

## Review Article

# Pesticide poisoning

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### ABSTRACT

Acute poisoning with pesticides is a global public health problem and accounts for as many as 300 000 deaths worldwide every year. The majority of deaths occur due to exposure to organophosphates, organochlorines and aluminium phosphide. Organophosphate compounds inhibit acetylcholinesterase resulting in acute toxicity. Intermediate syndrome can develop in a number of patients and may lead to respiratory paralysis and death. Management consists of proper oxygenation, atropine in escalating doses and pralidoxime in high doses. It is important to decontaminate the skin while taking precautions to avoid secondary contamination of health personnel. Organochlorine pesticides are toxic to the central nervous system and sensitize the myocardium to catecholamines. Treatment involves supportive care and avoiding exogenous sympathomimetic agents. Ingestion of paraquat causes severe inflammation of the throat, corrosive injury to the gastrointestinal tract, renal tubular necrosis, hepatic necrosis and pulmonary fibrosis. Administration of oxygen should be avoided as it produces more fibrosis. Use of immunosuppressive agents have improved outcome in patients with paraquat poisoning. Rodenticides include thallium, superwarfarins, barium carbonate and phosphides (aluminium and zinc phosphide). Alopecia is an atypical feature of thallium toxicity. Most exposures to superwarfarins are harmless but prolonged bleeding may occur. Barium carbonate ingestion can cause severe hypokalaemia and respiratory muscle paralysis. Aluminium phosphide is a highly toxic agent with mortality ranging from 37% to 100%. It inhibits mitochondrial cytochrome c oxidase and leads to pulmonary and cardiac toxicity. Treatment is supportive with some studies suggesting a beneficial effect of magnesium sulphate. Pyrethroids and insect repellants (e.g. diethyltoluamide) are relatively harmless but can cause toxic effects to pulmonary and central nervous systems. Ethylene dibromide—a highly toxic, fumigant pesticide—produces oral ulcerations, followed by liver and renal toxicity, and is almost uniformly fatal. Physicians working in remote and rural areas need to be educated about early diagnosis and proper

management using supportive care and antidotes, wherever available.

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### INTRODUCTION

A pesticide is usually defined as a chemical substance, biological agent, antimicrobial or disinfectant used against pests including insects, plant pathogens, weeds, molluscs, birds, mammals, fish, nematodes (roundworms) and microbes that compete with humans for food, destroy property, have a propensity for spreading or are a vector for disease or simply a nuisance. The term insecticide is used to denote agents designed to kill only insects, but the term pesticide has a broader connotation and also includes herbicides, rodenticides, fumigants, nematocides, algaecides, ascaricides, molluscicides, disinfectants, defoliant and fungicides.<sup>1</sup>

### HISTORY AND USAGE OF PESTICIDES

The first known pesticide was probably elemental sulphur dust used in Sumeria about 4500 years ago. In recorded history, nicotine sulphate was extracted from tobacco leaves for use as an insecticide in the seventeenth century. In the nineteenth century, pyrethrum derived from chrysanthemums, and rotenone derived from the roots of tropical vegetables were introduced. After its discovery in 1939 by Paul Muller, dichlorodiphenyltrichloroethane (DDT) found widespread use. However, with the recognition that it was a threat to biodiversity, its use has declined considerably.

In India, the use of pesticides began in 1948 with the introduction of DDT for the control of malaria and benzene hexachloride (BHC) for locusts. Production of these substances in India started in 1952.<sup>2</sup>

The increase in pesticide use for agriculture has paralleled the increase in quality and quantity of food products over the years. At the same time, there has been an increase in the use of these products for deliberate self-harm (DSH). At times, pesticides have been accidentally consumed and on rare occasions have even been used for homicidal purposes. Despite a high rate of pesticide poisoning, not enough is known about the management. This article reviews the current evidence on the management of acute pesticide poisoning.

### EPIDEMIOLOGY

Acute, deliberate self-poisoning with agricultural pesticides is a global public health problem but reliable estimates of the incidence are lacking. Pesticide poisoning accounts for as many as 300 000 deaths worldwide every year.<sup>3</sup> Most estimates of the extent of acute pesticide poisoning have been based on data from hospital

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admissions, which would include only the more serious cases and hence merely reflect a fraction of the real incidence. On the basis of a survey of self-reported minor poisoning in the Asian region, it is estimated that there could be as many as 25 million agricultural workers in the developing world who suffer from an episode of poisoning each year.<sup>4</sup>

Of the total burden of acute pesticide poisoning, the majority of deaths are from deliberate self-poisoning with organophosphorus pesticides (OP), aluminium phosphide and paraquat. Exposure to pesticides is usually occupational, accidental or suicidal. When suicidal, it is termed as deliberate self-harm (DSH), and results in a higher mortality than when accidental.<sup>2</sup> The case fatality rate in pesticide poisoning is between 18% and 23%.<sup>5</sup> The highest case fatality rates have been reported with poisoning due to aluminium phosphide, endosulphan and paraquat.<sup>6-8</sup>

In a study of pesticide poisoning cases, 8040 patients were reported from Warangal district of Andhra Pradesh over a period of 6 years.<sup>7</sup> The overall case fatality rate was 22.6%. In the year 2002 alone, 1035 cases were recorded with a case fatality rate of 22%. Extrapolating these data to the whole of Andhra Pradesh, it was estimated that more than 5000 people die of pesticide poisoning in Andhra Pradesh alone every year.

#### ACUTE PESTICIDE POISONING: GENERAL PRINCIPLES OF MANAGEMENT

The management of pesticide poisoning is similar to other forms of poisoning, with gastric decontamination, supportive care and antidotes where available. Gastric lavage may be useful within 1–2 hours of ingestion and is done after aspiration of the gastric contents with an orogastric tube using 200–300 ml of tap water (5 ml/kg of normal saline in young children). Larger quantities of saline should be avoided since they push the gastric contents into the intestine, or may induce vomiting leading to aspiration. Lavage with potassium permanganate (1:10 000 solution) may be of benefit in poisoning due to some substances and lavage should be continued till the aspirate remains pink. Comatose patients should be intubated prior to gastric lavage to reduce the risk of aspiration. The use of cathartics is not recommended when the poisoning is suspected to be due to substances that cause diarrhoea (organophosphates and carbamates) or lead to ileus (paraquat or diquat). Sorbitol in a single dose of 1–2 ml/kg as a solution may be used as a cathartic. Charcoal is beneficial when given within 60 minutes of ingestion of the poison. Ipecac is not recommended for use in pesticide poisoning.

In addition to absorption from the gut, most pesticides are also absorbed through the cutaneous route. Therefore, skin decontamination is important and is done by washing the skin with large volumes of soap and water. Skin folds, areas under the fingernails, axillae and groins as well as other areas of the body that trap and retain chemicals should be carefully washed. Healthcare workers involved in decontamination must take adequate personal protection measures. Latex gloves give inadequate protection and rubber gloves should be used while decontaminating patients. The use of a full face mask with an organic vapour/high efficiency particulate filter has been recommended during skin decontamination.<sup>9</sup> However, these are seldom available in resource-restricted, developing countries where poisoning due to such substances is common.

The label of the pesticide container is an invaluable resource to guide management and should be inspected whenever available, although at times, the information available about management after exposure may be inadequate, outdated and even misleading

and incorrect.<sup>10</sup> A classification of pesticides is given in Table I.

#### ACETYLCHOLINESTERASE (CHOLINESTERASE) INHIBITORS

Cholinesterase inhibitors, the most common group of agricultural pesticides involved in poisoning, consist of two distinct chemical groups—organophosphates (OPs) and carbamates.

#### ORGANOPHOSPHATE (OP) PESTICIDES

OP pesticides are the most commonly available over-the-counter insecticides in India for agricultural and household use. They are responsible for the largest number of deaths following pesticide ingestion.<sup>3,11</sup> The fatality rate in DSH with OP compounds is reported to be as high as 46% in some hospital-based studies.

The commonly used OP insecticides are acephate, anilophos, chlorpyrifos, dichlorvos, diazinon, dimethoate, fenitrothion, methylparathion, monocrotophos, phenthoate, phorate, primiphos, quinalphos, temephos, etc. The replacement of an oxygen atom in the organophosphorus structure by sulphur leads to the formation of organothiophosphorus compounds such as malathion and parathion, which have a lower lethal potential but *in vivo* metabolism to the oxon metabolite enhances their toxicity.<sup>1</sup> Most OPs can be divided into two types: diethyl (e.g. chlorpyrifos, diazinon, parathion, phorate and dichlorfenthion) and dimethyl (e.g. dimethoate, dichlorvos, fenitrothion, malathion and fenthion).

#### *Mechanism of toxicity*

OP compounds inhibit acetylcholinesterase (AChE) which hydrolyses acetylcholine. Acetylcholine is a neurotransmitter at many nerve endings. These include the postganglionic parasympathetic and cholinergic sympathetic nerves, and both sympathetic and parasympathetic preganglionic fibres. Acetylcholine is also released at the myoneural junctions of skeletal muscle and functions as a neurotransmitter in the central nervous system. Inhibition of AChE by OPs results in accumulation of acetylcholine at various sites. Acetylcholine released from

TABLE I. Classification of pesticides

<i>Insecticides</i>
Acetylcholinesterase inhibitors: Organophosphates, carbamates
Organochlorines
Pyrethrins and pyrethroids
<i>Herbicides</i>
Dipyridyl pesticides: Paraquat and diquat
Chlorphenoxyacetate weed killers: Bromoxynil, 2,4-D
<i>Fungicides</i>
Substituted benzene: Chloroneb, chlorothalonil
Thiocarbamates
Organomercurials: Methylmercury, phenylmercuric acetate
<i>Molluscicides</i>
Metaldehyde
<i>Rodenticides</i>
Aluminium phosphide
Zinc phosphide
Warfarin and superwarfarin compounds
Heavy metal: Thallium-containing pesticides
Yellow phosphorus
<i>Insect repellants</i>
Diethyl toluamide (DEET)
<i>Miscellaneous</i>
Anilides
Avermectins

postganglionic parasympathetic and cholinergic sympathetic nerves acts on the muscarinic receptors present on various smooth muscles and glands. The postsynaptic sites of preganglionic fibres and neuromuscular junctions have nicotinic receptors while the central neurons have both muscarinic and nicotinic receptors. A difference in toxicity has been found between individual OP poisons, but the cause of this difference has not been clearly identified.<sup>12</sup>

Binding of OP with AChE leads to phosphorylation of the enzyme and this reaction is not easily reversible. The rate of spontaneous reactivation of AChE is very slow with diethyl OPs while it is relatively fast with dimethyl OPs. Further, there is ageing of the phosphorylated enzyme after which the enzyme cannot be reactivated by oximes. The half-life of ageing of dimethylphosphorylated and diethylphosphorylated AChE *in vitro* is 3.7 hours and 33 hours, respectively, and the therapeutic windows therefore are 13 and 132 hours, respectively (4 times the half-life).<sup>13</sup>

#### *Clinical features of poisoning*

**Acute toxicity.** The acute features of poisoning generally develop within 1–2 hours of exposure and can be grouped as those related to the muscarinic, nicotinic and central nervous system.

Muscarinic or parasympathetic features include salivation, lacrimation, urination, defaecation, gastrointestinal cramps and emesis, and can be remembered by the acronym SLUDGE. Another acronym, DUMBLES (diarrhoea, urination, miosis, bronchorrhoea, lacrimation, emesis and seizures/sweating/salivation) also includes all the clinical features.<sup>1</sup> Bronchorrhoea and bronchospasm may be severe. Miosis, hypotension and bradycardia are key features and need to be assessed.

Nicotinic or somatic motor and sympathetic features include fasciculations, muscle cramps, fatigue, paralysis, tachycardia, hypertension and rarely mydriasis.

Neurological features include headache, tremors, restlessness, ataxia, weakness, emotional lability, confusion, slurring, coma and seizures.

ECG changes in the form of small voltage complexes and ST–T changes may develop. Other changes include idioventricular rhythms, ventricular extrasystoles, prolonged PR interval and polymorphic ventricular complexes. Hyperglycaemia, hyperamylasaemia, clinical acute pancreatitis and hypothermia may be seen in some patients.

**Intermediate syndrome.** An important condition that should be kept in mind once the acute cholinergic symptoms have subsided but before the features of delayed polyneuropathy have set in, is the intermediate syndrome seen in 20%–47% of patients after ingestion of OP. It is probably related to a toxin-induced myopathy, or action at both the presynaptic and postsynaptic junctions.<sup>14</sup>

The syndrome typically occurs after 1–4 days of exposure to OP poison but may occur even in the subsequent week. It is due to inhibition of neuropathic target esterase. The initial feature is weakness of neck flexion, which progresses to respiratory muscle weakness and respiratory failure. Other associated features include cranial nerve palsies (typically III, IV, VI, VII and X) and proximal muscle weakness.<sup>14</sup>

**Delayed effects.** An uncommon delayed complication of acute OP poisoning is organophosphate-induced delayed neuropathy (OPIDN), also called ginger paralysis syndrome.<sup>15</sup> It is a distal ascending neuropathy that occurs after 10–21 days of exposure. Paraesthesias and motor weakness are common.

Myonecrosis, personality changes, schizophrenia, depression

and confusion may occur as sequelae following ingestion of the poison.

As many as 10%–12% patients develop pancreatitis following OP ingestion. Painless pancreatitis often goes unnoticed in patients presenting with OP ingestion. Rarely, formation of a pseudopancreatic cyst has been reported.<sup>16</sup>

#### *Diagnosis*

Exposure to OP can be confirmed by measuring the activity of butyrylcholinesterase (pseudocholinesterase or plasma cholinesterase) and/or red cell cholinesterase but therapy should not be delayed pending investigation. Red cell cholinesterase levels that are 30%–50% of the normal indicate exposure and symptoms appear once the level falls to 20% of the normal.<sup>17</sup> Measurement of pseudocholinesterase is more easily available but is less reliable. Its levels may be low in chronic liver disease, pregnancy, malnutrition, neoplasms, infection and with the use of drugs such as morphine or codeine. The level of red cell cholinesterase may be falsely low in sickle cell disease, thalassaemia and in severe anaemia. Some OPs affect plasma cholinesterase more than erythrocyte acetylcholinesterase (e.g. diazinon).<sup>18</sup>

#### *Management*

**Initial management.** A patent airway, breathing and circulation should be ensured in a patient presenting with symptoms of poisoning following OP ingestion. The patient should be started on high-flow oxygen and monitored with a pulse oximeter. The risk of aspiration is reduced by placing the patient in a left lateral position with the head-end below the level of the body and the neck extended. The treating team should be vigilant to the occurrence of convulsions, which should be treated with intravenous diazepam or midazolam. Although it has been proposed that the use of regimens containing diazepam has a better outcome due to its effect on the GABA receptors, no clear reduction in mortality has been shown. Some case reports have shown a subjective reduction in fasciculations.<sup>19</sup> Recording the baseline Glasgow Coma Score helps in monitoring the patient's condition.

**Atropine.** The presence of any feature of cholinergic poisoning, i.e. bradycardia (<80/minute), hypotension (systolic blood pressure <80 mmHg), diaphoresis, bronchorrhoea and miosis, is an indication for intravenous administration of atropine.<sup>11</sup> The dose of atropine is 1.8–3 mg (three to five 0.6 mg vials). Although it is preferable that oxygen is given early to all ill patients, administration of atropine should not be delayed if oxygen is unavailable. In case the features of cholinergic poisoning are not present, the patient should be carefully monitored because these may appear once the poison is metabolized in the body to the active oxon form.

The speed of atropinization is of paramount importance while managing patients with poisoning due to OP compounds.<sup>20</sup> If the effect of atropine is not seen after 3–5 minutes of the initial dose and features of cholinergic poisoning persist, it is advisable to double every subsequent dose of atropine compared to the previous dose till such time as the desired effect is achieved. This protocol is useful because if the previous dose is merely repeated, the patient may die due to cholinergic poisoning before the desired effect of atropine is achieved. An advantage of bolus dosing is the necessity to evaluate the patient before each subsequent dose is administered. This may be important in a busy emergency department where the patient may otherwise be neglected if an unmonitored infusion is started.

Indicators for atropinization should be assessed 5 minutes

after the initial dose of atropine and every 3–5 minutes subsequently. The best guide to adequate atropinization is improvement in all the five parameters stated above. Therefore, adequate atropinization is indicated by a dry patient with drying of bronchial secretions, heart rate >80 per minute, systolic pressure >80 mmHg and pupils that are no longer constricted.<sup>11</sup> Maintaining a heart rate of 120–160 beats/minute is usually unnecessary as this suggests atropine toxicity rather than a simple reversal of cholinergic poisoning. It is unwise to follow only pupil size and heart rate during monitoring as these may be fallaciously related to the balance between the nicotinic and muscarinic receptors.

Tachycardia could lead to complications if there is pre-existing heart disease. Tachycardia is not a contraindication to atropine therapy if the other features indicate under-atropinization. The pupils may remain constricted if the eyes have been exposed to the poison, persistent crepitations in the chest may be due to aspiration pneumonia and tachycardia could be a result of hypoxia, agitation, alcohol withdrawal, pneumonia or even fast oxime administration.

Once the patient has been successfully atropinized, a maintenance dose of atropine calculated at 10%–20% of the total dose required for initial atropinization is given in divided doses every hour. A better method is to give a continuous infusion of atropine but care should be taken to avoid complacency in monitoring.

A confused, agitated, febrile patient with no bowel sounds and a full bladder with urinary retention certainly has atropine toxicity, indicating the need to reduce or stop atropine temporarily. After the atropine toxicity subsides, three-fourth of the previous dose should be started. Urinary retention and a distended bladder are common causes of agitation in patients with OP poisoning on atropine. An irritable patient may be calmed by simple catheterization.

Most deaths after ingestion of OPs are due to respiratory failure occurring due to cholinergic crisis, peripheral respiratory failure, aspiration, bronchorrhoea or bronchospasm.

**Glycopyrrolate.** This is a quaternary ammonium antimuscarinic agent with peripheral effects similar to those of atropine. It is a longer acting drug which does not cross the blood–brain barrier and therefore does not counteract the central nervous system effects of the poison. However, it is a more effective antisialagogue than atropine. It is less likely to cause much tachycardia and blocks bradyarrhythmias effectively. There are some data to suggest that addition of glycopyrrolate to atropine reduces the dose of atropine required and may also reduce the toxic effects on the central nervous system and the duration of ventilatory care.<sup>21</sup>

**Pralidoxime (PAM, 2-pyridine aldoxime methylchloride).** This commonly used oxime is a cholinesterase reactivator which reverses the nicotinic effects as well as some of the central nervous system effects of OP poisoning. However, the role of oximes in the treatment of OP poisoning remains controversial, and despite several studies on the subject, a clear indication for its use is not available.<sup>22,23</sup> de Silva *et al.* reported no clinical benefit of oximes in reducing mortality or morbidity at a time when PAM was not available for use in Sri Lanka.<sup>24</sup> In a small study, a high dose of PAM was found to be better than a low dose.<sup>25</sup> In a recent study, a high dose regimen of PAM iodide, consisting of a constant infusion of 1 g/hour for 48 hours after a 2 g loading dose, has been found to reduce morbidity and mortality in moderately severe cases of acute OP pesticide poisoning.<sup>26</sup> However, in this open-label randomized trial, no control group was included and no clear definition of moderately severe illness emerged. Besides,

the study group had a very low atropine requirement, suggesting a baseline dissimilarity between the groups studied.<sup>27–30</sup>

Most authorities including the World Health Organization (WHO) recommend a 30 mg/kg loading dose of PAM (chloride salt) over 15 minutes, followed by a continuous infusion of 10 mg/kg per hour till clinical recovery or for 7 days, whichever is later. The chloride salt of PAM is about 1.53 times more potent than the iodide salt, which is usually available in India. For obidoxime, the loading dose is 250 mg followed by an infusion of 750 mg every 24 hours.

Another important concept is the ageing of phosphorylated AChE, which blocks its reversal to the active form. AChE ageing is particularly rapid with dimethyl OPs, which may thwart effective reactivation by oximes. In contrast, patients with diethyl OP poisoning may particularly benefit from oxime therapy, even if no improvement is seen during the first few days when the poison load is high. The low propensity for ageing with diethyl OP poisoning may allow reactivation after several days, when the poison concentration drops.<sup>31</sup>

PAM is contraindicated in carbaryl poisoning. Its role in carbamate poisoning is unclear.

**Miscellaneous.** In a hyperthermic patient, cooling can be achieved by placing cold towels in the axillae and groins, and using the minimum required doses of atropine and sedation, if warranted, for agitation. Haloperidol is not preferred over diazepam for sedation because it has a non-sedating, pro-convulsant action, disturbs central thermoregulation and prolongs the QT interval.

Several other potential therapeutic agents such as sodium bicarbonate infusion, magnesium, clonidine and fluoride have been suggested to have a role in OP poisoning but their use is not universally recommended due to a lack of good clinical evidence.<sup>32–34</sup>

**Treatment of the intermediate syndrome.** Early institution of ventilatory support, which may be required for a prolonged duration, is essential for management. Close monitoring of respiratory function such as chest expansion, arterial blood gas monitoring and oxygen saturation is essential to identify the onset and monitor the progress of the intermediate syndrome. Some patients develop an offensive and profuse diarrhoea and it is important to maintain a close watch and a positive fluid balance. Recovery usually occurs without residual deficit.<sup>14</sup>

## CARBAMATES

Carbamates reversibly inhibit acetylcholinesterase and plasma pseudocholinesterase. They hydrolyse spontaneously from the enzymatic site within 48 hours. They cause increased activity of acetylcholine at the nicotinic and muscarinic receptors during this transient period. Aldicarb, benomyl, carbaryl, carbendazim, carbofuran, propoxur, triallate, etc. are the commonly used carbamates.

The clinical features of carbamate ingestion are similar to those of OP poisoning and the presenting symptoms include both muscarinic and nicotinic features. Central nervous system features are not very prominent in carbamate poisoning due to the poor permeability of these compounds across the blood–brain barrier.

Measuring enzymatic activity to arrive at a diagnosis may be misleading due to a transient anticholinesterase effect of carbamates.

Treatment is mainly supportive in addition to the use of atropine. The role of PAM in carbamate poisoning is unclear. Due to the short duration of action of carbamates, PAM is used only when the patient fails to respond adequately to atropine.

## ORGANOCHLORINE (OC) PESTICIDES

OC compounds are banned in many countries due to their toxicity and propensity for accumulation in various body tissues. However, they are widely used in India and poisoning with endosulphan, aldrin and endrin is common in several parts of central and southern India.

OC insecticides are chlorinated cyclic hydrocarbons with molecular weights of 300–550 D. The commonly used OC insecticides are endrin, aldrin, benzene hexachloride (BHC), endosulphan, dieldrin, toxaphene, DDT, heptachlor, kepone, dicofol, methoxychlor, etc. DDT, the most toxic OC, is available in dry powder form or as a mixture with other pesticides in powder or liquid form. BHC is available as powder, emulsion, dust and solution for use as a garden insecticide. Lindane is an isomer of hexachlorocyclohexane ( $\gamma$ -HCH), and used as an insecticide and disinfectant in agriculture, and in lotions, creams and shampoos for the treatment of lice and scabies. These agents can be absorbed transdermally, orally or via inhalation, depending on the solvents in which they are contained. The commonly used solvents for these pesticides are kerosene, toluene and other petroleum distillates which have their own toxic effects. This should be kept in mind while managing patients of OC poisoning.

### *Mechanism of toxicity*

OC compounds impair nervous system function by depolarization of the nerve membranes. They facilitate synaptic transmission and inhibit the GABA–chloride channel complex.<sup>35</sup> These agents accumulate within lipid-rich tissues. They also cause sensitization of the myocardium to both endogenous as well as exogenous catecholamines and predispose to arrhythmias. Lindane produces histological alterations in cardiac tissue and cardiovascular dystrophy (contracture, degeneration and necrosis), mainly in the left ventricular wall.

### *Clinical features of acute toxicity*

The clinical features of an acute overdose start early if the agent has been ingested on an empty stomach. These can appear as early as 30 minutes after exposure and include nausea, vomiting, dizziness, seizures, confusion or coma.<sup>36</sup> Seizures may occur without the prodromal features of gastrointestinal toxicity. Dizziness, tremors, myoclonus, opsoclonus, weakness, agitation and confusion may occur prior to or independent of seizures. Status epilepticus may be unresponsive to anticonvulsant therapy, and is associated with respiratory and cardiovascular insufficiency.<sup>37</sup> Lindane is particularly toxic to the central nervous system. It can also produce alterations in the ECG including rhythm abnormalities and changes in ST–T waves suggesting hyperkalaemia. Besides the features related to OCs, associated solvents may produce aspiration pneumonitis.

### *Management*

The management of OC poisoning involves careful monitoring for seizures. It is important to maintain a patent airway and institute ventilatory support if required. Skin decontamination along with gastric decontamination is done once the airway, breathing and circulation have been secured to avoid further absorption of the poison. Epinephrine should be avoided as OCs sensitize the myocardium. If required, dopamine may be given to control hypotension. Oximes have no role in the management of OC poisoning. Cholestyramine resin accelerates the biliary–faecal excretion of some OC compounds.<sup>38</sup> It is usually administered in 4 g doses, 4 times a day. Prolonged treatment (several weeks or

months) may be necessary. Recovery is usually complete and occurs without sequelae.

## HERBICIDES

Herbicides are used to control wild plants. Most herbicides belong to two classes: bipyridyl (or dipyrilidium) and chlorophenoxyacetic compounds. Of the bipyridyl herbicides, paraquat is the most widely used.

### DIPYRIDILIUM OR BIPYRIDYL HERBICIDES

This group includes paraquat and diquat. These herbicides were first developed in Britain and revolutionized the practice of agriculture by eliminating the need for a plough. These herbicides act on weeds and are inactivated upon contact with soil.<sup>39</sup> They are highly effective pesticides, but have been reportedly used for DSH in many parts of the world including India. Paraquat is widely used and is easily available as a granular powder or as a water-soluble concentrate which is an odourless brown liquid and can be mistaken for cola if stored in an empty soft-drink bottle.<sup>40</sup> In liquid form it is available in concentrations of 5% or 25% weight by volume. Uncommon routes of exposure include cutaneous exposure,<sup>41,42</sup> or intravenous<sup>43</sup> and intramuscular<sup>44</sup> injection.

### *Mechanism of toxicity*

Paraquat is freely available in the Indian market as a pesticide for agricultural use. When consumed orally it causes oxidant free radical damage which results in hepato/nephrotoxicity besides pulmonary fibrosis. Absorbed paraquat is sequestered in the lungs and causes release of hydrogen and superoxide anions which cause lipid damage in the cell membranes.<sup>45</sup> An acute alveolitis develops causing haemorrhagic pulmonary oedema or acute respiratory distress syndrome (ARDS). Death after ingestion is due to hypoxaemia secondary to lung fibrosis.

### *Clinical features*

Ingestion results in severe inflammation of the tongue, oral mucosa and throat, corrosive injury to the gastrointestinal tract, renal tubular necrosis, hepatic necrosis and pulmonary fibrosis.<sup>45</sup> Immediately after ingestion, patients complain of burning and ulceration of the throat, tongue and oesophagus. A pharyngeal membrane is formed which is distinct from the diphtheria membrane as it affects the tongue.

Mild poisoning occurs with ingestion of <20 mg of paraquat per kg body weight (<1.5 g). Patients remain largely asymptomatic though a transient fall in vital capacity may occur. In moderate poisoning, ingestion is around 20–40 mg/kg (1.5–3 g). Early signs include vomiting, diarrhoea and dysphagia, followed by mild renal tubular damage with respiratory symptoms that start 3 weeks after ingestion with cough, breathlessness and pulmonary opacities on chest X-ray. Death may occur as late as 6 weeks after ingestion. Severe poisoning occurs with ingestion of 40–80 mg/kg (3–6 g) and there is marked ulceration and multiorgan dysfunction. The course of illness is more protracted. Respiratory symptoms begin within a week of ingestion and death is imminent with renal failure and hepatocellular damage. Rarely, perforation of the oesophagus and mediastinitis may occur. Fulminant poisoning is seen after ingestion of more than 80 mg/kg of paraquat (>6 g). Corrosive injury with painful ulceration is rapidly followed by renal failure and metabolic acidosis and dyspnoea. Death occurs within 24–48 hours.<sup>45</sup>

Systemically absorbed diquat is not selectively concentrated

in the lung tissue, as is paraquat, and pulmonary injury due to diquat is less prominent. However, diquat has severe toxic effects on the central nervous system that are not typical of paraquat poisoning. These include nervousness, irritability, restlessness, combativeness, disorientation, nonsensical statements, inability to recognize friends or family members and diminished reflexes. Neurological effects may progress to coma accompanied by tonic-clonic seizures, and result in death.<sup>46</sup> Other features include a corrosive effect on the gut leading to burning pain in the mouth, throat, chest and abdomen, intense nausea and vomiting, and diarrhoea. Renal and liver injury is common.

#### Diagnosis

To identify absorption of paraquat, 1 ml of urine is added to 1 ml of a solution of 100 mg sodium dithionite in 10 ml 1 M sodium hydroxide.<sup>45</sup> A blue-green colour indicates poisoning. If the test is negative 4–6 hours following ingestion, it implies that not enough paraquat has been absorbed to cause toxicity.

Urinary excretion is helpful in prognostication. Excretion rates of >1 mg/hour in the urine after 8 hours of ingestion signify a higher mortality.<sup>47</sup> A plasma concentration of >1.6 µg/ml 12 hours after ingestion has been found to be universally fatal.<sup>48</sup>

#### Management

The management of paraquat poisoning is mainly supportive and includes gastric decontamination with bentonite (1 L of 7% aqueous suspension) or Fuller earth (1 L of a 15% aqueous solution), haemodialysis<sup>49</sup> and the use of N-acetylcysteine.

Oxygen is contraindicated early in the poisoning because of progressive oxygen toxicity to the lung tissue. It may be given if the patient develops severe hypoxaemia. There may be some advantage in placing the patient in a moderately hypoxic environment, i.e. 15%–16% oxygen, although the benefit of this treatment has not been established in human poisoning.

Intravenous methylprednisolone 15 mg/kg/day for 3 consecutive days along with intravenous cyclophosphamide 10 mg/kg/day for 2 consecutive days, followed by intravenous dexamethasone 4 mg thrice a day has been proposed for management.<sup>50</sup> Several variations of this regimen, including a Caribbean regimen (cyclophosphamide, dexamethasone, furosemide, vitamins B and C),<sup>51</sup> exist in the literature and clear guidelines on dose and use are not available.<sup>52–54</sup> S-carboxymethylcysteine has been used by some authorities for treatment.<sup>55</sup>

Mortality remains high even with prompt management. Oesophageal rupture<sup>56</sup> and neutropenia<sup>57</sup> following paraquat ingestion have been reported. Morbidity in survivors is difficult to manage and is usually in the form of a restrictive lung disease.<sup>58</sup> However, this may be improved with newer modalities that help in attenuating paraquat-induced lung inflammation.<sup>50</sup> In case of severe pulmonary toxicity, the only treatment may be lung transplantation. However, the transplanted lung is susceptible to subsequent damage due to redistribution of paraquat.<sup>59</sup>

#### CHLOROPHENOXYACETIC HERBICIDES

These are popularly known as 'hormonal' weed killers. 2,4-D (2,4-dichlorophenoxyacetic acid) is the most commonly used agent besides dichloroprop, mecoprop and trichlorophenoxyacetic acid.

#### Clinical features of acute toxicity

Ingestion of 50–60 mg/kg of 2,4-D causes burning, nausea, vomiting, facial flushing and profuse sweating. Ingestion of

larger quantities causes headache, dizziness, muscle weakness, central nervous system depression, coma, rhabdomyolysis and respiratory distress. Renal injury produces oliguria and proteinuria.<sup>60</sup>

#### Diagnosis

Chromatographic identification of the poison helps in the diagnosis.

#### Management

Urinary alkalization substantially enhances the elimination of 2,4-D. Haemodialysis should be considered in such patients.

#### OTHER HERBICIDES

##### Chlorates

Sodium chlorate is found in weed killers and used in dye production. Chlorates are highly toxic oxidant compounds. Ingestion of 20 g of chlorate is fatal. Patients present with nausea, vomiting, diarrhoea and abdominal pain. Methaemoglobinaemia, haemolysis with haemoglobinaemia, jaundice and acute renal failure are seen.<sup>61</sup>

Monitoring of haemoglobin, haematocrit and plasma potassium concentration are essential during management. Methaemoglobinaemia exceeding 30% is managed with 1–2 mg/kg methylene blue given by slow intravenous injection. Haemodialysis is helpful in the management of severe cases.

##### Propanil

Propanil is an aromatic anilide herbicide used for rice farming which produces methaemoglobinaemia, tissue hypoxia, respiratory depression and depression of the central nervous system if ingested. Poisoning is rare and usually mild with most cases having been reported from Sri Lanka.<sup>62,63</sup> However, ingestion of large amounts is fatal and may need exchange transfusion for management. Treatment is with methylene blue.

#### RODENTICIDES

Two major types of rodenticides are used to kill rats, mice, moles, voles and squirrels. Single-dose rodenticides are fatal for rodents after a single feed. These include sodium monofluoroacetate, fluoroacetamide, norbromide, red squill, thallium sulphate, aluminium phosphide and zinc phosphide, and some of the superwarfarins. The multiple-dose types require repeated dosing. The commonly used ones are the warfarins and superwarfarins.

##### Thallium

Thallium poisoning tends to have a more insidious onset with a wide variety of toxic manifestations. Alopecia is a fairly consistent feature of thallium poisoning that is often helpful in diagnosing thallium poisoning. However, it occurs 2 weeks or more after poisoning and is not helpful in making an early diagnosis. In addition to hair loss, the gastrointestinal, central nervous, cardiovascular and renal systems, and skin are prominently affected by the intake of toxic amounts.<sup>64</sup>

Early symptoms include abdominal pain, nausea, vomiting, bloody diarrhoea, stomatitis and salivation. Ileus may appear later on. The liver enzymes may be elevated indicating tissue damage. Some patients may experience signs of central nervous system toxicity including headache, lethargy, muscle weakness, painful paraesthesias, tremor, ptosis and ataxia. These usually occur several days to more than a week after exposure. Myoclonic movements, convulsions, delirium and coma indicate more severe

neurological involvement.<sup>65,66</sup> Cardiovascular effects include early hypotension, due at least in part to toxic myocardial damage. Ventricular arrhythmias may occur. Patients may also develop ARDS.<sup>64</sup>

Treatment is supportive with careful correction of electrolytes and fluid deficit, and control of seizures. Potassium ferric ferrocyanide (Prussian blue) given orally enhances the faecal excretion of thallium by exchanging potassium for thallium in the gut. Haemodialysis is effective in removing thallium from the body.

#### Warfarins

These are multiple-dose rodenticides which produce a haemorrhagic state in rats after repeated ingestion by inhibiting vitamin K-dependent clotting factors II, VII, IX and X, and by direct capillary damage.

Warfarins are used therapeutically in humans for their anticoagulant effect. As rodenticides they are available in powder form containing 0.025%–0.5% hydroxycoumarin. The clinical features after toxic ingestion may be delayed by a few hours to days. The most common presentation is an asymptomatic prolongation of the prothrombin time. Overt bleeding from multiple sites can occur with ingestion of larger doses. A careful search should be done for petechial haemorrhages, haematuria and occult blood in the stools.<sup>67</sup>

A single ingestion of a warfarin compound does not mandate a gastric lavage. The toxicity of the ingested poison is monitored by serial measurements of the prothrombin time. If it remains normal after 24 hours and there is no clinical bleeding, the patient may safely be discharged. Vitamin K<sub>1</sub> (phyloquinone or phytonadione) 10 mg i.v. up to 5 times a day is administered if the prothrombin time is prolonged. Vitamin K<sub>1</sub>, specifically, is required. Neither vitamin K<sub>3</sub> (menadiol) nor vitamin K<sub>4</sub> (menadiol) is an antidote for these anticoagulants. Fresh frozen plasma may be administered in case phyloquinone is not available.

#### Superwarfarins

Superwarfarins are more potent than warfarins and have a longer duration of action. Like warfarin, these compounds also inhibit synthesis of factors II, VII, IX and X in the liver. However, due to their long duration of action, these act as single-dose rodenticides. The compounds in this category include bromadiolone, brodifacoum, difenacoum and diaphacinone. These are usually available as 'cakes'. Most patients who ingest superwarfarins do not get any major symptoms. A few may develop bleeding from different sites. Prolongation of the prothrombin time can be demonstrated after 36–48 hours and may persist for long periods.<sup>67,68</sup>

Since most ingestion involves small amounts of poison, no specific treatment is required. In case the amount ingested is larger (>1 'cake'), the patient may be admitted for 48–72 hours for observation and monitored with serial estimation of the prothrombin time. The management is similar to that for warfarin poisoning.

#### Aluminium phosphide

Aluminium phosphide is a commonly used, low cost, solid fumigant rodenticide that is used as a grain preservative in northern India and is available as pellets and powder. After fumigation, non-toxic residues comprising phosphate and hypophosphite of aluminium are left in the grain. A 3 g pellet contains 57% aluminium phosphide and is available under the common names of celphos, alphos, quickphos and phosfume. Less than 500 mg of an unexposed pellet of aluminium phosphide is lethal for an adult human.

However, the pellets rapidly lose their potency on exposure to air.

*Mechanism of toxicity.* On exposure to atmospheric moisture, aluminium phosphide liberates phosphine which may be absorbed by inhalation or through the skin. Upon ingestion, aluminium phosphide liberates phosphine gas which is absorbed into the circulation. It is a protoplasmic poison which inhibits various enzymes and protein synthesis. It is a potent respiratory chain enzyme inhibitor with its most important effect on cytochrome c oxidase. Inhibition of cytochrome c oxidase and other enzymes leads to the generation of superoxide radicals and cellular peroxides, and subsequent cellular injury through lipid peroxidation and other oxidant mechanisms.<sup>69</sup> Increased activity of superoxide dismutase and decreased levels of catalase<sup>70</sup> have been found, indicating that free radical-mediated cellular toxicity is responsible for hypoxic damage to various organs.

Since a small amount of aluminium phosphide is also absorbed and metabolized in the liver, slow release of phosphine can occur in the body, which may result in delayed features of toxicity.

*Clinical features of phosphine inhalation.* The gaseous nature of phosphine poses a potential risk to healthcare providers doing gastric decontamination; this fact should be borne in mind while undertaking the activity. Even 'off gassing' in a patient's exhaled breath may lead to contamination of healthcare staff. In the USA, the occupational permissible exposure limit for phosphine gas is 0.3 ppm.<sup>71</sup> Phosphine inhalation is dangerous at a concentration of 300 ppm and is usually fatal at a concentration of 400–600 ppm for 30 minutes.

Symptoms of mild intoxication are irritation of the mucous membranes, tightness in the chest, respiratory distress, dizziness, headache, nausea and vomiting.<sup>71</sup> In moderate intoxication, patients often complain of diplopia, ataxia and tremors. In severe cases, ARDS, cardiac arrhythmias, convulsions and coma occur, followed by death. Occasionally, systemic toxicity in the form of liver and renal failure occurs.

*Clinical features of aluminium phosphide ingestion.* Toxic features usually develop within 30 minutes of ingestion and include severe epigastric pain, repeated vomiting, diarrhoea, hypotension, tachycardia and metabolic acidosis. The presence of severe hypotension unresponsive to dopamine is a poor prognostic marker in these patients.<sup>72</sup> Toxic myocarditis resulting in life-threatening arrhythmias,<sup>73</sup> ST–T changes<sup>74</sup> and subendocardial infarction have been reported.<sup>75</sup> Respiratory features include cough, dyspnoea, cyanosis, pulmonary oedema and ARDS. Typically, patients remain conscious till the late stages. Aluminium phosphide ingestion can lead to intravascular haemolysis and this could mimic hepatic failure if this diagnosis is not considered during management.<sup>76</sup>

*Diagnosis.* The silver nitrate test on the gastric analysate is used for diagnosis.<sup>77</sup> To perform this test, 5 ml of gastric contents are diluted with 15 ml of water in a flask. Two round strips of a filter paper, one impregnated with 0.1 N silver nitrate and other with 0.1 N lead acetate are placed alternately on the mouth of the flask, which is heated at 50 °C for 15–20 minutes. If phosphine is present in the gastric contents, the silver nitrate paper turns black (due to conversion to metallic silver) while the lead acetate paper does not change colour. If hydrogen sulphide is present, both the papers turn black.

A variant of the gastric test is the breath test. The patient is asked to breathe through a filter paper impregnated with silver nitrate (0.1 N) for 15 minutes. In the presence of phosphine in the breath, the filter paper turns black. The test on gastric aspirate is much more sensitive than the breath test.<sup>77</sup> However, therapy

should not be delayed for want of the test in case the history and clinical examination support the diagnosis.

**Management.** If the victim has been exposed to phosphine gas, he should immediately be removed to an open area. Otherwise, management for both inhalation of phosphine and ingestion of aluminium phosphide is mainly supportive as no specific antidote is available. The objective is to support life till the time the body excretes the phosphine gas naturally through the lungs and kidneys.

Absorption of unabsorbed poison from the gut is reduced by gastric decontamination using potassium permanganate in 1:10 000 dilution for gastric lavage. Shock should be managed by infusing a large amount of saline, preferably under monitoring of the central venous pressure or pulmonary artery wedge pressure. Most patients require 4–6 L of fluids over 4–6 hours. If there is no response to fluids, dopamine may be started. Metabolic acidosis should be corrected with intravenous sodium bicarbonate.

Magnesium sulphate has been shown to stabilize cell membranes and reduce the incidence of arrhythmias. However, there is no clear evidence to support its use.<sup>78,79</sup> A 3 g bolus dose followed by a 6 g infusion over the next 12 hours for 5–7 days may be used.

N-acetylcysteine and magnesium<sup>78</sup> have been suggested as potential therapies for the management of poisoning but no effective treatment has been found and the mortality remains high.<sup>79</sup> Coconut oil has been reported to prevent rapid absorption of unabsorbed phosphine from the gut,<sup>80</sup> but the strength of evidence is at best weak.

Mortality remains high after ingestion of aluminium phosphide and death is common even after ingestion of as little as half a tablet provided it has been freshly opened and has not been exposed to the atmosphere. Serum levels of 1.6 mg/dl of phosphine correlate with mortality.<sup>81</sup> Complications are frequently seen in survivors. Benign oesophageal strictures have been reported due to local corrosion and can be corrected by endoscopic dilatation.<sup>82</sup>

#### *Barium compounds*

Carbonate, hydroxide and chloride forms of barium are used in pesticides. Barium carbonate is also used in glazing pottery while barium sulphide is used in depilators for external application.

**Mechanism of toxicity.** Barium ions interface with the sodium–potassium pump, producing a change in membrane permeability followed by paralysis of muscles.

**Clinical features of acute toxicity.** In humans, barium chloride is toxic in a dose of 1–10 g, whereas barium carbonate is toxic in as small a dose as 500 mg. Patients present with repeated vomiting, loose motions and abdominal pain following ingestion. There is tightness of the muscles of the face and neck, muscle tremors, anxiety and difficulty in breathing. Convulsions and cardiac arrhythmias have also been reported. Wide-complex tachyarrhythmias are seen including ectopics, ventricular tachycardia and even ventricular fibrillation. A prolonged QTc interval, prominent U waves and evidence of myocardial damage are present on ECG. Perioral paraesthesia that spreads to other parts of the body may be seen. Ascending quadriplegia with respiratory muscle involvement may occur in barium poisoning.<sup>83,84</sup> Hypokalaemia is common in patients with barium poisoning.

**Management.** This includes gastric lavage (in the early stages) followed by instillation of magnesium sulphate in the gut to precipitate insoluble barium sulphate, which is not absorbed in the gastrointestinal tract. Magnesium sulphate should not be given intravenously as it may precipitate barium sulphate leading to acute renal failure. Monitoring for arrhythmias and adequately correcting hypokalaemia are required.

#### *Zinc phosphide*

Zinc phosphide is a crystalline powder with an odour resembling rotten fish. It is available as a powder or as pellets that release phosphine gas on contact with water. The clinical features of zinc phosphide poisoning are similar to those of aluminium phosphide but slower in onset since the release of phosphine is slower. Nausea and vomiting are early features and can occur after ingestion of as little as 30 mg. Patients complain of tightness in the chest and may be excited, agitated and thirsty. Shock, oliguria, coma and convulsions may develop.<sup>85</sup> Pulmonary oedema, metabolic acidosis, hypocalcaemia, hepatotoxicity, thrombocytopenia and ECG changes are seen. The management of zinc phosphide poisoning is mostly supportive and symptomatic.

#### INSECT REPELLENTS

With the changing pattern of vector-borne diseases and increasing travel to tropical destinations, there has been an increasing use of personal protective measures against insects. Personal protection from malaria and scrub typhus has plagued military campaigns throughout history and has given rise to the term 'extended duration topical insect/arthropod repellents' (EDTIARs). The most widely used component in most EDTIARs is diethyltoluamide, popularly known as DEET.<sup>86</sup>

Poisoning with DEET has been reported after oral intake, topical application on non-intact skin, contact with eyes and by inhalation. The lethal dose of DEET is 2–4 g/kg in rats. After topical application, it has been shown that women experience lesser protection against mosquito bites over time compared with men.<sup>86</sup> It would, therefore, be reasonable to expect gender variability in the symptoms of toxicity.

Acute poisoning manifests with hypotension, respiratory depression and central nervous system toxicity. Toxic encephalopathy manifests as behavioural disorders including headache, restlessness, irritability, ataxia, rapid loss of consciousness and seizures. In some cases there may be flaccid paralysis and areflexia. Systemic toxicity after topical application is rare. Bullous eruptions have been reported in the skin flexures and antecubital fossae after an overnight application. However, only as little as 8% of the substance is absorbed after application and it is almost completely eliminated within 4 hours.

Management of DEET poisoning involves decontamination of the skin and supportive care. No specific antidote is available.<sup>87</sup>

#### MISCELLANEOUS POISONS

##### *Ethylene dibromide (EDB)*

Ethylene dibromide, also known as 1,2-dibromomethane, is a common pesticide used as a fumigant and preservative for storage of cereals and grains in India. It is a colourless liquid with a distinctive sweet odour.

In humans EDB is absorbed by all routes, easily penetrates the clothes and no effective antidote is available.<sup>88</sup> Ingestion of small amounts of EDB may be non-fatal<sup>89</sup> but exposure to 5–10 ml is usually fatal. Fatal exposure to EDB has been reported as an occupational hazard among grain storers and handlers.<sup>90</sup>

Cutaneous exposure to EDB can cause ulcerations, conjunctivitis, gastrointestinal and mucosal irritation, central nervous system irritation and depression.

Ingestion of EDB leads to vomiting, diarrhoea and burning in the throat soon after ingestion. These features may last for 1–3 days. Patients also develop tremors and central nervous system depression. Examination of the oral cavity may reveal ulceration of the mouth and throat. Within a few hours, the patient develops

hypotension and altered consciousness, followed by oliguria and jaundice in the next 24–48 hours.<sup>91,92</sup> Uncommon features include pulmonary oedema, muscle necrosis and hyperthermia. In the first 24–48 hours, death is due to respiratory or circulatory failure while later on, it is due to liver and kidney injury.<sup>92</sup>

Laboratory investigations show elevated levels of serum bromide (due to metabolism to bromine), urea and creatinine. The anion gap is low as bromides falsely elevate chloride levels. The bilirubin is elevated, and SGOT, SGPT and alkaline phosphatase may show mild-to-marked elevation. There may be proteinuria and haematuria.<sup>92</sup>

If EDB has been ingested in the past 2 hours, gastric lavage is recommended after which activated charcoal should be administered. Multiple doses of charcoal have been used in several cases of EDB poisoning. The most important aspect of management is to provide supportive care to the patient. This includes administration of intravenous fluids to correct the intravascular volume, maintenance of oxygenation and correction of acidosis.<sup>92</sup> If a patient develops hepatic encephalopathy, treatment for hepatic coma should be initiated. Haemodialysis is indicated to correct abnormalities associated with renal failure and reduce bromide levels. If the patient complains of severe retrosternal burning, an endoscopy should be done to look for oesophageal burns.

#### Pyrethrins and pyrethroids

Pyrethrum is the oleoresin extract of dried chrysanthemum flowers. The extract contains about 50% active insecticidal ingredients known as pyrethrins. Synthetically derived compounds such as deltamethrin, cypermethrin or fenvalerate have a longer half-life and are called pyrethroids. These substances are a common component of the mosquito repellent creams and coils available in the market. Commercial formulations usually contain piperonyl butoxide, which inhibits the metabolic degradation of the active ingredients. They disrupt nervous system function by altering membrane permeability to sodium.<sup>93</sup>

Pyrethrins are poorly absorbed from the gut, respiratory tract and skin. Their use indoors and in enclosed spaces has produced toxicity. Pyrethrins are thought to act on sodium channels causing central nervous system overactivity. The possibility that they also induce hypersensitivity is controversial.

Topical application may cause paraesthesias and a stinging sensation, especially on the hands and face. Pyrethroids may also cause various forms of dermatitis.<sup>94,95</sup> Inhalation causes breathlessness, headache, irritability and may precipitate fatal acute severe asthma.<sup>96</sup> Ingestion causes nausea, vomiting, palpitations, headache, fatigue and tightness of the chest. Ingestion of large amounts may even cause coma, convulsions and pulmonary oedema.

Management of pyrethrin toxicity is with skin decontamination. Seizures are controlled with benzodiazepines. Oxygen and bronchodilators may be necessary in cases presenting with respiratory distress or acute severe asthma.

#### CONCLUSION

Poisoning with pesticides is frequent in India and carries a high mortality and morbidity. Aggressive resuscitation and the use of antidotes where available are the keys to reducing mortality. It is important to sensitize physicians working in the periphery and rural hospitals to advances in the diagnosis and management, as newer means become available to fight the morbidity and mortality induced by pesticide poisoning.

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