

targets for ascertained or suspected effects of OPs. The inhibition of the esterase activity carried by transferrin has been correlated with the promotion of axonopathies caused by certain OPs and by other, structurally unrelated, pesticides. It is not known whether substrate accumulation or other effects on this protein are involved in the mechanisms of promotion.

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THE LACK OF TRANSLATIONAL RESEARCH ON ANTIDOTES FOR PESTICIDE POISONING

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Pesticide poisoning kills hundreds of thousands of people each year. There is next to no evidence for benefit from any antidote other than atropine. There is an urgent need for better evidence on the effects of current treatments and also newer, more effective, antidotes. Animal studies have revealed many compounds offering clear benefits, yet no new treatment has reached the bedside during the last 30 years, and no new treatment is in clinical trials. For example, in animal models, organophosphate (OP) hydrolases break down OPs and speed up reactivation of AChE, reversible anticholinesterases (e.g. the carbamate pyridostigmine) reduce re-inhibition of AChE, and glutamate antagonists and agonists for adenosine and alpha-2 receptors limit damage to the central nervous system.

There are many perspectives on the priorities for drug development for OP poisoning. An international health perspective would prioritise finding out whether currently used treatments such as activated charcoal and oximes are safe and effective. From a military perspective, treatments that are effective and safe as both pre and post-treatment in the field are ideal. Reversible anticholinesterases and OP hydrolases seem the most promising from the animal data. From a pharmaceutical industry perspective, the most attractive agents will be neuro-protective agents that might be useful in other forms of brain injury. Finally, from a developing world perspective, bicarbonate and lactate might be the most cost-effective potential antidotes. The massive expenditure on unproven antidotes in the West provides a sound financial rationale for more research.

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RELATIVE CLINICAL TOXICITY OF ORGANOPHOSPHORUS COMPOUNDS

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Organophosphorus (OP) pesticide self-poisoning causes thousands of deaths each year, with a case fatality ratio (CFR) often exceeding 10% even in the best ICUs. Textbooks treat OP poisoning as a homogeneous entity, separating pesticides by their animal toxicity using the WHO's classification of toxicity. We assessed whether animal toxicity was an accurate measure of human toxicity for individual OP pesticides. All OP pesticide-poisoned patients

admitted to two secondary hospitals were observed prospectively for 11 months. Outcome and need for intubation were recorded for each patient. 546 OP-poisoned patients were admitted; 71 died (CF 13%). The three most commonly ingested OPs were chlorpyrifos ($n = 234$; animal LD₅₀: 135 mg/kg), dimethoate ($n = 122$; animal LD₅₀: 150 mg/kg) and fenthion ($n = 60$; animal LD₅₀: 586 mg/kg), all classified as having WHO Class II toxicity. Compared to patients poisoned with chlorpyrifos, patients poisoned with dimethoate and fenthion had greater need for intubation (chlorpyrifos 12.4%; dimethoate 32.0%, odds ratio 3.32 [95% confidence interval 1.9–5.7]; fenthion 26.7%, OR 2.57 [1.3–5.1]) and higher CFR (chlorpyrifos 6.8%; dimethoate 21.3%, OR 3.69 [1.9–7.2]; fenthion 16.7%, OR 2.73 [1.2–6.4]). Reactivation of acetylcholinesterase was more successful with chlorpyrifos, likely due to its diethyl structure. OP pesticides have previously been considered as a homogeneous group, varying only according to their animal toxicity. This study shows that the human toxicity of OP pesticides differs significantly from their animal toxicity, and that this difference is important for ventilation and outcome. Each OP pesticide should therefore be considered separately, as an individual poison. This conclusion has major consequences for both pesticide regulation and clinical trials of new interventions for OP poisoning.

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MEDICAL PREPARATION FOR MASS CASUALTIES FROM CHEMICAL WARFARE AGENTS

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Chemical war and terrorism have become a world problem, following major chemical attacks at war (Iraq-Iran) and terrorism (Japan). In order to prevent exposure and to manage the intoxicated patients, the following steps must be applied: 1. Public awareness by education and providing facilities such as personal protective devices and shelters. 2. Special group training of all staff in different sectors that may be involved in a chemical war or terrorism including health professionals, regulators, coordinators, armed forces, police, fire brigades and first aid helpers. 3. Coordination between different departments involved in a chemical war or terrorism. 4. Providing facilities for the protection and management of a major chemical attack including protective devices, chemical diagnostic tools (kits, GC-Mass), antidotes, mobile clinics, emergency means of transport (ambulances, helicopters), decontaminating tools (showers, chemical neutralizers, fire engines) and emergency hospitals with highly trained personnel. 5. Practical guidelines for different groups involved in a chemical war or terrorism. 6. Physical protection of all medical and paramedical staff. 7. Rapid clinical assessment and triage, antidotes (auto-injectors), supportive and symptomatic treatment from the field to the hospital. 8. Follow a flow chart of management a CWA (nerve agents) that is described by the author. 9. Consultations with relevant medical specialists. 10. Regular simulation exercises for a chemical war or terrorism every season/year.