu, et al. (2013). "Renal biomarkers predict nephrotoxicity after paraquat." Toxicol Lett **222**(3): 280-288.

Paraquat is a widely used herbicide which has been involved in many accidental and intentional deaths. Nephrotoxicity is common in severe acute paraquat poisoning. We examined seven renal injury biomarkers, including cystatin-C, kidney injury molecule-1, beta2-microglobulin, clusterin, albumin, neutrophil gelatinase-associated lipocalin and osteopontin, to develop a non-invasive method to detect early renal damage and dysfunction and to compare with the conventional endogenous marker creatinine. Male Wistar rats were dosed orally with four different doses of paraquat, and the biomarker patterns in urine and plasma were investigated at 8, 24 and 48h after paraquat exposure. By Receiver Operating Characteristic analysis, urinary kidney injury molecule-1 was the best marker at predicting histological changes, with areas under the Receiver Operating Characteristic curve of 0.81 and 0.98 at 8 and 24h (best cut-off value>0.000326mug/ml), respectively. Urinary kidney injury molecule-1, urinary albumin and urinary Cystatin-C elevations correlated with the degree of renal damage and injury development. Further study is required to compare biomarkers changes in rats with those seen in human poisoning.

Yucel, I., Y. Demiraran, et al. (2008). "Suicide attempt with injection of insecticide in both wrists." Orthopedics **31**(2): 174.

Organophosphates that are commonly used in agriculture, houses, gardens, and in veterinary medicine worldwide, may be used for suicidal purposes. But suicide attempt with self-injection of organophosphates is rare. This article presents a case of a suicide attempt of a young man with self-injection of an organophosphate insecticide (dichlorvos) to both his wrists.

Zawadzki, M., J. Magdalan, et al. (2007). "[Poisonings with anticoagulant rodenticides]." Arch Med Sadowej Kryminol **57**(4): 427-429.

Anticoagulant rodenticides are commonly used in extermination of rodents. Failure to adhere to safety principles and sometimes a deliberate use of these compounds may be a reason of severe poisonings in human.

Diagnosis is based on a characteristic clinical course of the disease and postmortem examinations.

Zerin, T., Y. S. Kim, et al. (2012). "Protective effect of methylprednisolone on paraquat-induced A549 cell cytotoxicity via induction of efflux transporter, P-glycoprotein expression." Toxicol Lett **208**(2): 101-107.

Paraquat (PQ) is the third most extensively used herbicide in the world, causing thousands of deaths due to accidental or intentional self-poisoning in developing countries. Although many therapeutic treatments for PQ-induced poisonings have been proposed and developed, the efficacy of these treatments is still poor and requires further investigation. Methylprednisolone (trade name Solumedrol, hereinafter MP) is a widely used steroid for the treatment of various diseases but the function of MP has not yet been studied in the context of PQ-induced intoxication. The aim of this study was to determine if MP can ameliorate PQ-induced toxicity in an alveolar A549 cell line by inducing ATP-dependent transporter P-glycoprotein (P-gp) expression. P-gp expression and activity in the PQ-treated A549 cell line were enhanced by MP treatment and cytotoxicity by PQ was dramatically decreased. We also found that MP per se or together with PQ induced P-gp expression by both Western blot and qRT-PCR analyses. In addition, induced P-gp transporter was shown to improve the efflux effect on PQ-treated A549 cell lines as was demonstrated using the Calcein-AM fluorescence accumulation assay. In summary, MP induces the transmembrane ATP-dependent transporter P-gp expression, which greatly improves PQ-treated A549 cell viability, reduces accumulation of intracellular PQ and prevents PQ induced cytotoxicity but it should be further evaluated in in vivo studies.

Zhang, Y., M. Su, et al. (2011). "Tetramine poisoning: A case report and review of the literature." Forensic Sci Int **204**(1-3): e24-27.

BACKGROUND: Tetramethylene disulfotetramine (TETS), a banned neurotoxic rodenticide, has accounted for numerous intentional and unintentional poisonings in mainland China. Since the first known case of human illness caused by tetramine occurred in NewYork, in May 2002, TETS has caused more than 50 human poisonings in Western countries. AIM: To analyze pathological changes of TETS poisoning and to provide evidence for forensic identification. METHODS: We report the case of a 28-year-old female who suffered from tetramine poisoning and died of multi-organ failure. We also performed a retrospective study of 40 cases of poisoning, from pathological autopsy reports, by analyzing and summarizing the related the literature from 1996 to 2010. Based on pathologic autopsies and the literature, we summarize the pathological changes related to tetramine poisoning. RESULTS: Signs of asphyxia were obvious upon pathological examination. Edema and congestion of organs, particularly in the brain, were seen in all cases. Subarachnoid and cerebral hemorrhaging were also common signs of tetramine poisoning. CONCLUSION: In forensic practice, tetramine poisoning should be considered when the patient has signs of abnormal excitation of the central nervous system, convulsions, hyperspasmia, and cerebral hemorrhage.

Zhao, Y., W. Zhang, et al. (2013). "The vital function of Fe3O4@Au nanocomposites for hydrolase biosensor design and its application in detection of methyl parathion." Nanoscale **5**(3): 1121-1126.

A nanocomposite of gold nanoparticles (AuNPs) decorating a magnetic Fe(3)O(4) core was synthesized using cysteamine (SH-NH(2)) as linker, and characterized by TEM, XPS, UV and electrochemistry. Then a hydrolase biosensor, based on self-assembly of methyl parathion hydrolase (MPH) on the Fe(3)O(4)@Au nanocomposite, was developed for sensitive and selective detection of the organophosphorus pesticide (OP) methyl parathion. The magnetic nanocomposite provides an easy way to construct the enzyme biosensor by simply exerting an external magnetic field, and also provides a simple way to renew the electrode surface by removing the magnet. Unlike inhibition-based enzyme biosensors, the hydrolase is not poisoned by OPs and thus is reusable for continuous measurement. AuNPs not only provide a large surface area, high loading efficiency and fast electron transfer, but also stabilize the enzyme through electrostatic interactions. The MPH biosensor shows rapid response and high selectivity for detection of methyl parathion, with a linear range from 0.5 to 1000 ng mL(-1) and a detection limit of 0.1 ng mL(-1). It also shows acceptable reproducibility and stability. The simplicity and ease of operation of the proposed method has great potential for on-site detection of P-S containing pesticides and provides a promising strategy to construct a robust biosensor.

Zhou, Y., C. Zhan, et al. (2010). "Intravenous lipid emulsions combine extracorporeal blood purification: a novel therapeutic strategy for severe organophosphate poisoning." Med Hypotheses **74**(2): 309-311.

Organophosphorus (OP) pesticide self-poisoning is a major clinical problem in rural Asia and it results in the death of 200,000 people every year. At present, it is lack of effective methods to treat severe organophosphate poisoning. The high mortality rate lies on the amount of toxic absorption. Intravenous lipid emulsions can be used as an antidote in fat-soluble drug poisoning. The detoxification mechanism of intravenous lipid emulsions is "lipid sink", which lipid emulsions can dissolve the fat-soluble drugs and separate poison away from the sites of toxicity. Most of organophosphorus pesticides are highly fat-soluble. So, intravenous lipid emulsions have the potentially clinical applications in treatment of OP poisoning. Extracorporeal blood purification especially charcoal hemoperfusion is an efficient way to eliminate the poison contents from the blood. We hypothesize that the combination of intravenous lipid emulsions and charcoal hemoperfusion can be used to cure severe organophosphate poisoning. This novel protocol of therapy comprises two steps: one is obtained intravenous access to infuse lipid emulsions as soon as possible; another is that charcoal hemoperfusion will be used to clear the OP substances before the distribution of OP compounds in tissue is not complete. The advantages of this strategy lie in three points. Firstly, it will alleviate the toxic effect of OP pesticide in the patients by isolation and removal the toxic contents. Secondly, the dosage of antidotes can be reduced and its side-effects will be eased. Thirdly, a large bolus of fatty acids provide energy substrate for the patients who are nil by mouth. We consider that it would become a feasible, safe and efficient

detoxification intervention in the alleviation of severe organophosphate poisoning, which would also improve the outcome of the patients.