

**HIGHLIGHTS**

- Easily absorbed in lung, gut, skin

**Signs and Symptoms:**

- Highly variable based on agent
- Many are irritants
- Carbon disulfide, chloroform, hydrogen cyanide, and naphthalene may have serious CNS effects
- Methyl bromide and aluminum phosphide (phosphine gas) cause pulmonary edema
- Hydrogen cyanide causes severe hypoxia without cyanosis in early stages

**Treatment:**

- Skin and eye decontamination
- Oxygen and diuresis for pulmonary edema
- Specific measures needed for various agents

**Contraindicated:**

- Ipecac should not be used in cyanide poisoning

# Fumigants

Fumigants have remarkable capacities for diffusion, a property essential to their function. Some readily penetrate rubber and neoprene personal protective gear, as well as human skin. They are rapidly absorbed across the pulmonary membrane, gut, and skin. Special adsorbents are required in respirator canisters to protect exposed workers from airborne fumigant gases. Even these may not provide complete protection when air concentrations of fumigants are high.

The packaging and formulation of fumigants are complex. Fumigants which are gases at room temperature (methyl bromide, ethylene oxide, sulfur dioxide, hydrogen cyanide, sulfuryl fluoride) are provided in compressed gas cylinders. Liquids are marketed in cans or drums. Solids which sublime, such as naphthalene, must be packaged so as to prevent significant contact with air before they are used.

Mixtures of fumigants have several advantages. Carbon tetrachloride reduces the explosiveness of carbon disulfide and acrylonitrile. Chloropicrin, having a strong odor and irritant effect, is often added as a “warning agent” to other liquid fumigants.

Liquid halocarbons and carbon disulfide evaporate into the air while naphthalene sublimates. Paraformaldehyde slowly depolymerizes to formaldehyde. Aluminum phosphide slowly reacts with water vapor in the air to liberate phosphine, an extremely toxic gas. Metam sodium, also a fumigant, is covered under thiocarbamates in Chapter 15, Fungicides.

## Toxicology *(in alphabetical order)*

**Acrolein** (acrylaldehyde) is an extremely irritating gas used as a fumigant and an aquatic herbicide. The vapor causes lacrimation and upper respiratory tract irritation, which may lead to laryngeal edema, bronchospasm, and delayed pulmonary edema. The consequences of ingestion are essentially the same as those that follow ingestion of formaldehyde. Contact with the skin may cause blistering.

**Acrylonitrile** is biotransformed in the body to hydrogen cyanide. Toxicity and mechanisms of poisoning are essentially the same as for cyanide (see under hydrogen cyanide below), except that acrylonitrile is irritating to the eyes and to the upper respiratory tract.

**Carbon disulfide** vapor is only moderately irritating to upper respiratory membranes, but it has an offensive “rotten cabbage” odor. Acute toxicity is due

chiefly to effects on the central nervous system. Inhalation of high concentrations for short periods has caused headache, dizziness, nausea, hallucinations, delirium, progressive paralysis, and death from respiratory failure. More prolonged exposure to lesser amounts has led to blindness, deafness, paresthesia, painful neuropathy, and paralysis. Carbon disulfide is a potent skin irritant, often causing severe burns. Long-term occupational exposures have been shown to accelerate atherosclerosis, leading to ischemic cardiomyopathy, polyneuropathy, and gastrointestinal dysfunction.<sup>1</sup> Toxic damage to the liver and kidneys may result in severe functional deficits of these organs. Reproductive failure has been noted.

**Carbon tetrachloride** is less toxic than chloroform as a central nervous system depressant, but is much more severely hepatotoxic, particularly following ingestion. Liver cell damage is apparently due to free radicals generated in the process of initial dechlorination.<sup>2</sup> Cardiac arrhythmias, progressing to fibrillation, may follow inhalation of high concentrations of carbon tetrachloride or ingestion of the liquid. Kidney injury also occurs sometimes with minimal hepatic toxicity. The kidney injury may be manifested by acute tubular necrosis or by azotemia and general renal failure. Even topical exposure has resulted in acute renal toxicity.<sup>3</sup>

**Chloroform** has an agreeable sweet odor and is only slightly irritating to the respiratory tract. It is well absorbed from the lungs and is also absorbed from the skin and gastrointestinal tract. It is a powerful central nervous system depressant (in fact, an anesthetic).<sup>4</sup> Inhalation of toxic concentrations in air leads to dizziness, loss of sensation and motor power, and then unconsciousness. Inhalation of large amounts causes cardiac arrhythmias, sometimes progressing to ventricular fibrillation. Large absorbed doses damage the functional cells of the liver and kidney. Ingestion is more likely to cause serious liver and kidney injury than is inhalation of the vapor.

**Chloropicrin** is severely irritating to the upper respiratory tract, eyes, and skin. Inhalation of an irritant concentration sometimes leads to vomiting. Ingestion could be expected to cause a corrosive gastroenteritis.

**Dibromochloropropane** is irritating to skin, eyes, and the respiratory tract. Eye damage has resulted from repeated exposure to the vapors. When absorbed, it causes headache, nausea, vomiting, ataxia, and slurred speech. Liver and kidney damage are prominent features of acute poisoning. Chronic exposure to relatively low concentrations has led to temporary or permanent sterility of workers in a manufacturing plant, by causing diffuse necrosis of seminiferous tubule cells. Because it is much less odiferous than ethylene dibromide, exposure of workers to toxic concentrations of DBCP is more likely. Its use has been cancelled in the U.S.

**Dichloropropene and dichloropropane** are strongly irritating to the skin, eyes, and respiratory tract. Bronchospasm may result from inhalation of high concentrations. Liver, kidney, and cardiac toxicity are seen in animals, but there are limited data in humans. It appears that risk of such toxicity is relatively low for humans except via ingestion of large quantities.

## Commercial Products

### HALOCARBONS

carbon tetrachloride\*  
chloroform\*  
trichloromethane  
chloropicrin  
Aquinite  
Dojyopicrin  
Dolochlor  
Larvacide  
Pic-Clor  
dibromochloropropane\*  
Nemafume  
Nemanax  
Nemaset  
1,2-dichloropropane\*  
propylene dichloride  
1,3-dichloropropene  
D-D92  
Telone II Soil Fumigant  
ethylene dibromide\*  
Bromofume  
Celmide  
dibromoethane  
E-D-Bee  
EDB  
Kopfume  
Nephis  
ethylene dichloride\*  
dichloroethane  
EDC  
methyl bromide  
Celfume  
Kayafume  
Meth-O-Gas  
MeBr  
Sobrom 98  
methylene chloride\*  
paradichlorobenzene

### HYDROCARBONS

naphthalene

### NITROGEN COMPOUNDS

acrylonitrile\*  
hydrogen cyanide\*  
hydrocyanic acid  
prussic acid

(Continued on the next page)

## Commercial Products

(Continued)

### OXIDES AND ALDEHYDES

acrolein  
Magnacide B  
Magnacide H  
1,2-epoxyethane  
ethylene oxide  
ETO  
formaldehyde  
oxirane  
paraformaldehyde

### PHOSPHORUS COMPOUNDS

phosphine (liberated from aluminum phosphide or magnesium phosphide)  
Agtoxin  
Alphos  
Fumex  
Fumitoxin  
Phostoxin  
Quickfos  
Sanifume  
Shaphos  
others

### SULFUR COMPOUNDS

carbon disulfide\*  
sulfur dioxide  
sulfuryl fluoride  
Vikane

\* Discontinued in the U.S.

**Ethylene dibromide** is a severe irritant to skin, eyes, and respiratory tract. The liquid causes blistering and erosion of skin, and is corrosive to the eyes. Once absorbed, it may cause pulmonary edema and central nervous system depression. Damage to testicular tissue has occurred in animals.<sup>5</sup> Long-term exposure may have some damaging effect on testicular tissue. Persons poisoned by ingestion have suffered chemical gastroenteritis, liver necrosis, and renal tubular damage. Death is usually due to respiratory or circulatory failure. A powerful disagreeable odor is advantageous in warning occupationally exposed workers of the presence of this gas.

**Ethylene dichloride** is moderately irritating to the eyes and respiratory tract. Respiratory symptoms may have a delayed onset. It depresses the central nervous system, induces cardiac arrhythmias, and damages the liver and kidney, in much the same way as carbon tetrachloride. Symptoms and signs of poisoning include headache, nausea, vomiting, dizziness, diarrhea, hypotension, cyanosis, and unconsciousness.

**Ethylene oxide and propylene oxide** are irritants to all tissues they contact. Aqueous solutions of ethylene oxide cause blistering and erosion of the affected skin. The area of skin may thereafter be sensitized to the fumigant. Inhalation of high concentrations is likely to cause pulmonary edema and cardiac arrhythmias. Headache, nausea, vomiting, weakness, and a persistent cough are common early manifestations of acute poisoning. Coughing of bloody, frothy sputum is characteristic of pulmonary edema.

Airborne **formaldehyde** is irritating to the eyes and to membranes of the upper respiratory tract. In some individuals, it is a potent sensitizer, causing allergic dermatitis. In addition, it has been associated with asthma-like symptoms, though there remains some controversy as to whether these represent true allergic asthma caused by formaldehyde.<sup>6,7,8</sup> High air concentrations may cause laryngeal edema, asthma, or tracheobronchitis, but apparently not pulmonary edema. Aqueous solutions in contact with the skin cause hardening and roughness, due to superficial coagulation of the keratin layer. Ingested formaldehyde attacks the membrane lining of the stomach and intestine, causing necrosis and ulceration. Absorbed formaldehyde is rapidly converted to formic acid. The latter is partly responsible for the metabolic acidosis that is characteristic of formaldehyde poisoning. Circulatory collapse and renal failure may follow the devastating effects of ingested formaldehyde on the gut, leading to death. Paraformaldehyde is a polymer which slowly releases formaldehyde into the air. Toxicity is somewhat less than that of formaldehyde, because of the slow evolution of gas.

**Hydrogen cyanide** gas causes poisoning by inactivating cytochrome oxidase, the final enzyme essential to mammalian cellular respiration. The patient will have signs of severe hypoxia, however, and in some cases may not appear cyanotic. This is due to the failure of hemoglobin reduction in the face of loss of cellular respiration. This will result in a pink or red color to the skin and arteriolization of retinal veins. In addition to the suggestive physical findings,

one may also find an unusually high  $pO_2$  on a venous blood gas.<sup>9</sup> Cyanosis is a late sign and indicates circulatory collapse.

The cells of the brain appear to be the most vulnerable to cyanide action. Presenting signs are nonspecific and can be found with many poisonings. Unconsciousness and death may occur immediately following inhalation of a high cyanide concentration, respiratory failure being the principal mechanism. Metabolic acidosis is another common presenting sign. Lesser exposures cause a constriction and numbness in the throat, stiffness of the jaw, salivation, nausea, vomiting, lightheadedness, and apprehension. Worsening of the poisoning is manifest as violent tonic or clonic convulsions. Fixed, dilated pupils, bradycardia, and irregular gasping respiration (or apnea) are typical of profound poisoning. The heart often continues to beat after breathing has stopped.<sup>9,10</sup> A bitter almond odor to the breath or vomitus may be a clue to poisoning, but not all individuals are able to detect this odor.<sup>9</sup>

**Methyl bromide** is colorless and nearly odorless, but is severely irritating to the lower respiratory tract, sometimes inducing pulmonary edema, hemorrhage, or a confluent pneumonia. The onset of respiratory distress may be delayed 4–12 hours after exposure. It is a central nervous system depressant, but may also cause convulsions. Early symptoms of acute poisoning include headache, dizziness, nausea, vomiting, tremor, slurred speech, and ataxia. The more severe cases of poisoning exhibit myoclonic and generalized tonic clonic seizures, which are sometimes refractory to initial therapy. Residual neurological deficits including myoclonic seizures, ataxia, muscle weakness, tremors, behavioral disturbances, and diminished reflexes may persist in more severely poisoned patients.<sup>11,12</sup> If liquid methyl bromide contacts the skin, severe burning, itching, and blister formation occur. Skin necrosis may be deep and extensive.

**Methylene chloride** is one of the less toxic halocarbons. It is absorbed by inhalation and to a limited extent across the skin. Exposure to high concentrations may cause central nervous system depression, manifested as fatigue, weakness, and drowsiness. Some absorbed methylene chloride is degraded to carbon monoxide in humans, yielding increased blood concentrations of carboxyhemoglobin. However, concentrations are rarely high enough to cause symptoms of carbon monoxide poisoning. Ingestion has caused death from gastrointestinal hemorrhage, severe liver damage, coma, shock, metabolic acidosis, and renal injury. In laboratory animals, extraordinary dosage has caused irritability, tremor, and narcosis, leading to death. When heated to that point of decomposition, one of the products is the highly toxic phosgene gas that has caused a significant acute pneumonitis.<sup>13</sup>

**Naphthalene** is a solid white hydrocarbon long used in ball, flake, or cake form as a moth repellent. It sublimates slowly. The vapor has a sharp, pungent odor that is irritating to the eyes and upper respiratory tract. Inhalation of high concentrations causes headache, dizziness, nausea, and vomiting. Intensive prolonged inhalation exposure, or ingestion or dermal exposure (from contact with heavily

treated fabric) may cause hemolysis, particularly in persons afflicted with glucose-6-phosphate dehydrogenase deficiency.<sup>14</sup> The inheritance of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency is by a sex-linked gene with intermediate dominance. For this reason it is most commonly expressed in heterozygous males. However, homozygous females, who are far less common, will have a similar expression. Heterozygous females have only a mild depression of this enzyme. This illness is most common in non-white African and African-American ethnic groups. It is also seen in some Mediterranean ethnic populations.

It is actually the metabolites of naphthalene that are responsible for the hemolysis.<sup>15</sup> Secondary renal tubular damage may ensue from the naphthol and from the products of hemolysis. Convulsions and coma may occur, particularly in children. In infants, high levels of hemoglobin, methemoglobin, and bilirubin in the plasma may lead to encephalopathy. Kernicterus has been specifically described as a complication of exposure to naphthalene with severe hemolysis and resulting hyperbilirubinemia. Some individuals exhibit dermal sensitivity to naphthalene.

**Paradichlorobenzene** is solid at room temperature, and is now widely used as a moth repellent, air freshener, and deodorizer in homes and in public facilities. The vapor is only mildly irritating to the nose and eyes. Liver injury and tremor may occur following ingestion of large amounts. Although accidental ingestions, especially by children, have been fairly common, symptomatic human poisonings have been rare. Other stereoisomers of dichlorobenzene are more toxic than the para-isomer.

**Phosphine** gas is extremely irritating to the respiratory tract. It also produces severe systemic toxicity. It is used as a fumigant by placing solid aluminum phosphide (phostoxin) near produce or in other storage spaces. Through hydrolysis, phosphine gas is slowly released. Most severe acute exposures have involved ingestion of the solid aluminum phosphide, which is rapidly converted to phosphine by acid hydrolysis in the stomach. Poisoning due to ingestion carries a high mortality rate (50 to 90%).<sup>16,17</sup> Mechanisms of toxicity are not well understood. Extracellular magnesium levels have been found to be slightly elevated, suggesting a depletion of intracellular magnesium from myocardial damage.<sup>18</sup>

Poisonings had become quite frequent during the late 1980s and early 1990s in some parts of India.<sup>16,17</sup> The principal manifestations of poisoning are fatigue, nausea, headache, dizziness, thirst, cough, shortness of breath, tachycardia, chest tightness, paresthesia, and jaundice. Cardiogenic shock is present in more severe cases. Pulmonary edema is a common cause of death. In other fatalities, ventricular arrhythmias, conduction disturbances, and asystole developed.<sup>16,19</sup> Odor is said to resemble that of decaying fish.

**Sulfur dioxide** is a highly irritant gas, so disagreeable that persons inhaling it are usually prompted to seek uncontaminated air as soon as possible. However, laryngospasm and pulmonary edema have occurred, occasionally leading to severe respiratory distress and death. It is sometimes a cause of reactive airways disease in occupationally exposed persons.

**Sulfuryl fluoride** has been used extensively for structural fumigation. Although use experience has generally been good, some fatalities have occurred when fumigated buildings have been prematurely reentered by unprotected individuals.<sup>20</sup> Since this material is heavier than air, fatal hypoxia may follow early reentry. Manifestations of poisoning have been nose, eye, and throat irritation, weakness, nausea, vomiting, dyspnea, cough, restlessness, muscle twitching, and seizures. Renal injury may induce proteinuria and azotemia.

## Confirmation of Poisoning

There are no practical tests for absorbed **alkyl oxides, aldehydes, or phosphine** that would be helpful in diagnosis of poisoning.

**Carbon disulfide** can be measured in urine by gas chromatography, but the test is not generally available.

Cyanide ion from **cyanide** itself or **acrylonitrile** can be measured in whole blood and urine by an ion-specific electrode or by colorimetry. Symptoms of toxicity may appear at blood levels above 0.10 mg per liter.<sup>10</sup> Urine cyanide is usually less than 0.30 mg per liter in nonsmokers, but as much as 0.80 mg per liter in smokers. Thiocyanate, the metabolite of cyanide, can also be measured in blood and urine. It is elevated at blood levels exceeding 12 mg per liter.<sup>10</sup> Urine thiocyanate is usually less than 4 mg per liter in nonsmokers, but may be as high as 17 mg per liter in smokers.

**Methyl bromide** yields inorganic bromide in the body. Methyl bromide itself has a short half-life and is usually not detectable after 24 hours. The bromide anion is slowly excreted in the urine (half-life about 10 days), and is the preferred method of serum measurement.<sup>11</sup> The serum from persons having no exceptional exposure to bromide usually contains less than 1 mg bromide ion per 100 mL. The possible contributions of medicinal bromides to elevated blood content and urinary excretion must be considered, but if methyl bromide is the exclusive source, serum bromide exceeding 6 mg per 100 mL probably means some absorption, and 15 mg per 100 mL is consistent with symptoms of acute poisoning. Inorganic bromide is considerably less toxic than methyl bromide; serum concentrations in excess of 150 mg per 100 mL occur commonly in persons taking inorganic bromide medications. In some European countries, blood bromide concentrations are monitored routinely in workers exposed to methyl bromide. Blood levels over 3 mg per 100 mL are considered a warning that personal protective measures must be improved. A bromide concentration over 5 mg per 100 mL requires that the worker be removed from the fumigant-contaminated environment until blood concentrations decline to less than 3 mg per 100 mL.

**Methylene chloride** is converted to carbon monoxide in the body, generating carboxyhemoglobinemia, which can be measured by clinical laboratories.

**Naphthalene** is converted mainly to alpha naphthol in the body and promptly excreted in conjugated form in the urine. Alpha naphthol can be measured by gas

chromatography. Many halocarbons can be measured in blood by gas chromatographic methods. Some can be measured in the expired air as well.

**Paradichlorobenzene** is metabolized mainly to 2,5-dichlorophenol, which is conjugated and excreted in the urine. This product can be measured chromatographically.

A serum fluoride concentration of 0.5 mg per liter was measured in one fatality from **sulfuryl fluoride** fumigation. Serum fluoride in persons not exceptionally exposed rarely exceeds 0.1 mg per liter.

Large industrial concerns sometimes monitor human absorption of halocarbons by analysis of expired air. Similar technology is available in some departments of anesthesiology. These analyses are rarely needed to identify the offending toxicant, because this is known from the exposure history. In managing difficult cases of poisoning, however, it may be helpful to monitor breath concentrations of toxic gas to evaluate disposition of the fumigant. Testing of the urine for protein and red cells is needed to detect renal injury. Free hemoglobin in urine most likely reflects hemolysis, as from naphthalene. Elevations of alkaline phosphatase, lactate dehydrogenase (LDH), serum GGT, ALT, AST, and certain other enzymes are sensitive indices of insult to liver cells. More severe damage increases plasma concentrations of bilirubin. The chest x-ray may be used to confirm the occurrence of pulmonary edema. Electromyography may be useful in evaluating peripheral nerve injury. Sperm counts may be appropriate for workers exposed to **dibromochloropropane** and **ethylene dibromide**.

Some occupational health agencies now urge periodic neurologic and neuropsychologic testing of workers heavily exposed to fumigants and solvents to detect injury to the nervous system as early as possible. This would be particularly desirable in the case of exposures to such agents as methyl bromide and carbon disulfide which have well-documented chronic neurotoxic effects.

## Treatment

**1. Skin decontamination.** Flush contaminating fumigants from the skin and eyes with copious amounts of water or saline for at least 15 minutes. Some fumigants are corrosive to the cornea and may cause blindness. Specialized medical treatment should be obtained promptly following decontamination. Skin contamination may cause blistering and deep chemical burns. Absorption of some fumigants across the skin may be sufficient to cause systemic poisoning in the absence of fumigant inhalation. For all these reasons, decontamination of eyes and skin must be immediate and thorough. See Chapter 2.

**2. Physical placement.** Remove victims of fumigant inhalation to fresh air immediately. Even though initial symptoms and signs are mild, keep the victim quiet, in a semi-reclining position. Minimum physical activity limits the likelihood of pulmonary edema.

**3. Respiration.** If victim is not breathing, clear the airway of secretions and resuscitate with positive pressure oxygen apparatus. If this is not available, use chest compression to sustain respiration. If victim is pulseless, employ cardiac resuscitation.

**4. Pulmonary edema.** If pulmonary edema is evident, there are several measures available to sustain life. Medical judgment must be relied upon, however, in the management of each case. The following procedures are generally recommended:

- Put the victim in a sitting position with a backrest.
- Use intermittent and/or continuous positive pressure oxygen to relieve hypoxemia. (Do not give oxygen at greater concentrations or longer periods than necessary, because it may exaggerate the fumigant injury to lung tissue. Monitor arterial pO<sub>2</sub>.)
- Slowly administer furosemide, 40 mg, intravenously (0.5-1 mg/kg in children up to 20 mg), to reduce venous load by inducing diuresis. Consult package insert for additional directions and warnings.

Some patients may benefit from careful administration of anxiolytic drugs. Whenever possible, such patients should be managed by intensivists in an intensive care center. Limit victim's physical activity for at least 4 weeks. Severe physical weakness usually indicates persistent pulmonary injury. Serial pulmonary function testing may be useful in assessing recovery.

**5. Shock.** Combat shock by placing victim in the Trendelenburg position and administering plasma, whole blood, and/or electrolyte and glucose solutions intravenously, with great care, to avoid pulmonary edema. Central venous pressure should be monitored continuously. Vasopressor amines must be given with great caution, because of the irritability of the myocardium.

**6. Control convulsions.** Seizures are most likely to occur in poisonings by methyl bromide, hydrogen cyanide, acrylonitrile, phosphine, and carbon disulfide. See Chapter 2 for seizure management. In some cases of methyl bromide, seizures have been refractory to benzodiazepines and diphenylhydantoin, and the authors resorted to anesthesia using thiopental.<sup>11</sup>

**7. Gastrointestinal decontamination.** If a fumigant liquid or solid has been ingested less than an hour prior to treatment, consider gastric emptying, followed by activated charcoal, as suggested in Chapter 2.

**8. Fluid balance** should be monitored, and urine sediment should be checked regularly for indications of tubular injury. Measure serum alkaline phosphatase, LDH, ALT, AST, and bilirubin to assess liver injury.



**9. Extracorporeal hemodialysis** may be needed to regulate extracellular fluid composition if renal failure supervenes. It is probably not very effective in removing lipophilic fumigant compounds from blood, but it is, of course, effective in controlling extracellular fluid composition if renal failure occurs.

**10. Specific fumigants.** Certain specific measures are recommended in poisonings by particular fumigants (carbon disulfide, carbon tetrachloride, naphthalene, phosphine gas, and hydrogen cyanide and acrylonitrile):

- **Carbon Disulfide:** Mild poisonings by carbon disulfide inhalation may be managed best by no more than careful observation, even though sensory hallucinations, delirium, and behavioral aberrations can be alarming. Severe poisonings may require specific measures. If manic behavior threatens the safety of the victim, diazepam (5-10 mg in adults, 0.2-0.4 mg/kg in children), administered slowly, intravenously, may be helpful as a tranquilizer. Give as much as is necessary to achieve sedation. Do not give catecholamine-releasing agents such as reserpine and amphetamines.
- **Carbon Tetrachloride:** For carbon tetrachloride poisoning, several treatment measures have been suggested to limit the severity of hepatic necrosis. Hyperbaric oxygen has been used with some success.<sup>2</sup> Oral administration of N-acetyl cysteine (Mucomyst<sup>®</sup>) may be worthwhile as a means of reducing free radical injury.<sup>21</sup> Dilute the proprietary 20% product 1:4 in a carbonated beverage, and give about 140 mg/kg body weight of the diluted solution as a loading dose. Then give 70 mg/kg every 4 hours after the loading dose for a total of 17 doses. (This dosage schedule is used for acetaminophen poisonings.) Administration via duodenal tube may be necessary in a few patients who cannot tolerate Mucomyst.<sup>22</sup> Intravenous administration of N-acetyl cysteine may be used; more information is available through poison control centers.
- **Naphthalene:** Naphthalene toxicosis caused by vapor inhalation can usually be managed simply by removing the individual to fresh air. Skin contamination should be removed promptly by washing with soap and water. Eye contamination should be removed by flushing with copious amounts of clean water. Eye irritation may be severe, and if it persists, should receive ophthalmologic attention.

Examine the plasma for evidence of hemolysis: a reddish-brown tinge, especially in the blood smear for “ghosts” and Heinz bodies. If present, monitor red blood cell count and hematocrit for anemia, urine for protein and cells. Measure direct- and indirect-reacting bi-

lirubin in the plasma. Monitor fluid balance and blood electrolytes. If possible, monitor urinary excretion of naphthol to assess severity of poisoning and clinical progress.

If hemolysis is clinically significant, administer intravenous fluids to accelerate urinary excretion of the naphthol metabolite and protect the kidney from products of hemolysis. Use Ringer's lactate or sodium bicarbonate to keep urine pH above 7.5. Consider the use of mannitol or furosemide to promote diuresis. If urine flow declines, intravenous infusions must be stopped to prevent fluid overload and hemodialysis should be considered.<sup>15</sup> If anemia is severe, blood transfusions may be needed.

- **Phosphine Gas:** Recent experience in India suggests that therapy with magnesium sulfate may decrease the likelihood of a fatal outcome.<sup>16,19,23</sup> The mechanism is unclear, but may possibly be due to the membrane stabilization properties of magnesium in protecting the heart from fatal arrhythmias. In one series of 90 patients, magnesium sulfate was found to decrease the mortality from 90% to 52%.<sup>16</sup> Two controlled studies have been done, one of which showed a reduction in mortality from 52% to 22%.<sup>23</sup> The other study found no effect on mortality.<sup>24</sup> The dosage for magnesium sulfate is: 3 grams during the first 3 hours as a continuous infusion, followed by 6 grams per 24 hours for the next 3 to 5 days.<sup>16</sup>
- **Hydrogen Cyanide and Acrylonitrile:** Poisonings by hydrogen cyanide and acrylonitrile gases or liquids are treated essentially the same as poisoning by cyanide salts. Because cyanide is so promptly absorbed following ingestion, treatment should commence with prompt administration of oxygen and antidotes. Gastrointestinal decontamination should be considered if the patient presents within a short interval after ingestion, and **only** after the above life-saving treatment has commenced. Ipecac should be avoided due to the potential for rapid onset of loss of consciousness.

The three antidotes — amyl nitrite, sodium nitrite, and sodium thio-sulfate — are available as a kit called the Lilly Cyanide Antidote Kit, available from Eli Lilly and Company, Indianapolis, IN. The dosages vary between adults and children and are outlined below.

## Dosage of Cyanide Antidotes

### Adults:

- Administer **oxygen** continuously. Hyperbaric oxygen has been evaluated as effective in this condition.<sup>25</sup> If respiration fails, maintain pulmonary ventilation mechanically.
- Administer **amyl nitrite** ampules by inhalation for 15-30 seconds of every minute, while a fresh solution of 3% sodium nitrite is being prepared. This solution is ready prepared in commercial cyanide antidote kits.
- As soon as solution is available, inject intravenously 10 mL of 3% **sodium nitrite** solution over a 5-minute interval, keeping the needle in place.

**Caution:** Monitor pulse and blood pressure during administration of amyl nitrite and sodium nitrite. If systolic blood pressure falls below 80 mm Hg, slow or stop nitrite administration until blood pressure recovers.

- Follow sodium nitrite injection with an infusion of 50 mL of 25% aqueous solution of **sodium thiosulfate** administered over a 10-minute period. Initial adult dose should not exceed 12.5 g.
- If symptoms persist or recur, treatment by sodium nitrite and sodium thiosulfate should be repeated at half the dosages listed above.
- Measure hemoglobin and methemoglobin in blood. If more than 50% of total hemoglobin has been converted to methemoglobin, blood transfusion or exchange transfusion should be considered, because conversion back to normal hemoglobin proceeds slowly.

### Children:

- Give amyl nitrite, oxygen, and mechanical respiratory support as recommended for adults. The following dosages of antidotes have been recommended for children.<sup>26</sup>
- Children over 25 kg body weight should receive adult dosages of sodium nitrite and sodium thiosulfate.
- Children less than 25 kg body weight should first have two 3-4 mL samples of blood drawn and then, through the same needle, receive 0.15-0.33 mL/kg up to 10 mL of the 3% solution of sodium nitrite injected over a 5-minute interval. Following sodium nitrite, administer an infusion of 1.65 mL/kg of 25% sodium thiosulfate at a rate of 3-5 mL per minute.

... continued

- At this point, determine the hemoglobin content of the pretreatment blood sample. If symptoms and signs of poisoning persist or return, give supplemental infusions of sodium nitrite and sodium thiosulfate based on hemoglobin level, as presented in the table. These recommended quantities are calculated to avoid life-threatening methemoglobinemia in anemic children. They are aimed at converting approximately 40% of circulating hemoglobin to methemoglobin. If possible, monitor blood methemoglobin concentrations as treatment proceeds.

### RECOMMENDED DOSAGES OF SUPPLEMENTAL SODIUM NITRITE AND SODIUM THIOSULFATE BASED ON HEMOGLOBIN LEVEL

Initial Hemoglobin Concentration g/100 mL	Volume of 3% Sodium Nitrite mL/kg	Dose 25% Sodium Thiosulfate mL/kg
14.0	0.20	1.00
12.0	0.16	0.83
10.0	0.14	0.68
8.0	0.11	0.55

Although various cobalt salts, chelates, and organic combinations have shown some promise as antidotes to cyanide, they are not generally available in the United States. None has been shown to surpass the nitrite-thiosulfate regimen in effectiveness.

### References

1. Wilcosky TC and Tyroler HA. Mortality from heart disease among workers exposed to solvents. *J Occup Med* 1983;25:879-85.
2. Truss C and Killenberg P. Treatment of carbon tetrachloride poisoning with hyperbaric oxygen. *Gastroenterology* 1982;82:767-9.
3. Perez AJ, Courel M, Sobrado J, et al. Acute renal failure after topical application of carbon tetrachloride. *Lancet* 1987;1:515-6.
4. Dykes MH. Halogenated hydrocarbon ingestion. *Intern Anesthesiol Clin* 1970;8:357-68.
5. Amir D. The spermicidal effect of ethylene dibromide in bulls and rams. *Mol Reprod Dev* 1991;28:99-109.

6. Smedley J. Is formaldehyde an important cause of allergic respiratory disease? *Clin Exp Allergy* 1996;26:247-9.
7. Krzyzanowski M, Quackenboss JJ, and Lebowitz MD. Chronic respiratory effects of indoor formaldehyde exposure. *Environ Res* 1990;52:117-25.
8. Harving H, Korsgaard J, Pedersen OF, et al. Pulmonary function and bronchial reactivity in asthmatics during low-level formaldehyde exposure. *Lung* 1990;168:15-21.
9. Johnson RP and Mellors JW. Arteriolization of venous blood gases: A clue to the diagnosis of cyanide poisoning. *J Emerg Med* 1988;6:401-4.
10. Yen D, Tsai J, Wang LM, et al. The clinical experience of acute cyanide poisoning. *Am J Emerg Med* 1995;13:524-8.
11. Hustinx WNM, van de Laar RTH, van Huffelen A, et al. Systemic effects of inhalational methyl bromide poisoning: A study of nine cases occupationally exposed due to inadvertent spread during fumigation. *Br J Ind Med* 1993;50:155-9.
12. Deschamps FJ and Turpin JC. Methyl bromide intoxication during grain store fumigation. *Occupat Med* 1996;48:89-90.
13. Snyder RW, Mishel HS, and Christensen GC. Pulmonary toxicity following exposure to methylene chloride and its combustion product, phosgene. *Chest* 1992;101:860-1.
14. Shannon K and Buchanan GR. Severe hemolytic anemia in black children with glucose-6-phosphate dehydrogenase deficiency. *Pediatrics* 1982;70:364-9.
15. Gosselin RE, Smith HC, and Hodge HC (eds). Naphthalene. In: *Clinical Toxicology of Commercial Products*, 5<sup>th</sup> ed. Baltimore: Williams & Wilkins, 1984, pp. III-307-11.
16. Katira R, Elhence GP, Mehrotra ML, et al. A study of aluminum phosphide poisoning with special reference to electrocardiographic changes. *J Assoc Physicians India* 1990;38:471-3.
17. Singh S, Singh D, Wig N, et al. Aluminum phosphide ingestion: A clinico-pathologic study. *Clin Toxicol* 1996;34:703-6.
18. Singh RB, Singh RG, and Singh U. Hypermagnesemia following aluminum phosphide poisoning. *Int J Clin Pharmacol Ther Toxicol* 1991;29:82-5.
19. Gupta S and Ahlawat SK. Aluminum phosphide poisoning: A review. *Clin Toxicol* 1995;33:19-24.
20. Scheuerman EH. Suicide by exposure to sulfuryl fluoride. *J Forensic Sci* 1986;31:1154-8.
21. Ruprah M, Mant TGK, and Flanagan RJ. Acute carbon tetrachloride poisoning in 19 patients: Implications for diagnosis and treatment. *Lancet* 1985;1:1027-9.
22. Anker AL and Smilkenstein MJ. Acetaminophen: Concepts and controversies. *Emerg Med Clin North Am* 1994;12:335-49.
23. Chugh SN, Kumar P, Sharma A, et al. Magnesium status and parenteral magnesium sulphate therapy in acute aluminum phosphide intoxication. *Magnesium Res* 1994;7:289-94.
24. Siwach SB, Singh P, Ahlawat S, et al. Serum and tissue magnesium content in patients of aluminum phosphide poisoning and critical evaluation of high dose magnesium sulphate therapy in reducing mortality. *J Assoc Physicians India* 1994;42:107-10.
25. Myers RAM and Schnitzer BM. Hyperbaric oxygen use: Update 1984. *Postgrad Med* 1984;76:83-95.
26. Mofenson HC, Greensher J, Horowitz R, and Berlin CM. Treatment of cyanide poisoning. *Pediatrics* 1970;46:793-6.