

**4-Aminopyridine**  
**COMMERCIAL**  
**PRODUCTS**

Avitrol

**HIGHLIGHTS**

Toxic to all vertebrates

Used as bird repellent in grain baits or powdered sugar formulation

Rapidly absorbed across gut; less so on skin

Enhances cholinergic transmission in nervous system

**SIGNS & SYMPTOMS**

Severe muscle spasms

Reported abdominal discomfort, nausea, vomiting, weakness, dizziness, diaphoresis

**TREATMENT**

Decontaminate skin, eyes

Consider GI decontamination

Control seizures

Treat severe spasms in ICU

IV fluids if needed

CHAPTER 19

**Miscellaneous Pesticides, Synergists, Solvents and Adjuvants**

**MISCELLANEOUS PESTICIDES**

**4-Aminopyridine**

**Toxicology**

4-Aminopyridine is a highly toxic white powder used as a bird repellent. It works by making one or two birds acutely ill, and they warn off the remaining birds with their cries of distress.<sup>1</sup> It is toxic to all vertebrates.<sup>2</sup> It is usually added to grain baits in 0.5%-3.0% concentration, but 25% and 50% concentrates in powdered sugar are available. The avian LD<sub>50</sub> is between 1mg/kg and 8 mg/kg.<sup>1</sup> Information on human exposure has come from its use as an investigational drug in the treatment of multiple sclerosis.<sup>3,4</sup> It is rapidly absorbed by the gut and less effectively across skin. The chief mechanism of toxicity is enhancement of cholinergic transmission in the nervous system through the release of acetylcholine both centrally and peripherally. Because of enhanced transmission at neuromuscular junctions, severe muscle spasms may be a prominent manifestation of toxicity.<sup>3</sup> 4-aminopyridine is rapidly metabolized and excreted.

No human poisonings have occurred as a result of ordinary use, but toxic effects following intentional ingestion have been reported. In a report of ingestion of about 60 mg, patients experienced immediate abdominal discomfort, nausea and vomiting, weakness, dizziness and profuse diaphoresis. One went on to develop a tonic-clonic seizure and required ventilatory support. Acidosis was also present in those cases.<sup>2</sup> Dizziness and gait disturbances are additional reported findings. As seen above, seizures may also occur and be severe, although recovery with supportive therapy and ventilatory support has been the usual outcome.<sup>2,3,4</sup>

**Treatment of 4-Aminopyridine Toxicosis**

1. Decontaminate the skin with soap and water, as outlined in the **Chapter 3, General Principles**. Treat eye contamination by irrigating the exposed eyes with copious amounts of clean water or saline for at least 15 minutes. Remove contact lenses, if present, prior to irrigation. If irritation persists after irrigation, specialized medical treatment in a healthcare facility should be obtained.
2. If ingested, consider gastrointestinal decontamination as outlined in **Chapter 3**.
3. Control seizures with benzodiazepines. See **Chapter 3** for specific medications and dosages.
4. Treat severe muscular spasms that may occur with this agent with neuromuscular blockade in an intensive care unit setting.<sup>2</sup>
5. Treat dehydration with intravenous fluids if oral fluids cannot be retained.

## Calcium Cyanamide

This synthetic compound is marketed as granules containing 44% calcium cyanamide, yielding 19.5% nitrogen. It is incorporated into soil to serve as fertilizer, fungicide and herbicide. In contact with water, especially under acidic conditions, hydrogen cyanamide is released. Hydrogen cyanamide is a solid with considerable vapor pressure. It has toxic properties totally different from those of cyanide, and it does not degrade to cyanide.

### Toxicology

While the initial ingredient, **calcium cyanamide**, is only moderately irritating to skin, the byproduct hydrogen cyanamide is severely irritating and caustic to skin. Dermal and mucosal lesions in the mouth, tongue and upper esophagus have occurred after exposure. Contact dermatitis has been reported manifested by exfoliation. Additional symptoms include fever, pruritus, anorexia, insomnia and malaise.<sup>5</sup> Lichen planus has also been reported.<sup>6</sup> If hydrogen cyanamide is inhaled, it can be strongly irritating to mucous membranes.<sup>7</sup> Systemic poisonings have followed inhalation of hydrogen cyanamide and ingestion of the salt. Manifestations of systemic poisoning include flushing, headache, vertigo, dyspnea, tachycardia and hypotension, sometimes progressing to shock.<sup>7</sup>

Cyanamide is an inhibitor of acetaldehyde dehydrogenase; therefore, as with disulfiram (Antabuse), ingestion of alcohol may significantly worsen the toxic effects.<sup>8</sup> A pharmaceutical form of calcium cyanamide has been used in alcohol aversion therapy, and one patient treated with this experienced peripheral neuropathy.<sup>9</sup> Long-term use of cyanamide has been reported to cause hepatocellular damage.<sup>10</sup>

### Treatment of Cyanamide Toxicosis

1. Decontaminate the skin with soap and water, as outlined in the **Chapter 3, General Principles**. Treat eye contamination by irrigating the exposed eyes with copious amounts of clean water or saline for at least 15 minutes. Remove contact lenses, if present, prior to irrigation. If irritation persists after irrigation, specialized medical treatment in a healthcare facility should be obtained.
2. If ingested, consider gastrointestinal decontamination as outlined in **Chapter 3**.
3. If hypotension occurs, provide supportive care including intravenous fluids. If severe, the patient may need vasopressors and intensive care management.<sup>11</sup>

## Creosote

Creosote is a wood preservative that is registered as a restricted use pesticide, which limits its use to non-residential sites and requires strict worker protection standards. Creosote was first registered in 1948. It was used in the past as an animal dip and disinfectant, but is currently only registered for use on heavy-duty, pressure-treated industrial products, such as railroad ties and utility poles.<sup>12</sup>

### Toxicology

**Creosote** is obtained by distillation of the tar formed by heating wood or coal in the absence of oxygen. It is purified by extraction into oils. Creosote from wood consists of caustic phenol compounds, mainly guaiacol (methoxy phenol) and cresol (methyl

## Calcium Cyanamide COMMERCIAL PRODUCTS

cyanamide

nitrolime (has been discontinued)

## HIGHLIGHTS

Marketed as multi-function granules

Byproduct hydrogen cyanamide is severe skin irritant

Alcohol may worsen toxic effects

## SIGNS & SYMPTOMS

Mouth, tongue, upper esophageal lesions

Possible contact dermatitis with exfoliation

Fever, pruritus, anorexia, insomnia, malaise

Systemic: flushing, headache, vertigo, dyspnea, tachycardia, hypotension

## TREATMENT

Decontaminate skin, eyes, GI as appropriate

Supportive care, IV fluids for hypotension

## CHAPTER 19

### Miscellaneous Pesticides, Synergists, Solvents and Adjuvants

#### Creosote

#### HIGHLIGHTS

Restricted use pesticide

Used only on heavy-duty,  
pressure-treated industrial  
wood

Skin, eye, mucous  
membrane irritant

Absorbed by gut, lung

#### SIGNS & SYMPTOMS

Skin irritation, possible  
eruptions, pigmentation

GI lesions, pain

Systemic: salivation,  
vomiting, dyspnea,  
headache, dizziness, loss  
of pupil reflex, cyanosis,  
hypothermia, convulsions,  
coma

Dark, “smoky” urine

#### TREATMENT

Decontaminate skin, eyes

Consider GI  
decontamination with  
caution

ICU support may be  
indicated

phenol). Coal-derived creosote contains, in addition, some phenol, pyridine and pyridinol. Much of human exposure is in the form of various phenol compounds. Some phenolic compounds such as cresol are also used as disinfectants; more information on toxicity from these compounds is found in **Chapter 20, Disinfectants**. Creosote is carcinogenic in animals and epidemiological evidence has suggested an association with some human cancers. This is discussed in the **Chapter 21, Chronic Effects**.

Creosote is irritating to skin, eyes and mucous membranes. Workers in contact with technical creosote or with treated timbers sometimes develop skin irritation, vesicular or papular eruptions, dermal pigmentation and occasionally gangrene and skin cancer.<sup>13</sup> Photosensitization has been reported. Eye contamination has resulted in conjunctivitis and keratitis, sometimes resulting in corneal scarring.<sup>14</sup> The constituents of creosote are efficiently absorbed across the skin, but acute systemic poisonings following dermal absorption have occurred very rarely.

Absorption of ingested phenolic compounds from the gut occurs promptly, and there may be significant absorption of vapor by the lung. Conjugates of absorbed phenolic constituents are excreted mainly in the urine. Acute toxic effects are similar to those of Lysol, but the corrosive nature of creosote is somewhat less because of greater dilution of phenol in the creosote.<sup>15</sup> Irritation of the gastrointestinal tract including mucosal lesions, esophageal ulcers, abdominal pain, toxic encephalopathy and renal tubular injury are all principal effects following ingestion or inhalation exposure from phenolic compounds.<sup>16,17,18,19,20</sup>

Manifestations of acute systemic poisoning are salivation, vomiting, dyspnea, headache, dizziness, loss of pupillary reflexes, cyanosis, hypothermia, convulsions and coma. Death is due to multiorgan system failure as patients develop shock, acidosis, respiratory depression and anuric renal failure. Acute respiratory distress syndrome (ARDS) has also been reported and is potentially fatal.<sup>17,21,22</sup> Some reports of poisoning have been from related phenolic compounds as opposed to the wood preservative itself. A chronic toxicosis from continuing gastrointestinal absorption (creosote used medicinally) has been described, consisting of gastroenteritis and visual disturbances.<sup>19</sup>

#### Confirmation of Poisoning

The presence of phenolic oxidation products imparts a dark, smoky color to the urine.<sup>15,20</sup> If creosote poisoning is suspected, addition of a few drops of ferric chloride solution to the urine yields a violet or blue color indicating the presence of phenolic compounds. Methods to determine urinary levels of phenolic compounds using capillary gas chromatography have been described.<sup>23</sup> Data are limited in determining a “normal range”; however, in separate fatal cases of phenol poisoning, peak blood and urine levels were 58-60 µg/mL (blood) and 20-208 µg/mL (urine) using GC/MS.<sup>24,25</sup>

#### Treatment of Creosote Toxicosis

1. Decontaminate the skin with soap and water, as outlined in **Chapter 3, General Principles**. Treat eye contamination by irrigating the exposed eyes with copious amounts of clean water or saline for at least 15 minutes. Remove contact lenses, if present, prior to irrigation. If irritation persists after irrigation, specialized medical treatment in a healthcare facility should be obtained.
2. If ingested, consider gastrointestinal decontamination as outlined in **Chapter 3**. Given the corrosive nature of phenolic compounds such as creosote, efforts to use an adsorbent such as charcoal (or repeated use of charcoal) depend on whether there has been corrosive injury to the esophagus. If pharyngeal redness

and swelling are evident, emesis, whether induced or exacerbated by activated charcoal, is not advisable because of potential re-exposure of the esophagus to the creosote. Risk of perforation from a gastric tube precludes the use of gastric lavage.

3. Treat severe systemic creosote poisoning in an intensive care unit setting with appropriate supportive care including respiratory support, intravenous fluids, cardiac monitoring and renal function support as necessary.
4. Draw a blood sample to test for methemoglobinemia, to measure BUN and blood electrolytes and to check for signs of liver injury (bilirubin, GGT, LDH, ALT, AST and alkaline phosphatase). Examine the urine for protein and cells, and for “smoky” phenolic excretion products.
5. Control seizures with benzodiazepines. See **Chapter 3** for specific medications and dosages. Hemoperfusion over charcoal has been reported to be successful.<sup>26</sup>
6. Methemoglobinemia is rarely severe, but consider administration of methylene blue if 25%-30% of hemoglobin is converted.

### Dosage of Methylene Blue

- **1-2 mg/kg body weight, IV, over 5 minutes, repeated as needed every 4 hours.**

Methylene blue is contraindicated in patients with G6PD deficiency.

7. Refer patients for endoscopic evaluation following a deliberate ingestion. If there are any signs or symptoms suggestive of mucosal pharyngeal or esophageal injury (visible burns in the oral mucosa, stridor, drooling, dysphagia, refusal to swallow or abdominal pain) following inadvertent or unintentional ingestion, those patients should also have an endoscopy.<sup>27,28,29</sup>

## Endothall

As the free acid or as sodium, potassium or amine salts, endothall is used as a contact herbicide, defoliant, aquatic herbicide and algaecide. It is formulated in aqueous solutions and granules at various strengths.

### Toxicology

**Endothall** is irritating to skin, eyes and mucous membranes. It is well absorbed across abraded skin and from the gastrointestinal tract. Recognized systemic toxic mechanisms in mammals include a corrosive effect on the gastrointestinal tract (particularly from high concentrations of the free acid), cardiomyopathy and vascular injury leading to shock, and central nervous system injury, causing convulsions and respiratory depression. A single case has been reported of a lethal poisoning in a previously healthy 21-year-old man who died after ingestion of 7-8 grams of endothall. In this patient, hemorrhage and edema were noted in the gastrointestinal tract and lungs.<sup>30</sup>

## Endothall COMMERCIAL PRODUCTS

Accelerate  
Aquathol  
Des-i-cate  
Endothall Turf Herbicide  
Herbicide 273  
Hydrothol

## HIGHLIGHTS

Well absorbed by gut and abraded skin

GI corrosive

Cardiac, respiratory, CNS impacts

## SIGNS & SYMPTOMS

Convulsions

Respiratory depression

“Smoky” urine

## TREATMENT

Decontaminate skin, eyes

Consider GI decontamination with caution

ICU support may be indicated

Control seizures

## CONTRAINDICATED

Gastric lavage in most cases

## CHAPTER 19

### Miscellaneous Pesticides, Synergists, Solvents and Adjuvants

#### *Metaldehyde* COMMERCIAL PRODUCTS

Antimilace  
Biodehido Snailkill  
Cekumeta  
Halizan  
META  
Metason  
Namekil  
and others

#### HIGHLIGHTS

Slug baits and other uses  
Inhalation and ingestion  
hazard

#### SIGNS & SYMPTOMS

Nausea, vomiting, dizziness  
after ingestion  
Severe toxicity: pyrexia,  
seizures, metabolic  
acidosis, mental changes  
Possible headache,  
hypersalivation, facial  
flushing, tachypnea

#### TREATMENT

Consider GI  
decontamination  
ICU treatment may be  
indicated

#### **Confirmation of Poisoning**

There are no standards for endothall levels, and they are not considered useful in the management of acute poisoning.

#### **Treatment of Endothall Toxicosis**

1. Decontaminate the skin with soap and water as outlined in the **Chapter 3, General Principles**. Irrigate exposed eyes with copious amounts of clean water or saline for at least 15 minutes. Remove contact lenses, if present, prior to irrigation. If irritation persists after irrigation, obtain specialized medical treatment in a health-care facility.
2. If ingested, consider gastrointestinal decontamination as outlined in **Chapter 3**, but use treatment procedures appropriate for ingestions of corrosives (strong acids and alkalis). Due to the corrosive nature of this agent, gastric lavage is usually contraindicated, because of the risk of esophageal perforation. Refer patient to a surgeon or gastroenterologist for consideration of endoscopy.
3. Treat severe systemic endothall poisoning in an intensive care unit setting with appropriate supportive care, including respiratory support, intravenous fluids, cardiac monitoring and renal function support as necessary.
4. Draw a blood sample to test for methemoglobinemia, measure BUN and blood electrolytes and check for signs of liver injury (bilirubin, GGT, LDH, ALT, AST and alkaline phosphatase). Examine the urine for protein and cells and for “smoky” phenolic excretion products.
5. Control seizures with benzodiazepines. See **Chapter 3** for specific medications and dosages.

#### **Metaldehyde**

##### **Toxicology**

Metaldehyde is a 4-unit cyclic polymer of acetaldehyde long used to kill slugs and snails, which are attracted to it without the use of bait. Occasional poisonings of animals and children have resulted from ingestion of pellets intended as molluscicide, and tablets designed as a combustible fuel (“meta-fuel”) have also been responsible for human poisonings.<sup>31</sup> Another form of exposure is “snow storm tablets,” which the user places at the end of a lighted cigarette to create snow. Toxicity occurs through inhalation of metaldehyde fumes.<sup>32</sup> The biochemical mechanism of poisoning is not known. Both acetaldehyde and metaldehyde produced similar effects in dogs; however, acetaldehyde was not detected in the plasma or urine of the metaldehyde-poisoned dogs.<sup>33</sup> Poisoned animals show muscle tremors, ataxia, hyperesthesia, salivation, tachycardia and seizures.<sup>33,34</sup>

Ingestion of a toxic dose is often followed shortly by nausea, vomiting and dizziness, if symptoms are even present.<sup>35</sup> Primary features of severe toxicity include pyrexia, generalized seizures, metabolic acidosis and mental status changes such as irritability, sometimes progressing to coma.<sup>31,35,36,37</sup> Other signs and symptoms that may occur include headache, hypersalivation, facial flushing and tachypnea.<sup>31,32</sup> Pneumonitis has followed inhalational exposure to metaldehyde.<sup>32</sup> Most cases are either self limiting or with significant but controllable seizures, and fatal events are infre-

quent.<sup>31,35,36,37</sup> One patient survived what has been considered a lethal dose of 600 mg/kg.<sup>36</sup> Autopsy findings in fatal human poisonings indicate severe damage to liver cells and renal tubular epithelium.

### **Confirmation of Poisoning**

Metaldehyde can be measured in the serum, although there are very few reports of levels among poisoned humans. Saito described a method to measure metaldehyde in serum using headspace solid-phase microextraction and gas chromatography-mass spectrometry.<sup>38</sup> One patient who had severe tonic-clonic seizures and was comatose had a metaldehyde level in the serum of 125 mg/l, with a half-life of 27 hours. This patient did not have detectable acetaldehyde in the serum.<sup>37</sup>

### **Treatment of Metaldehyde Toxicosis**

There is no specific antidote for metaldehyde poisoning.

1. If ingested, consider gastrointestinal decontamination as outlined in **Chapter 3, General Principles**.
2. Treat severe systemic metaldehyde poisoning in an intensive care unit setting with appropriate supportive care, including respiratory support, intravenous fluids, cardiac monitoring and renal function support as necessary. Early and aggressive treatment of all of the above may be life saving following a massive ingestion.<sup>36</sup>
3. Consider sodium bicarbonate in the event of severe metabolic acidosis.<sup>36</sup> Monitor fluid balance and electrolytes carefully to avoid fluid overload if renal failure supervenes.
4. Order liver function tests and urine sediment examination to assess liver and kidney injury in poisoned patients.

## **Sodium Chlorate**

Sodium chlorate is used in agriculture as a defoliant, nonselective contact herbicide and semi-permanent soil sterilant. Because of its explosive nature, it must be formulated with a water-soluble, fire-retardant material such as sodium metaborate, soda ash, magnesium chloride or urea. It is usually applied in water solution.

### **Toxicology**

**Sodium chlorate** is irritating to skin, eyes and mucous membranes of the upper respiratory tract.<sup>39</sup> Dermal absorption is slight. Even though gastrointestinal absorption is also inefficient, severe poisoning, sometimes fatal, follows ingestion of a toxic dose, said to be about 20 grams in the adult human. Excretion is chiefly in the urine.

Sodium chlorate poisoning can manifest in many ways. The principal mechanisms of toxicity are hemolysis, coagulation disturbances methemoglobin formation, cardiac arrhythmia (partly secondary to hyperkalemia) and renal tubular injury.<sup>39,40,41</sup> The most common cause of death in early stages of toxicity is anoxia from methemoglobinemia and hemolysis, resulting in disseminated intravascular coagulation. Renal failure may occur afterwards and figure prominently as a cause of death.<sup>39,40,41</sup>

Following ingestion, sodium chlorate may have an irritant action on the gut, causing nausea, vomiting and abdominal pain. Once absorbed, hemoglobin is rapidly

### **Sodium Chlorate COMMERCIAL PRODUCTS**

Bladvel  
Defol  
De-Fol-Ate  
Dervan  
Drop-Leaf  
Fall  
KM  
Kusatol  
Leafex

## CHAPTER 19

### Miscellaneous Pesticides, Synergists, Solvents and Adjuvants

#### **Sodium Chlorate** **HIGHLIGHTS**

Forms methemoglobin in  
unique fashion

Destroys erythrocytes and  
enzymatic systems

Irritating to skin, eyes,  
mucous membranes

Many poisoning  
manifestations

#### **SIGNS & SYMPTOMS**

Nausea, vomiting,  
abdominal pain

Cyanosis

Dark brown plasma, urine

#### **TREATMENT**

Decontaminate skin, eyes

Consider GI  
decontamination

ICU may be appropriate

Consider oral or IV sodium  
thiosulfate

IV fluids and sodium  
bicarbonate

#### **CONTRAINDICATED**

Methylene blue unless very  
early

oxidized to methemoglobin, and hemolysis and intravascular hemolysis subsequently occur.<sup>39,40,41</sup> Cyanosis is prominent if methemoglobinemia is severe and may be the only presenting sign.<sup>41</sup> Acute tubular necrosis and hemoglobinuria may result from the hemolysis or direct toxic injury. Plasma and urine are dark brown from presence of free hemoglobin and methemoglobin.<sup>39,41,42,43</sup> One fatal case presented with 30% methemoglobinemia.<sup>42</sup> Release of potassium from red cell destruction results in hyperkalemia that may be severe enough to cause life-threatening arrhythmias.<sup>43</sup> The liver and spleen are often enlarged due to uptake of hemolyzed erythrocytes.<sup>41</sup> Hypoxemia may lead to convulsions. Death may be the result of shock, tissue hypoxia, renal failure, hyperkalemia or disseminated intravascular coagulation (DIC).<sup>39,40,41,43</sup>

Although other toxicants will induce methemoglobinemia formation, the mechanism associated with chlorates is unique. Chlorate not only forms methemoglobin, it also destroys erythrocytes and the enzymatic systems in the process.<sup>40</sup> Ordinarily, methylene blue is used as an antidote to reduce methemoglobin. This process depends on NADPH formation by the oxidation of glucose-6-phosphate. However, chlorate will denature the glucose-6-phosphate dehydrogenase, which will in turn render methylene blue ineffective.<sup>40</sup>

#### **Confirmation of Poisoning**

Sodium chlorate poisoning can be detected by ion chromatography, although this test may not be widely available.<sup>42</sup> Chlorate poisoning should be considered when patients present with methemoglobinemia. Dark brown-to-black staining of the plasma and urine indicates the action of a strong oxidizing agent on hemoglobin.<sup>41,44</sup>

#### **Treatment of Chlorate Toxicosis**

1. Decontaminate the skin with soap and water as outlined in **Chapter 3, General Principles**. Irrigate exposed eyes with copious amounts of clean water or saline for at least 15 minutes. Remove contact lenses, if present, prior to irrigation. If irritation persists after irrigation, obtain specialized medical treatment in a health-care facility.
2. If ingested, consider gastrointestinal decontamination as outlined in **Chapter 3**.
3. Treat severe systemic sodium chlorate poisoning in an intensive care unit setting, with appropriate supportive care including respiratory support, intravenous fluids, cardiac monitoring and renal function support as necessary.<sup>44</sup> In addition, monitor for methemoglobinemia.
4. Sodium thiosulfate has been used as an antidote against absorbed sodium chlorate.<sup>39,44</sup> Thiosulfate is thought to inactivate the chlorate ion to form the less toxic chloride ion.

#### **Dosage of Sodium Thiosulfate**

- **2-5 gm dissolved in 200 mL of 5% sodium bicarbonate, given orally or as an IV infusion over 60-90 minutes**<sup>39</sup>

5. Administer intravenous fluids and sodium bicarbonate.<sup>41,44</sup> Monitor urine production closely, so that intravenous fluids can be slowed or discontinued if renal failure occurs.

6. Transfuse blood if hemolysis and methemoglobinemia are severe. Exchange transfusion has been recommended to enhance clearance and treat DIC.<sup>43</sup>
7. Consider hemodialysis, which has been used in several cases of chlorate poisoning.<sup>42,44</sup>
8. Consider administration of methylene blue, which has been used to reverse methemoglobinemia if as much as 25%-30% of hemoglobin is converted.

### Dosage of Methylene Blue

- **1-2 mg/kg body weight, IV, over 5 minutes, q 4 hours prn**

Methylene blue is generally not helpful with sodium chlorate poisoning unless given very early because of the unique characteristics described above in the *Toxicology* subsection.<sup>40,44</sup>

## SYNERGISTS

### Piperonyl Butoxide

Synergists are chemical agents included in pesticide products to enhance the killing power of the active ingredients. The widely used insecticide synergist piperonyl butoxide acts by inhibiting the enzymatic degradation of pyrethrins, rotenone, N-methyl carbamates, organophosphates and possibly some other insecticides. There is limited dermal absorption on contact. Inherent toxicity in mammals is low, with an oral LD<sub>50</sub> in rats of >4,500 mg/kg.<sup>45</sup> Large absorbed doses may theoretically enhance the toxic hazard of the rapidly metabolized insecticides used today, although inhibition of human drug metabolizing enzymes by these agents has not actually been demonstrated. Their presence in pesticide products to which humans are exposed does not change the basic approach to management of poisoning with the focus of treatment based on the active ingredient involved. The notable exception is that care providers should be aware of some possibility of enhanced toxicity of the active insecticidal ingredients.

## SOLVENTS AND ADJUVANTS

Liquid materials in which pesticides are dissolved or the solids on which they are adsorbed (sometimes called carriers or vehicles) are chosen by producers to achieve stability of the active ingredient, convenience in handling and application, and maximum killing power following application. The solvents and adjuvants pesticide manufacturers choose can give their commercial products a competitive edge. For this reason, their inclusion in marketed products is usually proprietary information, not available to the general public except under emergency circumstances. In a poisoning emergency, pesticide companies will usually cooperate in supplying physicians with information needed to provide treatment. The physician should seek this information to assist in evaluating all possible exposures. A direct request to the producer is necessary to secure this information. Some companies put the inert ingredients on the Material Safety Data Sheet (MSDS).

## Solvents & Adjuvants HIGHLIGHTS

Petroleum distillates are commonly used for lipophilic pesticides

Hydrocarbon pneumonitis: rapid respiration, cyanosis, tachycardia, fever

Some solvents may enhance dermal absorption of some pesticides

Some adjuvants, penetrants, safeners irritate skin, eyes, mucous membranes

Dust formulations can result in systemic poisoning via gut absorption

## TREATMENT

Consider GI decontamination with caution, especially with petroleum distillates

Watch for and treat hydrocarbon pneumonitis

Monitor urine, heart

**Petroleum distillates** are the most commonly used solvents for lipophilic pesticides. (Most insecticides are lipophilic.) The distillates are mixtures of aliphatic and aromatic hydrocarbons with low boiling points.

Sometimes specific hydrocarbons, such as toluene or xylene (strongly odiferous), are added to stabilize the solution of insecticide or make it more emulsifiable. Hydrocarbon-dissolved pesticides are usually diluted for application by adding measured amounts of water to form emulsions. Some chlorinated hydrocarbons may be present in particular technical mixtures. A strong odor lingering after application of a structural pest control spray is often due to the solvent rather than the active ingredient. Rapid respiration, cyanosis, tachycardia and low-grade fever are the usual indications of frank hydrocarbon pneumonitis.<sup>46</sup>

Less lipophilic active ingredients are sometimes dissolved in mixtures of **alcohols, glycols, ethers** or **various chlorinated solvents**. It is possible that these enhance the dermal absorbability of some pesticides. A well-described example is increased dermal absorption of the insect repellent DEET when dissolved in 70% ethyl alcohol compared to the solvent polyethylene glycol.<sup>47</sup> Also, some solvents (*e.g.*, methanol and isopropanol) may represent a significant toxic hazard if swallowed in sufficient dosage. Symptoms may include central nervous system depression ranging from disorientation to lethargy and coma with severe overdose, as well as respiratory depression and ketosis.<sup>48</sup> The presence of chlorinated solvents in some formulations may add significantly to the toxic hazard, particularly if the product is ingested. Certain adjuvants are irritants to skin, eyes and mucous membranes and may account for the irritant properties of products with active ingredient(s) lacking this effect. With these exceptions, however, the presence of adjuvants in most finished pesticide products probably does not enhance or reduce systemic mammalian toxicity to any great extent.

**Granular formulations** utilize various clay materials that adsorb pesticide, retain it in more or less stable form until application and then desorb the material slowly into treated soil. There is some significant desorption when granules are in contact with human skin and very substantial desorption into gastrointestinal secretions if granules are swallowed. The clay materials themselves are not a toxic hazard.

**Dusts** are infrequently used today. Various forms of talc (magnesium silicate particles) have been used in the past to adsorb pesticides for application to foliage. Particle sizes are such that these dusts are usually trapped in the upper respiratory mucous when inhaled. When the mucous is swallowed, the particles desorb pesticide into gastrointestinal secretions. Dust formulations may, therefore, release enough of some pesticides to cause systemic poisonings.

**Stickers and spreaders** (film extenders) are organic substances added to formulations to disperse pesticide over treated foliage surfaces and enhance adhesion. The availability and persistence of residue on the leaf surfaces is thereby increased. Substances used include proteinaceous materials (milk products, wheat flour, blood albumin, gelatin), oils, gums, resins, clays, polyoxyethylene glycols, terpenes and other viscid organics. Some also include sulfated alcohols, fatty acid esters, alkyl and petroleum sulfonates. For persons exposed in the course of formulation or application of pesticides, these adjuvants probably add little or no toxic hazard to that inherent in the active pesticidal ingredients.

**Emulsifiers** serve to stabilize water-oil emulsions formed when water is added to technical hydrocarbon concentrates. Chemically, they are detergent-like (one part of the molecule lipophilic, the other hydrophilic). Long-chain alkyl sulfonate esters of polyethylene glycol and polyoxyethylene oleate are exemplary emulsifiers. They have low inherent mammalian toxicity, and their presence probably has little effect on the overall toxicity of formulated products that include them.

**Penetrants** facilitate the transfer of herbicide from foliage surface to the interior tissues. Some are lipids while others are detergent (surfactant) in nature. Substances

used include heavy petroleum oils and distillates, polyol fatty acid esters, polyethoxylated fatty acid esters, aryl alkyl polyoxyethylene glycols, alkyl amine acetate, alkyl aryl sulfonates, polyhydric alcohols and alkyl phosphates. Some of these are eye and skin irritants and may account for the irritant effects of particular herbicide formulations whose active ingredients do not have this property.

**Safeners** are substances added to mixtures of fertilizers with pesticides (commonly herbicides) to limit the formation of undesirable reaction products. Some substances used are alcohol sulfates, sodium alkyl butane diamate, polyesters of sodium thiobutane dioate and benzene acetonitrile derivatives. Some are moderately irritating to the skin and eyes. Systemic toxicities are generally low.

**Anticaking agents** are added to granular and dust formulations to facilitate application by preventing cakes and clumps. Among several products used are the sodium salt of mono- and di-methyl naphthalene sulfonate, and diatomaceous earth. Diatomaceous earth has little adverse effect except a drying action on the skin. Methyl naphthalenes are said to be skin irritants and photosensitizers; whether their derivatives have this effect is not known.

### **Treatment of Solvent and Adjuvant Toxicosis**

Petroleum distillates are mineral hydrocarbons that undergo limited absorption across the gut. In general, clinical toxicologists do not recommend induced emesis or gastric lavage in treating ingestions of these materials, because of the serious risk of hydrocarbon pneumonitis even if tiny amounts of the liquid are aspirated into the lungs. However, this injunction against emptying the stomach may be set aside when the petroleum distillate is a vehicle for toxic pesticides in significant concentration.

1. In such cases, if the patient is seen within 1 hour of exposure, consider gastrointestinal decontamination, as outlined in **Chapter 3, General Principles**.
2. Hospitalize patients with presumed hydrocarbon pneumonitis who are symptomatic. If the patient has pulmonary symptoms, order a chest X-ray to detect or confirm signs of pneumonitis. Mechanically assisted pulmonary ventilation with pure oxygen may be required. Hydrocarbon pneumonitis is sometimes fatal, and survivors may require several weeks for full recovery. In milder cases, clinical improvement usually occurs within several days, although radiographic findings will remain abnormal for longer periods.<sup>49</sup>
3. Examine the urine for protein, sugar, acetone, casts and cells; and examine an ECG for arrhythmias and conduction defects.

### **References**

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