

## Chapter 4

**T o x i n s**

Toxins are poisonous chemicals produced by many different types of living organisms. Toxins have been implicated as the means by which certain pathogenic microorganisms produce their effects. Toxins that are highly toxic to humans and that are stable, available, and manageable are important in the threat they present in biological warfare. This chapter contains information on some of the possible Threat toxins. These toxins represent the range of toxin agents that may be available to the sophisticated user of biological weapons. However, weapon systems could incorporate many other toxins.

**Section I. Background**

Many toxins were developed for medical use. This is especially true of toxins from microorganisms and fungi. Examples are atropine, morphine, streptomycin, and penicillin. As a result commercial processes in many countries prepare microbial and fungal products. The technology exists for bulk production of some toxins. As a general rule toxins are not chemically synthesized; they are extracted from their natural sources.

The chemical nature of toxins is diverse (see Appendix E). Some toxins are large proteins; some are smaller proteinlike (proteinaceous) compounds; others are non-proteins. The proteinaceous toxins are solids when pure but dissolve in water-based solutions. Protein-based toxins are generally less stable than nonprotein toxins. Some toxins are extremely stable and may retain their potency for years in storage. Toxins from plants and fungi tend to be more stable than those from animals.

Biological agents (including toxins) may be expected to be disseminated either as an aerosol, a liquid, or a powder (see Chapter 1). Based on the portals of entry, the characteristics of agents used, and the results desired, different methods of dissemination are feasible for biological attack. Toxins are tactical or strategic weapons. Some can effectively cover hundreds of square kilometers, and most could cover at least several square kilometers.

The Threat may use ground-bursting or airbursting munitions, aircraft spray tanks, or ground-level aerosol generators to produce aerosol clouds of toxins. Inhalation of these aerosols will produce casualties in a manner similar to that of chemical aerosols. The greatest threat occurs with exposure of individuals to the cloud. There is still a risk of respiratory, eye or oral exposure while the

aerosols dissipate and also through secondary aerosolization.

The body absorbs particulate or liquid aerosols of toxins through the respiratory tract, the skin, or mucous membranes. Because mechanical or heat stress inactivate some toxins, use of these toxins may require dissemination of large concentrations. Aerosol toxin attacks usually are not visible. However, because of the amount required to produce casualties and the color of the toxin or dissemination medium, aerosolized solids may be visible as a dust cloud or as powders on equipment and clothing.

Bursting munitions and spray tanks may produce large liquid drops to cause ground contamination, like ground contamination by chemical agents. Forces in southeast Asia and Afghanistan used this method of dissemination to employ "yellow rain" mycotoxins. The Threat could use ground-contaminating toxins to produce casualties or to deny terrain, equipment, or supply.

Droplets of a solution or a suspension of a toxin would cause surface contamination, including contamination of food or water, and the toxin could enter the body through the digestive tract. Some toxins (for example, mycotoxin T-2) are skin damaging and could penetrate the skin.

In addition to tactical or strategic employment, toxins pose a threat as weapons for covert, guerrilla, or terrorist operations. With the vast number of toxins and delivery options, the imagination of the user is the only limitation to covert dissemination of toxins. Saboteurs can contaminate closed ventilation systems, drinking water, lakes and rivers, and food supplies. Assassins can also use some agents.

Physical and environmental factors determine the effectiveness of these methods. Mechanical or heat stress inac-

tivate some toxins. (This does not apply to powdered toxin dissemination; it applies only to liquids.) Some toxins (for example, Staphylococcus enterotoxin, Type B) are stable in the environment and are more resistant than G- or V-agents to heat, hydrolysis, or vaporization. Others, such as botulinum toxin, have only a brief predictable persistence unless rendered resistant to environmental conditions. Appendix F, Table F-1, summarizes the physical and chemical properties of toxins.

The use of certain specialized techniques that are common to the production of pharmacological could influence the effectiveness of the toxin. Examples of these techniques are micronizing (air-milling) and microencapsulation. Micronizing is a technique used to reduce the particle size to increase absorption. This process is particularly important when exposure occurs primarily by inhalation. Microencapsulation can make aerosol distribution of biological agents technically more feasible. Encapsulation of agents in certain organic compounds could enhance agent survivability in the environment during dissemination. It could potentially allow more specific targeting of the agent within the body or enhance absorption and retention.

The actions and effects of toxins may closely resemble those of chemical warfare agents, such as nerve, blister, vomiting, or choking agents. Most toxins of military significance cause casualties in two general ways and can be classified by the way they act:

Neurotoxins ("nerve toxins") interfere with nerve impulse transmission. They have highly specific effects on the nervous system. All neurotoxins do not produce the same symptoms or have the same mechanism of action. For example, they may stimulate or inhibit the release of acetylcholine, block receptors, or interfere with the activity of ion channels. Neurotoxins may cause symptoms similar to

chemical nerve agents such as pinpointing of pupils, convulsions, and rigid paralysis; or they may cause other symptoms such as blurred vision and light sensitivity due to dilation of pupils, tremors, seizures, confused behavior, extreme muscle weakness, or rigid or limp (flaccid) paralysis.

Cytotoxins ("cell poisons") produce a variety of effects because of their distinct mechanisms. Some destroy cells. Others disrupt cell activities, such as protein synthesis, cell regulation, or other biochemical processes. Symptoms may resemble those of chemical blister, vomiting, or choking agents; or they may resemble food poisonings or diseases. Cytotoxins may cause nausea, vomiting, or diarrhea; rashes, inflammation, or blistering, jaundice; or bleeding or deterioration of tissue (necrosis). Appendix E discusses the chemical nature and mechanisms of action of toxins.

Toxins may produce lethal or nonlethal effects (Table 4-1). By weight, most toxins are thousands of times more toxic than standard chemical agents. These effects depend on the toxin, the dose received, and the route of entry. The time lapse between contamination and symptoms may vary from a few minutes to several hours. Many, if not most, of the toxins are principally a threat by aerosol. Most toxicity data for toxins, however, is not in air concentration times the time (LCt50). Essentially all toxins are at least as toxic by aerosol as by injected dose (LD50). Therefore, this manual expresses aerosol data as the dose of toxin actually received (LD50). Nearly all toxins of concern would require considerably higher oral doses than aerosol doses. Most of the large protein toxins are not a significant threat by dermal or oral exposure unless there is an open wound. Toxins, even though of biological origin, are nonliving chemical compounds; as such, they are not infectious or contagious after dissemination. A summary of selected toxin effects is in Appendix F, Table F-2.

**Table 4-1. Lethality and rate of action of selected toxins.**

<b>Toxin and Time to Toxic Effects</b>	<b>LD<sub>50</sub>* (<math>\mu</math>g/kg)</b>	<b>Type and Effects</b>
<b>Very rapid: 5 minutes</b>		
Anatoxin A (Very Fast Death Factor [VFDF])	170 to 250	Lethal paralytic neurotoxin; chemical nerve agent symptoms.
Conotoxin	3 to 6	Lethal snail neurotoxin; bleeding at injection site; muscle weakness.
Palytoxin	0.08	Lethal neurotoxin; muscle paralysis; collapse.
<b>Rapid: 5 minutes to 1 hour</b>		
Diphtheria toxin	0.03	Lethal; sore throat; swollen glands.
Batrachotoxin	0.1 to 2	Lethal; frog paralytic neurotoxin; neuromuscular block.
Ricin (injected)	0.1 to 3.7	Lethal cytotoxin.
Taipoxin	2	Lethal; snake paralytic neurotoxin.
continued		

**Table 4-1, Lethality and rate of action of selected toxins continued**

Saxitoxin	5 to 12 (oral) 1 (aerosol)	Lethal; numbness; muscle weakness; incoordination; respiratory distress.
Tetrodotoxin	8 (injected) 30 (oral)	Lethal neuromuscular block; numbness; loss of muscle control; loss of voice.
Alpha-latrotoxin	10	Lethal spider neurotoxin; paralytic chemical agent symptoms.
Notexin	20	Lethal snake neurotoxin; paralytic.
Beta-bungarotoxin	20	Lethal snake neurotoxin; paralytic.
Cobrotoxin	75	Lethal snake neurotoxin; paralytic.
Microcystin (Fast Death Factor [FDF])	50 to 100	Lethal cytotoxin; shivering; stupor.
<b>Delayed: 1 to 12 hours</b>		
Ricin (aerosol, skin, oral)	3.0 (oral)	Lethal cytotoxin; nausea; vomiting; cramps.
Staphylococcus enterotoxin B	20 (injected)* 200 (aerosol)*	Incapacitant; acute food poisoning symptoms.
Botulinum (oral)	0.0003 to .01	Lethal neurotoxin; drooping eyelids; double vision; dilated pupils; fever; paralysis.
T-2 (skin, aerosol, oral)	50 to 240 (aerosol)	Incapacitant/lethal cytotoxin; skin reddening, rash, blisters; nausea; bloody vomit, diarrhea.
<b>Very delayed: 12 hours</b>		
Tetanus toxin (injected)	0.0025 (human)	Lethal neurotoxin; painful muscle contractions; "lockjaw."

\*In mice if no other information is given.

We know little about the persistency of toxins. Persistency depends on the physical and chemical properties of the toxin in question. Protein-based toxins are usually more sensitive to UV light, heat, and oxidation than nonprotein toxins, and would be less persistent in the environment.

Individual defensive measures normally associated with a persistent chemical agent attack will protect personnel against toxins. Upon recognition of an air- or ground-contaminating attack or onset of symptoms, personnel should immediately mask and put on all protective equipment (MOPP4). Apply standard MOPP analysis procedures to determine the MOPP level required to continue operations.

Normal field equipment and procedures cannot decontaminate water taken from sources exposed to toxins (such as rivers, ponds, or wells). Therefore, do not drink water from exposed sources. Do not consume food suspected of contamination. Water and food in approved closed containers are safe for consumption after exterior decontamination of the containers and inspection by qualified medical personnel.

## Section II. Sources of Toxins

Toxin sources (Table 4-2) include bacteria, dinoflagellates, algae, molds and fungi, plants, and animals. Section III presents descriptions of specific toxins.

Use soap and water or standard decontaminants (DS2, STB, or HTH) to decontaminate equipment or supplies. Washing the skin with soap and water (or flushing the skin with copious amounts of water) will reduce the effectiveness of the toxins. Evacuate contaminated casualties in accordance with unit SOP governing the evacuation of chemical casualties.

The discussion on specific toxin characteristics outlines the sensitivity of each toxin to decontaminants. Some toxins are sensitive to alkalis, some to acids, and others to heat. However, because the sensitivities are agent-dependent, the recommended method of decontamination is removal by scrubbing with soap and water.

Medical care for victims of toxin poisoning consists primarily of supportive care. Treat or prevent shock. Monitor and support cardiac and respiratory functions as necessary. Definitive medical care requires precise identification of the toxin, a capability not available in the field for all potential toxins. Antitoxin therapy is available for some toxins after identification of the agent.

Table 4-2. Classification of selected toxins by source.

Source	Toxin
<b>Bacteria</b>	
<i>Bacillus anthracis</i>	Anthrax toxin
<i>Clostridium botulinum</i>	Botulinum A, B, C, D, E
<i>Clostridium tetani</i>	Tetanus toxin
<i>Corynebacterium diphtheria</i>	Diphtheria toxin
<i>Escherichia coli</i>	Heat-labile enterotoxin LT Heat-stable enterotoxin ST
<i>Shigella dysenteriae</i>	<i>Shigella dysenteriae</i> toxin
<i>Staphylococcus aureus</i>	<i>Staphylococcus</i> enterotoxin A, B, C, D, E
<i>Vibrio cholerae</i>	Cholera toxin
<b>Dinoflagellates</b>	
<i>Gambierdiscus toxicus</i>	Ciguatoxin; maitotoxin
<i>Gonyaulax tamarensis</i> , <i>Gonyaulax catanella</i> and other species	Saxitoxin (shellfish poison)
<i>Ptychodiscus brevis</i> (formerly <i>Gymnodinium breve</i> )	Brevetoxin (red tide toxin)
<i>Takifugu poecilonotus</i>	Tetrodotoxin
<b>Algae</b>	
<i>Anacystis</i> species, <i>Anabaena flos-aquae</i>	Anatoxin A (VFDF)
<i>Microcystis aeruginosa</i> , <i>Microcystis cyanea</i>	Microcystin (FDF)
<i>Lyngbya gracillis</i> (seaweed)	Debromoaplysiatoxin
<b>Fungi</b>	
<i>Aspergillus flavus</i>	Aflatoxins
<i>Fusarium</i> species	Trichothecene toxins
<b>Plants</b>	
<i>Abrus precatorius</i> (tropical legume)	Abrin
<i>Aconitum napellus</i>	Aconitine
<i>Ricinus communis</i> (castor bean)	Ricin
<i>Rhododendron ericaceae</i> and other Ericaceae	Grayanotoxin
<i>Veratrum album</i> (lily)	Veratridine
<b>Animals</b>	
<i>Palythoa</i> (soft corals)	Palytoxin
<i>Aplysia</i> (sea hare)	Debromoaplysiatoxin; aplysiatoxin
	<b>continued</b>

Table 4-2, Classification of selected toxins by source continued

<i>Conus geographus</i> ; <i>Conus magnus</i> (fish-hunting cone snails)	Conotoxins
<i>Mytilis</i> , <i>Saxidomus</i> , other mussels	Saxitoxin (shellfish poison)
<i>Arothron</i> species (puffer fish)	Tetrodotoxin
<i>Phyllobates aurotaenia</i> and <i>Phyllobates terribilis</i> (Colombian frog)	Batrachotoxin
<i>Bungarus multicinctus</i> (banded krait)	Alpha-bungarotoxin Beta-bungarotoxin
<i>Crotalus</i> species (rattlesnakes)	Crotoxin
<i>Naja naja atra</i> (Formosan cobra)	Cobrotoxin
<i>Laticauda semifasciata</i> (sea snake)	Erabutoxin

## Bacterial Toxins

Toxins produced by microorganisms cause a number of bacterial diseases. In the past these toxins have been classed into two types - exotoxins and endotoxins. Classification of these toxins depends upon their chemical composition, resistance to heat, and method of release from the pathogen. The toxins produced by microorganisms may be excreted into the surrounding medium (exotoxins) or retained with the cell (endotoxins).

### Exotoxins

Exotoxins are poisonous compounds that can diffuse and that the cells that produce them can eliminate into the surrounding medium. Bacterial exotoxins are proteins of varied molecular weights. They are a normal part of the metabolic activities of the pathogen; some are enzymes. Various *Clostridium* species produce exotoxins associated with disease. *Clostridium botulinum* toxins are responsible for botulism; *Clostridium tetani* toxins cause tetanus; *Clostridium perfringens* (causing gas gangrene) can produce ten different exotoxins. Some of these attack and destroy red blood cells; others cause death (necrosis) of

tissue. *Escherichia coli* and *Staphylococcus aureus* are two bacterial species that produce heat-stable exotoxins that have their primary action upon the digestive tract (enterotoxins). These toxins produce severe nausea, vomiting, and diarrhea, but the possibility of death is remote. Humans normally acquire these enterotoxins following ingestion of contaminated food or water, but these enterotoxins may be aerosolized for warfare. Heat, acids, or alkalis can detoxify many exotoxins because they are proteins.

### Endotoxins

Many organisms (particularly certain classes of bacteria) do not elaborate a soluble toxin from the living intact cells. Instead, their toxins are associated with their cell wall and are not released until the cell disintegrates. *Rickettsia prowazekii*, which causes typhus fever, produces an endotoxin. This endotoxin causes the rapid destruction of the red blood cells and increases the permeability of blood vessels, resulting in hemorrhage.

## Algal Toxins

Algal toxins are by-products of algae. Most algae grow either in fresh water or in salt water. An algal bloom may produce enough toxin to kill fish or any animals that drink the water. The types of molecules involved are diverse, ranging from simple ammonia to complicated polypeptides and polysaccharides. Production of some is rather easy; some are quite potent. Little testing has been done on the ability to weaponize them. No specific means of detection is available. The greatest potential for the algal toxins as agents lies in a subversive role. These agents could upset

the normal ecology of an area, contaminate potable water supplies, and contaminate fishing areas of indigenous populations. The physiological effects vary. These effects range from the acute toxicity of paralytic shellfish poison, which produces death in a short period, to those that induce tissue changes after long exposure. Several of the toxins have undergone extensive study because of their dramatic effect on sodium-ion channels. These sodium-ion channels help to control differences between levels of sodium and potassium ions inside and outside normal cells.

The blue-green algae and dinoflagellates represent the two groups with the greatest potential as biological agents.

### Blue-Green Algae

Algae in this group are very similar to bacteria. The group contains most of the toxic freshwater algae along with some of the toxic marine species. At least eight genera have exhibited toxic characteristics. The toxins of the blue-green algae *Microcystis*, *Anabaena*, and *Aphanizomenon* affect the nervous system and represent potential sources of agents. Examples of toxins from blue-green algae include Anatoxin A, microcystin, and debromoaplysiatoxin.

### Dinoflagellates

Most of the toxic dinoflagellates are marine organisms within the range of 40 to 60 microns in diameter. *Gym-*

*nodium breve* (*Ptychodiscus brevis*) and *Gonyaulax* are primary sources of toxins. Their toxins are best known in the United States as the causes of red tide and paralytic shellfish poisoning (saxitoxin). A dinoflagellate (*Takifugu poecilonotus*) may produce tetrodotoxin, associated with puffer fish.

Several basic differences exist between the red tide toxin and saxitoxin. The red tide toxin is an endotoxin; it is insoluble in water and very unstable. Saxitoxin is an exotoxin; it is very water soluble and stable to heat and acids. Saxitoxin had been believed to be the most potent algal toxin known. However, maitotoxin from the dinoflagellate *Gambierdiscus toxicus* is now believed to be the most potent marine toxin.

## Mycotoxins

Mycotoxins include a wide variety of chemical substances produced by molds or fungi. The toxins are exotoxins. Many molds produce more than one toxin, and in numerous cases, combinations of mycotoxins enhance toxicity. Many of these toxins and/or their producing species are threats as anticrop or antianimal agents. Some, however, are threats as antipersonnel agents. Trichothecene mycotoxins, aflatoxins, and tremorgens may be of greatest concern.

### Trichothecenes

The trichothecenes came to the attention of the military primarily because of reports in the mid-1970s of yellow (and other color) powder, dust, and "rain" incidents in Southeast Asia. Historically, the main interest in trichothecenes resulted from health problems in humans and animals after they ate food contaminated with molds. *Fusarium*, *Stachybotrys*, and related fungi that infect food and grains, such as corn, rye, barley, oats, millet, straw, and hay, produce the toxins. These toxins are easily produced and moderately potent. They cause damage by ingestion, by eye or skin contact, or by inhalation. They are highly persistent and difficult to decontaminate. T-2 toxin is a highly toxic member of the very large family of trichothecene mycotoxins. This manual describes it chiefly because of it has been identified in the areas of attack; it also is a specifically defined chemical that chemical or biological means can produce. However, employment is

more likely of mixtures of agents than of a single agent; these mixtures come from crude biological extracts.

### Aflatoxins

Aflatoxins are toxic nonproteinaceous compounds produced by strains of *Aspergillus flavus*. Natural grain contamination by the fungus and its toxin represents a serious problem in the USSR and other countries of the world. Aflatoxins are not only toxic; they also induce cancers, malformations, and mutations. Because their effects, although severe, are relatively slow to appear, aflatoxins may not be viable as agents. The aflatoxins have enhanced effects in combination with other mycotoxins, notably with T-2 toxin.

### Tremorgens

Tremorgenic mycotoxins affect the nervous system; they produce severe trembling and loss of coordination and consciousness. Some *Aspergillus* and *Penicillium* molds produce tremorgenic mycotoxins. Tremorgens probably cause naturally occurring disorders of cattle and sheep known as "staggers." Symptoms appear in laboratory animals in about 30 minutes. Tremors and hypersensitivity to stimuli, such as noise or touch, usually last from 4 to 24 hours and then subside. At lethal dosages animals have intermittent seizures leading to death. Some tremorgens cause immobility that may last for hours; recovery follows, and the victim appears to be normal.

## Plant Toxins

Many plants have parts that are poisonous if they enter the body. Potential agents include the proteinaceous toxins ricin and abrin (from castor beans and *Abrus* seeds) and

certain lipid-soluble toxins from members of the lily family. See descriptions under Ricin.

## Animal Toxins

A number of animals produce toxins that are described in this manual. These toxins include batrachotoxin from the Colombian frog, palytoxin from soft corals, saxitoxin from various shellfish, conotoxins from marine snails, and

tetrodotoxin from puffer fish. Snake venoms also contain a large variety of toxic substances that affect nerves or damage muscles and membranes.

### Section III. Specific Toxin Characteristics

This section describes specific toxins. Descriptions include the use, source, physical and chemical properties, route of entry, symptoms, and treatment. The descriptions

also include the rate of action, mode of action, toxicity, stability, decontamination, and comments where applicable. Figures show the structures of some of the toxins.

#### Anatoxin A (Very Fast Death Factor; VFDF)

##### Use

Anatoxin A is a lethal, very rapid, paralytic neurotoxin.

##### Source

A freshwater, blue-green algae, *Anabaena flos-aquae* produces Anatoxin A. Culturing the algae can produce significant quantities of Anatoxin A. Chemical synthesis could probably produce large quantities.

##### Physical and Chemical Properties

Anatoxin A is a bicyclic alkaloid with a molecular weight of 165. It is water-soluble, but heat, light, and alkalis will destroy it.

##### Route of Entry

This toxin usually enters the body by ingestion. The toxic algal blooms have caused the deaths of fish, livestock, and birds.

##### Rate of Action

Symptoms begin in less than five minutes.

##### Symptoms

When ingested, Anatoxin A causes symptoms typical of chemical nerve agents. These symptoms are twitching, incoordination, tremors, paralysis, and respiratory arrest. Death results from paralysis; it may occur within minutes or up to three hours, depending upon the dose. Death in mice occurs in two to five minutes.

##### Treatment

There is no specific treatment.

##### Mode of Action

This toxin binds to the same receptor as acetylcholine; it stimulates the nerves and muscles in a similar manner. Acetylcholinesterase does not hydrolyze Anatoxin A, so stimulation continues until the neuron becomes depolarized. Evidence shows that this toxin also inhibits acetylcholinesterase.

##### Toxicity

The LD<sub>50</sub> in mice ranges from 170 µg/kg to 250 µg/kg, when injected intraperitoneally (ip). Dermal LD<sub>50</sub> is greater than 2,100 µg/kg oral LD<sub>50</sub> is 5,000 µg/kg. The CAS registry number is 64285-06-9, and the RTECS number is KM5527000.

##### Decontamination

Use hot, soapy water.

##### Comments

The magnitude of the threat from Anatoxin A depends on its toxicity. If the toxicity for humans is equal to the value for mice, this toxin could be a serious threat. If the human toxicity is closer to that for ducks (LD<sub>50</sub> of 50 mg/kg ip), the threat is considerably less. Figure 4-1 shows the structure.

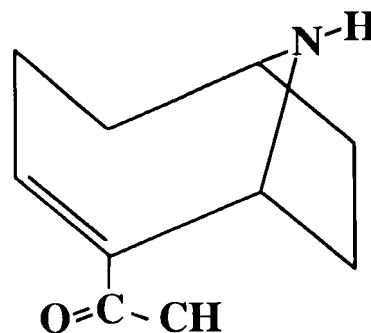


Figure 4-1. Anatoxin A (VFDF).

#### Batrachotoxin

##### Use

Batrachotoxin is a rapid-acting, lethal, paralytic neurotoxin.

##### Source

Batrachotoxin comes from the skin of the Colombian arrow frog (*Phylllobates aureotaenia* and related species).

South American Indians cover the points of hunting darts with a mixture of toxins secreted by these frogs. Dried natural toxin remains active for at least a year. Chemical synthesis can produce the toxin.

### Physical and Chemical Properties

Batrachotoxin is a nonprotein, three-ring compound. It has a low molecular weight of 538. Batrachotoxin is not soluble in water; however, it can dissolve in nonpolar organic reagents, such as fuels, fats, and oils. Because batrachotoxin is lipid-soluble, it is probably cumulative in the body. Figure 4-2 shows the structure.

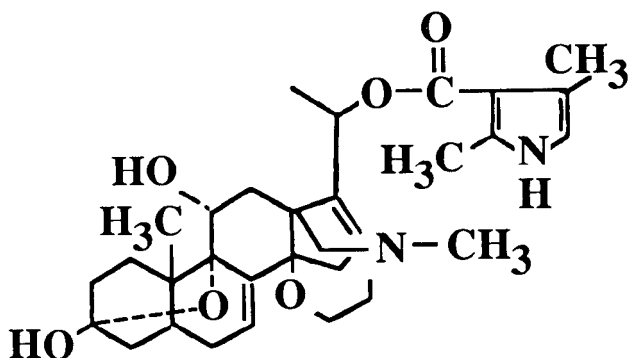


Figure 4-2. Batrachotoxin.

### Route of Entry

In experiments, this toxin is usually injected. Inhalation effects should be similar.

### Rate of Action

Batrachotoxin is rapid acting.

### Symptoms

When given to animals, batrachotoxin causes loss of balance and coordination, profound weakness, irregular

heart rhythms, convulsions, and cyanosis (bluish skin) in rapid succession. A lethal dose in mice causes death in five to ten minutes by respiratory failure.

### Treatment

Victims should receive general supportive care. They may require artificial respiration and/or cardiac resuscitation and support. No antidote or antitoxin is available. In laboratory cultures tetrodotoxin blocks the effects of this toxin.

### Mode of Action

Batrachotoxin binds to sodium channels of nerve and muscle cells. It inhibits closure of the channels so the neuron becomes completely depolarized and unable to transmit a signal.

### Toxicity

Batrachotoxin is about 10,000 times more lethal than Sarin. Its LD<sub>50</sub> is 0.1 to 2 µg/kg intravenously (in mice). Combining batrachotoxin with scorpion venom makes it twenty times more toxic. The CAS registry number is 23509-16-2, and the RTECS number is CR3990000.

### Stability

Batrachotoxin is stable under both acidic and moderately alkaline conditions and is more active under alkaline conditions. It is somewhat nonpersistent.

### Decontamination

Use soap and water to remove contamination from personnel. Because the toxin is nonpersistent, equipment would likely not require decontamination. Should decontamination prove necessary, use organic solvents if soap and water are not available.

## Other Similar Toxins

*Veratridine*, *Aconitine*, and *Grayanotoxin* are lipid-soluble, channel-activating toxins similar to batrachotoxin; they probably have a common site and similar mechanism. These toxins are much less toxic than batrachotoxin.

- *Veratridine* is the most potent of the lipid-soluble toxins. It comes from the lily family, genus *Veratrum*; its molecular weight is 673.

- *Aconitine* comes from the plant *Aconitum napellus*; its molecular weight is 633.
- *Grayanotoxin* comes from the leaves of rhododendron and other Ericaceae; its molecular weight is 398.

## Botulinum Toxin

### Use

Botulinum toxin is a lethal, delayed-action, paralytic neurotoxin. It is considerably more poisonous than nerve

gases. It causes botulism, a specific and often fatal food poisoning. Dispersion could be by aerosol.

## Source

Botulinum comes from the bacteria *Clostridium botulinum* and *Clostridium parbotulinum*. These bacteria are rod-shaped, slightly motile, spore-forming, gram-positive, anaerobic bacilli. The principal reservoir of these bacteria is soil. Because these bacteria cannot grow in the presence of oxygen, natural encounter with the toxin is in improperly preserved, canned foods. The bacteria grow and produce toxin while the food sits on the shelf. Growth requires a neutral to moderately alkaline medium. Acid conditions reduce the resistance of the bacteria to sterilization by heat, which helps explain why outbreaks never implicate preserved acid fruits. Large-scale production is possible.

## Physical and Chemical Properties

Botulinum toxin is a large protein (molecular weight 900,000) that has smaller subunits of molecular weights from 70,000 to 150,000. There are seven known types of toxin (A through G); type A is of greatest military interest. The molecular weight of type A toxin is 150,000. The structures of botulinum and tetanus toxins are very similar.

Purified toxin may be a white powder or a colorless needlelike crystal. It readily dissolves in water when finely powdered. It is stable in solution up to seven days when protected from heat and light. It can be used in solutions or freeze-dried as a powder.

## Route of Entry

This toxin normally enters the body through the digestive system in contaminated food. Fresh, well-cooked foods are not involved, as heat destroys the toxin. The bacteria do not grow or reproduce in the human body poisoning comes entirely from the toxin already formed in the ingested material. Botulinum toxin differs from other bacterial toxins in that digestive tract secretions do not destroy it. The toxin could possibly enter the body through breaks in the skin or by inhalation, as in the case of laboratory accidents. Botulinum toxin in its powder form lends itself to entry by inhalation or contamination of wounds.

## Rate of Action

Symptoms usually begin 12 to 72 hours after ingestion of contaminated food; the delay may range from 2 hours to 8 days. The delay in symptoms depends upon the amount of toxin and its absorption from the digestive tract. If toxin dispersal is by aerosol, the onset is much more rapid (averaging 3 to 6 hours), although symptoms remain the same. Introduction of botulinum through the skin is unlikely unless the skin is broken.

## Symptoms

Initial symptoms include weakness, malaise, dizziness, and in some cases nausea and profuse vomiting. Other

symptoms include difficulty swallowing and speaking, blurred or double vision, sensitivity to light, and muscular weakness progressing from the head downward. In severe cases, death results from respiratory paralysis. All personnel possibly exposed to the toxin should seek immediate medical attention, because it is difficult to treat once symptoms appear.

## Treatment

Medical care consists of supportive measures, including mechanical respiration. Antitoxin is available; its administration should take place immediately upon suspecting botulism poisoning. Upon recognizing a case of botulism, immediately search for all other possibly exposed persons. Treatment after severe symptoms set in is usually ineffective; the antitoxin will not reverse existing paralysis. Recovery is very slow, and several months may pass before a victim regains certain muscle movements.

## Mode of Action

Botulinum toxin inhibits acetylcholine release. The toxin is highly specific for the nerve-muscle junctions and synaptic ganglia. The toxin acts presynaptically. Botulinum toxin probably does not cross the blood-brain barrier.

## Toxicity

This toxin is among the most potent biological toxins known. The exact lethal dose for humans is unknown, but it may be as low as 1 to 10 nanograms. Mortality rate is 60 percent or higher. Animal studies show an LD<sub>50</sub> of 0.001 to 1 ng/kg. The LD<sub>50</sub> in mice is about 0.3 ng/kg. Humans are less sensitive to botulinum toxin than mice are. The oral LD<sub>50</sub> for humans is about 1 µg/kg. Studies show that inhaled toxin is ten times to a hundred times more toxic than ingested toxin. The RTECS number is ED9300000.

## Stability

The persistency of this toxin varies. Botulinum toxin decomposes within 12 hours in the air. It is stable for a week in nonmoving water. It may persist indefinitely in food when not exposed to air. This toxin is probably not UV-light sensitive; it is easily stabilized to environmental conditions. However, heat may destroy the toxin.

## Decontamination

Basic skills decontamination for personnel would prove effective in neutralizing this toxin. If mustard may be present, use a 1-percent to 2-percent hypochlorite solution (from household bleach, STB, or HTH). The toxin can withstand acids, but bleach or other alkaline solutions can destroy it. This toxin is sensitive to heat. Boiling for 15 minutes or, when in food, cooking for 30 minutes at 80°C (176°F) will destroy it.

## Comments

Because of its intense toxicity, water volatility, and difficulty in detection, this agent could present a particularly

great hazard. Immunization with botulinum toxoid is possible for types A through E.

## Other Clostridium Species

Other *Clostridium* species, which are anaerobic spore-forming bacteria that produce toxins, include *Clostridium tetani* and *Clostridium perfringens*. Employment of these toxins is less likely. *Clostridium tetani* produces tetanus toxin, a lethal delayed-action paralytic neurotoxin, causing "lockjaw." Tetanus toxin is produced after introduction of the tetanus spores into the body. They grow at the site of an injury, usually a puncture wound contaminated with soil,

street dust, or feces. The purified (crystalline) toxin is relatively unstable and very sensitive to heat. Its toxicity is about the same as crystalline botulinum toxin. The lethal oral dose for humans is probably 0.2 to 0.3 mg. *Clostridium perfringens* toxin causes gas gangrene in tissues surrounding a wound. *Clostridium perfringens* is similar to tetanus in its mode of transmission.

## Conotoxins

Conotoxins are small, proteinaceous neurotoxins from fish-hunting sea snails (*Conus*). The toxins are 13 to 14 amino acids long; they can easily be chemically synthesized or produced by genetic engineering. Conotoxins are water-soluble and highly stable; dissemination could be by

aerosols. Alpha-conotoxin blocks the acetylcholine receptors and produces extreme muscle weakness (flaccid paralysis) and respiratory and circulatory failure. The LD<sub>50</sub> in mice is 15 to 30 µg/kg. The estimated lethal dose for humans is 3 to 6 µg/kg.

## Microcystin (Fast Death Factor; FDF)

### Use

Microcystin is a lethal, rapid-acting cytotoxin.

### Source

A freshwater, blue-green alga, *Microcystis (Polycystis) aeruginosa*, produces microcystin. Other freshwater, blue-green algae may also produce it. Lyophilized (freeze-dried) microcystin retains its toxicity. See comments.

### Physical and Chemical Properties

Microcystin appears to be a family of small, cyclic peptides. The most common toxin in the family has a molecular weight of 994; others are similar. Microcystin is derived from a polypeptide with a molecular weight of 1,790 to 2,950. It is soluble in water, acids, bases, and some polar solvents, such as alcohol and acetone.

### Route of Entry

Microcystin is potent in air-dried material. If Threat forces use it as a warfare agent, it would presumably enter the body through the respiratory system. There are reports of human exposure in which the victims drank water from contaminated reservoirs.

### Rate of Action

See symptoms.

### Symptoms

Microcystin causes severe and rapid liver damage with resulting shock, liver enlargement, and death in a matter of hours. Symptoms would vary with the dose received. Symptoms in test animals include shivering and increased breathing rate and depth. These symptoms precede muscle twitching, convulsions, and gasping respiration before death. In test animals given twice the lethal dose, death occurs one to three hours after exposure.

### Treatment

Victims should receive general supportive care. No antidote or antitoxin is available. Substances that protect against the mushroom alkaloid phalloidin (for example, rifampicin and deoxycholate) reduce cell deformation.

### Mode of Action

Microcystin deforms and disrupts cell membranes in the liver. Test animals have shown extensive liver damage leading to circulatory collapse.

### Toxicity

Its LD<sub>50</sub> in mice is 25 to 100 µg/kg (ip) with a survival time of 30 to 90 minutes. The LD<sub>50</sub> is much higher by oral or dermal routes. Each gram of lyophilized cells contains about 1 to 4 milligrams of toxin; toxicity of cellular material is about 50 mg/kg. The RTECS number is XW5810000.

**Stability**

Microcystin is heat-stable when dry but unstable to heat when wet. It is stable to acid but sensitive to highly alkaline conditions.

**Decontamination**

Use large amounts of soap and water. Because microcystin is soluble in water and sensitive to alkalis, large amounts of water, STB, or DS2 will decontaminate supplies and equipment.

**Comments**

We know relatively little about the physical and chemical properties of this toxin. However, reports indicate the Soviets have done considerable research with it. Toxicity appears to be associated with a plasmid. If it is, it should be possible to clone the gene and have it expressed in another organism.

**Palytoxin****Use**

Palytoxin is a lethal, rapid-acting neurotoxin.

**Source**

A bacterium associated with soft corals of the genus *Palythoa*, which inhabit the digestive tract of filefish, produce palytoxin. It can be isolated from the corals. See comments.

**Physical and Chemical Properties**

Palytoxin is a relatively large, nonproteinaceous toxin; its molecular weight is 2,677. It is a polyhydroxy, long-chain macromolecule with a cyclic structure. It is soluble in water or alcohol. See Figure 4-3 for the structure.

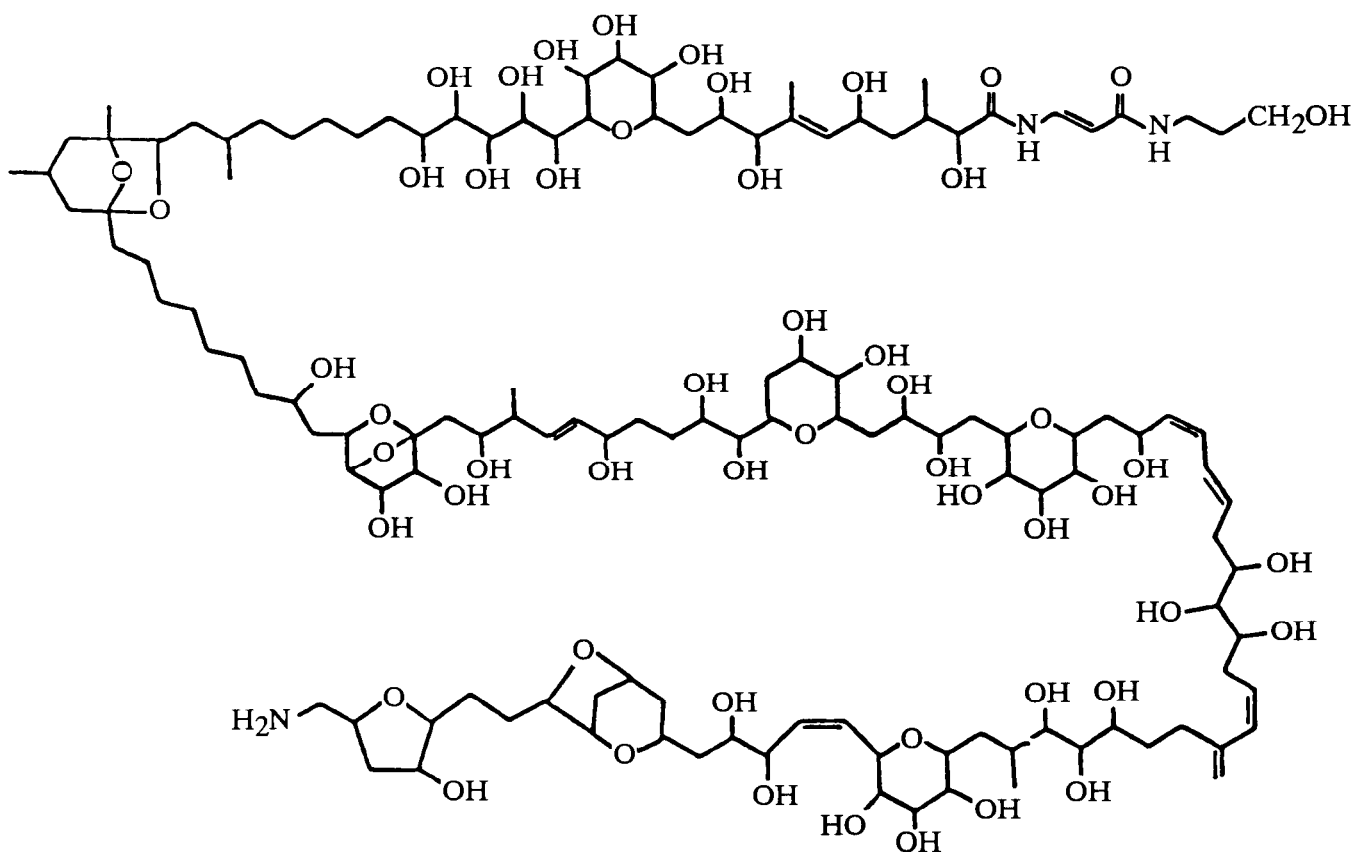


Figure 4-3. Palytoxin.

### Route of Entry

This toxin could enter the body by inhalation (as aerosolized toxin), ingestion, or absorption through the skin or eyes. Absorption through intact skin requires high doses.

### Symptoms

There have been no reported cases of human poisoning. Experimental animals show symptoms of drowsiness, weakness, vomiting, respiratory distress, diarrhea, convulsions, shock, low body temperature, and death within 30 to 60 minutes after intravenous injection. Death may result from constrictions of the blood vessels of the heart.

### Treatment

Victims should receive general supportive care. There is no definitive human treatment. However, rapid administration of steroids has reduced the severity of effects.

### Mode of Action

This toxin has a very potent effect on the coronary artery. It apparently causes irreversible depolarization of nerve and muscle tissue by an unknown mechanism, possibly affecting sodium channels. Palytoxin in high concentra-

tions exhibits delayed effects, causing the disintegration of red blood cells.

### Toxicity

The LD<sub>50</sub> is about 0.08 µg/kg in monkeys, 0.2 µg/kg in cats, and 0.4 µg/kg in mice. Mouse LD<sub>50</sub> through the skin is 1,270 µg/kg. The CAS registry number is 11077-03-5, and the RTECS number is RT647500.

### Stability

Palytoxin is stable to heat, acids, and alkalis.

### Decontamination

Because of the stability of this toxin in a variety of conditions, decontamination should include large amounts of water.

### Comments

The exotic nature of the biological source limits the possibilities for extraction of this toxin. However, advances in genetic engineering could make the manufacture of this toxin possible.

## Ricin

### Use

Ricin is a lethal, delayed-action cytotoxin; it is persistent in the environment.

### Source

This toxin comes from the seeds of the castor bean plant, *Ricinus communis*. This relatively inexpensive, accessible, natural source allows easy preparation of large quantities of ricin; therefore, there is little motivation to produce it synthetically. Large-scale production of ricin by recombinant DNA techniques is probably possible.

### Physical and Chemical Properties

Ricin is a lectin - a plant glycoprotein that binds and agglutinates animal cells. This toxin has a molecular weight of 65,000. It consists of two polypeptide chains linked by a disulfide bond. It is soluble and stable in water or dilute acid.

### Route of Entry

Ricin normally enters the body by ingestion. Aerosolized ricin would enter the body by inhalation. The toxin attaches to cell surfaces of a variety of tissues, particularly the stomach lining if ingested or the moist, upper respiratory tissues if inhaled.

### Rate of Action

Initial symptoms usually appear between 6 to 10 hours and 3 days. Clinical signs appear as early as 45 minutes after oral administration if the victim has an empty stomach.

### Symptoms

The symptoms may include nausea, vomiting, bloody diarrhea, abdominal cramps, breathing difficulty, renal failure, and circulatory collapse. Victims may linger for 10 to 12 days before death or recovery, depending upon the dose received.

### Treatment

Victims should receive general supportive care including fluid input and support of circulation and respiration. Antitoxin is available; its early administration is necessary to prevent severe tissue damage. Fluid input is critical, as fluid losses of up to 2-½ liters are probable.

### Mode of Action

Ricin inhibits protein synthesis.

### Toxicity

The oral LD<sub>50</sub> for humans is 1 mg/kg; a single seed can be fatal. The LD<sub>50</sub> in mice is about 3 µg/kg by injection or aerosol. The CAS registry number is 9009-86-3, and the RTECS number is VJ262500.

### Stability

Ricin is stable in water or dilute acid.

### Decontamination

As for most other toxins, use soap and water to remove contamination from personnel, equipment, and supplies,

## Saxitoxin (Paralytic Shellfish Poison)

### Use

Saxitoxin is a lethal, rapid-acting, paralytic neurotoxin.

### Source

The first isolation of saxitoxin was from the toxic Alaska butter clam, contaminated by dinoflagellates of the genus *Gonyaulax*. (Shellfish and mussels become contaminated while feeding on them.) Recently puffer fish that had ingested *Protogonyaulax* revealed saxitoxin. The toxin has also been identified in a freshwater, blue-green alga. See comments.

### Physical and Chemical Properties

This nonprotein compound is structurally related to tetrodotoxin. Saxitoxin normally appears as the dihydrochloride salt, a white powder that would lend to its use in an aerosol. The toxin is very soluble in water and slightly soluble in alcohols. Figure 4-4 shows the structure.

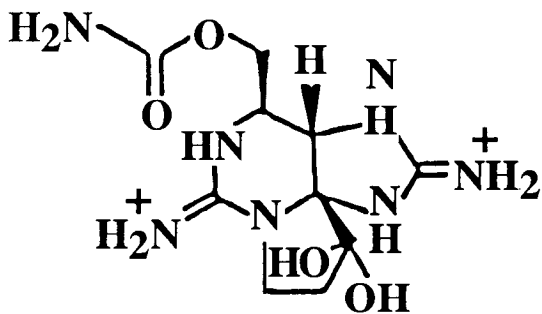


Figure 4-4. Saxitoxin.

### Route of Entry

This toxin usually enters the body by ingestion, but inhalation is also possible. It also can enter the body through wounds.

### Rate of Action

Symptoms occur between ten minutes and four hours (average 30 minutes) after ingestion of this toxin. Inhalation of the toxin will produce a more rapid onset. Injection may cause death in less than 15 minutes.

### Comments

Immunizations are highly effective in animals.

### Symptoms

Ingested saxitoxin causes tingling or burning sensations of the lips, face, and tongue. The sensations occur in fingertips and gradually change to numbness, spreading to the arms, legs, and neck. Incoordination and associated symptoms may occur. These associated symptoms include a feeling of lightness, dizziness, vomiting, nausea, headache, drooling, rapid pulse, and abdominal pain. Severe, generalized muscle weakness (flaccid paralysis) can lead to death from respiratory failure in 1 to 24 hours. If the casualty survives 18 hours, recovery is usually rapid and complete.

### Treatment

Induce vomiting and provide general supportive care. Artificial respiration may be necessary. **Faulty identification of this toxin as nerve gas with resultant use of atropine would increase fatalities.**

### Mode of Action

Upon entry this toxin blocks transient sodium-ion channels and causes paralysis by blocking depolarization. Its action is similar to that of tetrodotoxin.

### Toxicity

The LD<sub>50</sub> in mice is about 1 µg/kg through aerosol exposure, about 8 µg/kg by injection, and 322 µg/kg orally. Toxicity in humans (LD<sub>50</sub> 5.7 µg/kg) is similar to that in mice when introduction of saxitoxin is directly into the body. However, to humans it is much more toxic by mouth (LD<sub>50</sub> 7 µg/kg), equivalent to direct introduction into the body. A single contaminated mussel can contain up to 50 lethal human doses. If aerosolized, the estimated LC<sub>50</sub> by inhalation is 5 mg-min/m<sup>3</sup>. The estimated LC<sub>50</sub> by wound contamination is 0.05 mg/person. As the dihydrochloride salt, the CAS registry number is 35554-08-0. The RTECS number is UY8708600.

### Stability

Saxitoxin is relatively persistent. It is resistant to heat and acid but very sensitive to alkaline solutions.

### Decontamination

Decontaminate with soap and water. Any standard decontaminant is also acceptable, because saxitoxin is very sensitive to alkalis.

### Comments

Although chemical synthesis of saxitoxin is feasible, the cost would probably prohibit production. Dinoflagellates are difficult to culture. However, production of the toxin by culturing dinoflagellates will probably become feasible in the future.

## Scorpion Venom Toxins

### Use

Scorpion toxins are delayed-action neurotoxins.

### Source

Toxins can be extracted from various scorpions. Large-scale manufacture of scorpion toxins would require genetic engineering techniques.

### Physical and Chemical Properties

Scorpion venom consists of a family of small, basic proteins that are rigid in structure. The chemical structures of over 30 distinct scorpion toxins have been identified. They are very similar with molecular weights of about 7,000. The toxin components are water-soluble and heat-stable.

### Route of Entry

These toxins usually enter the body by injection. They could also be aerosolized and would enter the body by inhalation.

### Rate of Action

This toxin has a somewhat delayed action; therefore, determining the nature of the attack could be difficult.

### Symptoms

Localized pain and swelling usually occur upon injection. Mainly, scorpion toxins affect the cardiovascular and neuromuscular systems, similar to the effects of chemical nerve agents. Initial symptoms in cases of exposure by inhalation are unknown. Eyes may water and vision may dim. The pulse rate becomes rapid and irregular, and blood pressure increases. Breathing becomes difficult; respiratory or congestive heart failure may occur in about 20 hours. Rigid paralysis may also result from exposure.

### Treatment

Atropine counters some toxic effects *in vitro* (cell cultures). Prevent and treat shock, and provide artificial respiration. Relieve pain with procaine. **Do not use narcotics.** Barbiturates will lessen patient stress. Antivenin are available, but maximum effectiveness requires administration within two hours of exposure.

### Mode of Action

These toxins disseminate through the bloodstream to the nervous system. They modify the sodium-ion channels, resulting in continuous release of acetylcholine and other neurotransmitters.

### Toxicity

The lethality of venom is 0.34 to 1.2 mg/kg in mice. The potency of the toxic components varies between species; the most potent toxins have LD<sub>50</sub> values of 0.02 mg/kg.

### Stability

Scorpion venom would be relatively persistent. Scorpion toxins are very stable to heat, acids, bases, and denaturants. They also are stable to enzymes that digest proteins (proteases).

### Decontamination

Use soap and water to remove contamination from personnel, equipment, and supplies.

### Comments

If combined with batrachotoxin and related toxins, the venom is twenty times more toxic.

## Snake Venoms and Toxins

### Use

Snake venoms consist of a rapid-acting mixture of toxins.

### Source

A variety of poisonous species could serve as sources for biological toxins. These species include the cobras, kraits,

and coral snakes (elapids) and the rattlesnakes, copperheads, and other vipers (crotalids). Whole snake venoms are relatively unavailable. The toxins might be more available. See comments.

## Physical and Chemical Properties

Generally, snake venoms are extremely complex mixtures of water, low-molecular-weight protein toxins, enzymes, and salts. These venoms may contain a variety of water-soluble toxins, including neurotoxins, cardiotoxins, and toxins that cause severe tissue destruction and hemorrhage. The mixture of these toxins varies widely between species.

The toxic protein components of snake venom vary in size and stability. Some are small proteins (for example, cobra cardiotoxin with a molecular weight of 6,000 to 7,000). Others are much larger (for example, textilotoxin with a molecular weight of 80,000). Large proteins are usually less stable than small ones. Myotoxin is a small polypeptide (with a molecular weight of 4,600) and is very stable. Cobratoxin (molecular weight of about 7,000) is relatively heat-stable. However, cardiotoxins (basic proteins with a molecular weight of 6,000 to 7,000) lose their toxicity when heated to 90°C for 30 minutes. Exposure to ultraviolet light for 15 to 20 minutes will also cause them to lose their toxicity.

### Route of Entry

These toxins usually enter the body by injection. However, they could possibly be aerosolized and enter the body by inhalation. These toxins disseminate throughout the body through the bloodstream and affect target tissues.

### Rate of Action

Snake venoms and toxins produce effects rapidly.

### Symptoms

Cobras, kraits, mambas, and coral snakes (elapids) produce venom that primarily affects the nervous system. The active compounds of these venoms are neurotoxins, cardiotoxin, and enzymes. Venoms of most pit vipers, such as rattlesnakes and copperheads, contain very small amounts of neurotoxins. These venoms tend to cause severe local tissue destruction (necrosis), including muscle destruction, and hemorrhage.

Upon injection of neurotoxic components, initial symptoms usually include pain and swelling at the site of injection. Inhalation would probably result in several symptoms. These symptoms include fluid accumulation in the lungs, painful and difficult breathing, drowsiness, drooping eyelids, blurred vision, vomiting, and difficulty in speaking. A severe drop in blood pressure and shock frequently follow. Convulsions and paralysis may occur. Death may result from cardiac or respiratory failure or shock.

Cardiotoxins reduce the blood pressure and heart rate, cause heart irregularities, and eventually stop the heartbeat; however, they have no direct neurotoxic activity.

Cobra, mamba, and coral snake venoms contain cardiotoxins.

Necrotic toxins from pit viper venoms cause severe local tissue destruction, including muscle destruction and hemorrhaging. Myotoxin destroys muscles but not blood vessels. Dozens of hemorrhagic toxins, zinc-containing enzymes (proteases) that act on proteins, have been isolated.

### Treatment

Initial care for victims normally consists of measures for the treatment and prevention of shock. The victim should be calmed and evacuated. Circulation and/or respiration may require support. Antisera are available, and administration should take place as soon as possible. Experimentally, neostigmine and atropine have been used in the treatment of victims of cobra neurotoxin.

### Mode of Action

The neurotoxins usually act by blocking transmission at the synapse. The other components have a variety of destructive (necrotic and hemolytic) effects against target tissues.

Snake neurotoxins inhibit transmission before (presynaptic) or after (postsynaptic) the synapse. Presynaptic inhibitors initially increase acetylcholine and then block acetylcholine release, causing a flaccid (limp) paralysis leading to circulatory and respiratory failure. Venomous snakes, such as the tiger snake and taipan from Australia, the Asiatic banded krait, and the South American rattlesnake produce presynaptic neurotoxins.

Postsynaptic inhibitors block the receptor for the neurotransmitter acetylcholine, almost irreversibly. Examples of postsynaptic inhibitors are cobratoxin from the Formosan cobra, erabutoxin from the sea snake, and alpha-bungarotoxin from the banded krait.

### Toxicity

The potencies of snake venoms vary considerably. Variations range from 0.05 mg/kg for the brown snake, 0.1 for the Taipan, 0.16 for the sea snake, and 0.56 for the cobra to 11.4 for the Eastern diamondback rattlesnake. As little as 1 to 20 milligrams of a purified toxin component will usually prove fatal to the average human. The LD<sub>50</sub> in mice of some snake toxins are: taipoxin 1 µg/kg; beta-bungarotoxin 14 µg/kg; crotoxin 50 µg/kg; erabutoxin 150 µg/kg; cardiotoxin 1,500 µg/kg; myotoxin 5,000 µg/kg.

### Stability

The complex nature of whole snake venoms should make them relatively nonpersistent in the environment. The stability of the components varies.

### Decontamination

If required, decontaminate with soap and water.

### Comments

The isolation or manufacture of individual components might produce these toxins. Genetic engineering techniques could enhance the process.

## Staphylococcus Enterotoxin Type B (SEB)

### Use

This toxin is a rapid-acting toxin. The vomiting, diarrhea, and painful cramps associated with staphylococcal toxins make them effective incapacitants. The incapacitating effects (about a day) would last longer than those of many potential chemical incapacitants.

### Source

The bacteria *Staphylococcus aureus* produces Staphylococcus enterotoxin type B (SEB). Staphylococcal food poisoning usually results from ingestion of the toxins rather than ingestion of the bacteria. Foods contaminated with SEB have a normal appearance, odor, and taste. A potential natural hazard exists in situations involving mass feedings and lack of refrigeration; improper food handling is responsible for many natural outbreaks. Large-scale production of the enterotoxin appears possible by recombinant DNA techniques.

### Physical and Chemical Properties

The staphylococcal enterotoxins are a group of globular proteins with molecular weights ranging from 27,000 to 35,000. There are at least eight types: A, B, C1, C2, C3, D, E, and F. Purified Staphylococcus enterotoxin, type B is a white, fluffy material. The toxin is water-soluble and stable in heat, cold, acids, and bases.

### Route of Entry

Victims normally encounter this toxin as a food poisoning. However, inhalation of aerosolized toxin is possible.

### Rate of Action

Symptoms usually occur within one-half to six hours (average three hours) after ingestion. Symptoms can appear within a few minutes after exposure to large doses by aerosol. The use of purified toxin would probably result in simultaneous incapacitation of all the troops. Use of the bacteria would produce a longer effect, with some troops recovering as others became ill.

### Symptoms

Victims experience a sudden onset of vomiting, abdominal cramps, nausea, explosive watery diarrhea, and severe weakness. The symptoms usually continue 6 to 8 hours, rarely longer than 48 hours. Recovery usually occurs spontaneously within a day with no residual effects. However, the victim may be weak for another few days, especially

when the loss of body fluids is severe. Difficulty breathing, because of fluid accumulation in the lungs, may occur in severe inhalation cases.

### Treatment

Rest and fluids will promote recovery. Seek medical care if there is respiratory distress. Production of an antitoxin or toxoid vaccine should be possible, although none is currently available.

### Mode of Action

The toxin interacts with receptors in the gut, causing a massive loss of fluids. The toxin also stimulates intense vomiting.

### Toxicity

Animals vary in susceptibility to this toxin. Humans appear to be more sensitive to SEB than laboratory animals (see Table 4-3). This toxin is unusual in that lethal doses by ingestion are hundreds of times higher than incapacitating doses. Deaths rarely occur in healthy individuals with normal exposure to this toxin. However, if exposed through tactical employment, victims could receive massive doses that could cause death.

**Table 4-3. Susceptibilities to Staphylococcus enterotoxin type B.**

	Rhesus monkey	Cynomolgus monkey	Human (estimated)
<b>ED<sub>50</sub></b>			
Intravenous	0.1 µg/kg	0.08 µg/kg	
Aerosol	6.0 µg/kg	3.0 µg/kg	30 ng/person
Oral	1.0	1.0 µg/kg	20 to 25 µg/person
<b>LD<sub>50</sub></b>			
Intravenous	24 µg/kg	11 µg/kg	
Aerosol	27 µg/kg	11 µg/kg	1.7 µg/person
Oral	—	—	—
<b>ICt<sub>50</sub></b>			0.1 to 1 mg-min/m <sup>3</sup>
<b>LCt<sub>50</sub></b>			5 mg-min/m <sup>3</sup>

### Stability

The toxin resists acids, bases, and chlorine in amounts found in potable water. The toxin is quite stable to heat and

freezing its destruction in food or water requires boiling longer than 30 minutes. The organisms that produce the toxin remain viable after 67 days of refrigeration.

### Decontamination

Use large amounts of soap and water to decontaminate personnel, equipment, and supplies. SEB is difficult to decontaminate with active chlorine (STB, HTH). Formaldehyde detoxifies SEB.

## Tetrodotoxin (TTX); Fugu Poison

### Use

Tetrodotoxin is a rapid-acting, lethal, neurotoxic agent.

### Source

Tetrodotoxin comes primarily from the liver and ovary of puffer fish (*Arothron*). It also comes from some species of newt, octopus, frogs, and goby. Dinoflagellates (*Takifugu poecilonotus*) also may produce it.

### Physical and Chemical Properties

Tetrodotoxin is a water-soluble, three-ring nonprotein compound with a molecular weight of 319. Purified toxin may occur as colorless crystals or a white powder (lending itself to aerosol delivery). It is soluble in dilute acetic acid and slightly soluble in water or ether. Strong acids and in alkaline solutions destroy it. Figure 4-5 shows the structure.

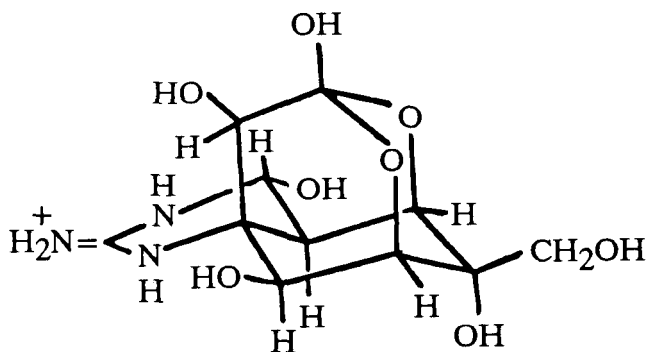


Figure 4-5. Tetrodotoxin.

### Route of Entry

The toxin usually enters the body by ingestion, but inhalation or entry through abraded skin is also possible. See comments.

### Rate of Action

The onset of symptoms occurs within minutes after injection (and presumably after inhalation) of the toxin.

### Comments

The protective mask provides adequate protection from inhalation of SEB disseminated as an aerosol. In the context of biological warfare, several measures will reduce the likelihood of casualties. These measures include effective protection of food and water supplies (and containers for transportation of food to remote sites), and the boiling of all water (even if chlorinated). Measures also include the use of high temperatures for cooking followed by immediate serving.

Symptoms develop more slowly with ingested toxin, taking 10 to 45 minutes.

### Symptoms

Symptoms include nausea, vomiting, dizziness, paleness, and malaise. The victim may experience tingling and prickling sensations that proceed to general numbness. Weakness, dilation of pupils, twitching, tremor, and loss of coordination follow. Severe, generalized muscle weakness leading to death by respiratory arrest may occur within minutes of the onset of symptoms. Symptoms and mechanisms are similar to saxitoxin poisoning, although tetrodotoxin also produces severe shock.

### Treatment

Victims will require general supportive care with particular attention paid to maintaining respiration. Except at very high doses, this toxin does not normally affect cardiac function. No antidote or antitoxin is available. Anticholinergics, such as atropine, are not effective.

### Mode of Action

Once inside the body, tetrodotoxin inhibits sodium-ion channels in nerves and muscles. As a result, the nerve impulse is lost and paralysis occurs. (It does not affect the neuromuscular junction.)

### Toxicity

The inhaled toxin is extremely potent with an LD<sub>50</sub> of about 100 to 200 µg/person (1.5 to 3 µg/kg). Ingested tetrodotoxin requires a much larger dose (30 µg/kg) because of the destruction of the toxin by the acid in the stomach. The ingested toxin is still highly toxic, however. The oral LD<sub>50</sub> in mice is 435 µg/kg. Injected LD<sub>50</sub> is 8 to 14 µg/kg in mice, dogs, and rabbits. The CAS registry number for tetrodotoxin is 4368-28-9, and the RTECS number is 101450000.

### Stability

The toxin is stable to heat, but strong acids and alkaline

## Decontamination

Use water with STB to decontaminate equipment. DS2 will also break down tetrodotoxin. Decontaminate skin with soap and water.

## Comments

The Japanese especially value puffer fish, called fugu in the Orient, as a delicacy. The sensations of eating fugu probably result from the narcotic effect caused by ingestion of low levels of tetrodotoxin. Tetrodotoxin is common in Haitian voodoo as a toxin that creates zombies by direct introduction into the blood through abraded skin.

## Trichothecene (T-2) Mycotoxins

### Use

Trichothecene (T-2) mycotoxin may be suitable as a nonlethal harassing agent. There is a marked difference between the very low, effective (incapacitating) dose and the high, lethal dose. Therefore, there may be many ill casualties who will not die.

### Source

The trichothecenes are a family of about 40 rapidly acting, fungal toxins (mycotoxins). They are primarily isolated from molds of the genus *Fusarium* found on infected grain. Harvesting and extracting infected grain can produce large amounts of these toxins.

### Physical and Chemical Properties

These cytotoxins are nonproteins. Volubility in water or other solvents depends on the structure of the toxin (that is, any hydroxyl, acetyl, and ester groups attached). Figure 4-6 shows the structure. These toxins are heat-stable, usually water-soluble, but sensitive to strong acids. Purified T-2 toxin may occur as colorless crystals or as a clear to yellowish oil. The molecular weight of T-2 is 466. Figure 4-6 shows the structure.

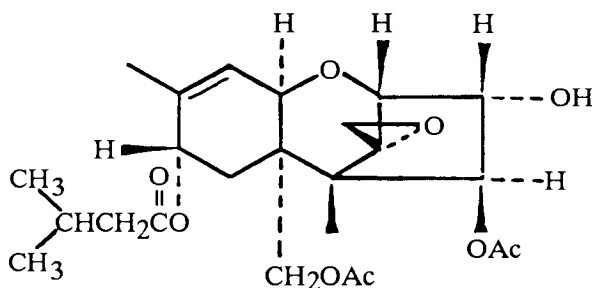


Figure 4-6. Trichothecene (T-2).

### Route of Entry

Dissemination of trichothecenes is likely to be in powder or smoke aerosol form or as large, liquid drops as a ground contaminant. (They have sometimes been called "yellow rain.") These toxins enter the body by absorption through

the skin or eyes, inhalation (aerosols), or ingestion in contaminated food or water.

### Protection

Upon recognition of an attack or onset of symptoms, personnel should immediately mask and put on all protective equipment (MOPP4). Skin exposure to toxins may result in severe itching. This itching would make the protective mask uncomfortable to wear. If vomiting occurs, a damp cloth held over the nose and the mouth may help limit additional inhalation of toxins until the victim can control the vomiting and redon the protective mask.

### Rate of Action

Time to effects after exposure depends on the dose. Initial symptoms may occur within 1 hour after inhalation or as long as 12 to 24 hours after skin contact. High doses produce vomiting, dizziness, rapid heart beat, and chest pain within 10 to 30 minutes. Skin irritation is delayed 12 to 24 hours; death may occur within a day. After low, single-dose exposure, peak effects tend to occur in 1 to 3 days; skin irritation may be the first symptom.

### Symptoms

Low-dose symptoms include nausea; shortness of breath; dizziness; eye and skin irritation; formation of small, hard blisters; and chest pains. Although trichothecene symptoms may resemble those of blister agents, nausea commonly occurs with exposure to these toxins. Trichothecenes are "radiomimetics"; that is, they mimic the effects of ionizing radiation. High doses can result in additional symptoms, such as bloody vomit or diarrhea and blistering of the skin, within hours. Death may follow rapidly from high doses because of massive hemorrhaging and shock, or it may occur weeks later. The delayed death would result from bone marrow suppression (leading to anemia and reduction in immunity), liver failure, and/or internal bleeding.

### Treatment

Victims require general supportive care. No antidote or antitoxin is available. For ingested toxin, repeated doses of oral charcoal can be helpful.

### Mode of Action

The precise mode of action is unknown. One effect is inhibition of protein synthesis. The toxin also affects clotting factors in the blood, leading to hemorrhage. The most pronounced effects occur in rapidly dividing cells (that is, blood and bone marrow cells).

### Toxicity

The best estimate for the human lethal dose is 3 to 35 milligrams. The ED<sub>50</sub> for vomiting is 0.1 mg/kg; and for skin irritation it is tenths of a microgram. Microgram doses can cause irreversible injury to the eyes. Doses as low as 5 nanograms (10<sup>9</sup> gram) may cause skin irritation. Doses as low as 14 µg/kg can cause sustained nausea for days. Aerosol doses may well be ten times more potent than parenteral doses. The CAS registry number for trichothecene mycotoxins is 21259-20-1, and the RTECS number is YD0100000. Table 4-4 shows susceptibilities to this toxin.

Note: Small repeated doses may accumulate to lethal levels.

### Stability

The trichothecenes are very stable; storage for years at room temperature produces no loss of activity. Environmental persistency of T-2 is five to seven days. They are heat-stable with no loss of activity noted after heating at 100°C for one hour. They are quite stable in solution. Strong acids will abolish all toxic effects.

### Decontamination

Rapid removal of toxins from the skin and eyes is essential. Use water or saline for the eyes; use soap and water with repeated flushing for the skin. Flushing the skin with water is an acceptable field expedient procedure for T-2 toxin if done within five minutes after exposure. The M258 and M258A1 skin decontamination kits are effective in

removing T-2 toxin from the skin. The use of absorbents, such as diatomaceous earth, is not effective.

Usually, soap and water will effectively remove toxin from equipment and supplies. Total destruction requires strong bleach and sodium hydroxide (NaOH; lye) or strong acids. STB and DS2 are effective decontaminants (30 minutes at 70°F [21°C] to 80°F [27°C] on nonporous surfaces). Household bleach diluted 50 percent with water or a mixture of bleach, vinegar, and water makes an effective field expedient decontaminating agent for T-2 for a four-hour contact time. T-2 resists decontamination even at very high temperatures. If contamination appears oily, fuels would effectively remove it.

**Table 4-4. Susceptibilities to trichothecene (T-2).**

	Mouse	Rat	Humans (estimated)
<b>LD<sub>50</sub></b>			
Aerosol	0.24 mg/kg	0.05 mg/kg	25 to 50 µg/kg
Intravenous	4.2 mg/kg	1.2 mg/kg	500 µg/kg
Intraperitoneal (ip)	5.2 mg/kg	2.6 mg/kg	
Oral	10.5 mg/kg	2.3 mg/kg	1.6 mg/kg
Dermal	> 67 mg/kg	4.3 mg/kg	2.4 to 8 mg/kg if in carrier
<b>Incapacitation</b>			
Skin reddening and burning			10 ng/cm <sub>2</sub>
Nausea and/or vomiting			50 to 100 µg/kg
Eye damage			1 µg/eye