Toxins of concern to animals and people

T. Garland (1) & E.M. Bailey (2)

(1) Indiana Board of Animal Health, 805 Beachway Drive, Indianapolis, IN 46224, United States of America
(2) Department of Veterinary Physiology and Pharmacology, College of Veterinary Medicine, Texas A&M University, College Station, TX, 77843-4466, United States of America

Summary
Historically veterinarians have diagnosed accidental poisonings and identified possible terrorist events before they have come to the attention of public health authorities. There are many toxins that pose a threat to both humans and animals and the authors examine several of them here, namely, anthrax, tricothecenes, staphylococcal enterotoxin B, botulinum toxins, ricin, saxitoxin and dinoflagellate toxins. By discussing exposure routes, clinical signs and differential diagnoses the authors demonstrate how veterinarians are in a unique position to recognise zoonotic diseases, toxin exposure, and acts of bioterrorism. The work of veterinarians protects the food supply and contributes to human health and this article highlights the importance of coordination and communication between veterinarians and physicians. Sharing information is critical in confirming diagnoses and, in the case of intentional toxin attacks, could also be beneficial in identifying the perpetrators of the crime.

Keywords

Introduction
Veterinarians are in a unique position to be the first to observe an act of bioterrorism. They are trained to recognise zoonotic diseases and are in contact with animals that may be sentinels or targets of diseases spread by terrorists. The devastating effect on the livestock industry and the people associated with the industry was witnessed in the United Kingdom with foot and mouth disease, and has been seen in the western United States of America (USA) with Newcastle disease virus. However, with as much devastation and destruction as has happened, it was not as terrible as it could have been if either of these diseases had been a significant zoonotic disease.

There are a number of weaponised zoonotic diseases available to our enemies. Some of the diseases of concern to both humans and animals are anthrax, plague, smallpox, brucellosis and botulism. Toxins of concern to both humans and animals include T-2 toxin (also known as ‘yellow rain’), ricin, staphylococcus enterotoxin B (SEB), botulinum, saxitoxin, aflatoxin and endotoxins, which are associated with some diseases such as anthrax.

Toxins are substances produced by an animal, plant or microbe, but which do not reproduce themselves. Toxins can be natural or man-made and produced by molecular biological techniques or by chemical synthesis. Generally, toxins are not volatile and do not directly affect the skin. Exceptions are the tricothecene mycotoxins and some of the algal toxins.

Some could be food or water contaminants. Some toxins are not regarded as the ideal weapon of mass destruction, possibly because they may be difficult to manufacture or to effectively disseminate. Toxins not considered here include those associated with the blue-green alga, some plant toxins such as abra or aconitine, and such marine toxins as tetraodotoxin.

When one considers the epidemiology of toxins, there are a few things to consider. Toxins are dose dependant, so large doses will produce a more rapid response than small doses. Also, some toxins, such as botulism, are so potent, that even tiny amounts may cause death very quickly. Toxins are pre-formed, so there is no incubation time necessary; there may be a latent period, largely dependent on dose and route of exposure, between exposure and the
onset of clinical signs. Toxins are not contagious between animals. Rather, animals must encounter the toxin individually. Therefore, it is often appropriate to look for a common source, such as food, feed, or water. Aerosolised toxins are likely to produce the same clinical signs in animals over a wide area, at essentially the same time. In the case of aerosolised toxins, multiple species may be affected. However, in the case of contaminated feedstuffs a particular species of animal is more likely to be affected more than any other species. Investigations into the possible source of a toxin should examine a change in source of feed, or commodities, or even employees handling the feedstuffs. Investigations should also examine water sources, including algae found on or in the source of water.

Some specific toxins

**Anthrax**

In 2001 anthrax made the news with events possibly related to terrorism. Anthrax can be acquired by contact, ingestion, or inhalation. Clinical signs vary depending upon the method by which the bacterium is acquired. When inhaled, the affects are much more rapid. Animals generally acquire the disease through ingestion of the spores. However, animals are also susceptible to the disease by inhalation. Clinical signs in animals are dyspnoea, trembling, collapse, convulsive movements, and sudden death. Cardiac and respiratory distress may be evident, and possibly a rise in body temperature. The body may not bleed from its orifices, depending upon the strain of anthrax. Signs and symptoms in human beings are dyspnoea, chest pain, headaches, as well as possible cardiac disturbances and a rise in body temperature.

Recently, a series of three toxic protein factors associated with anthrax have been identified. The three proteins are the protective antigen (PA), oedema factor (EF) and lethal factor (LF). The PA binds to the cell-surface receptors on the host's cell membranes. Following cleavage by a protease, PA binds to the two toxic enzymes EF and LF and mediates their transportation into the cytosol where they exert their pathogenic effects. The LF, the crucial pathogenic enzyme of anthrax toxin, and the EF cause cellular disruptions and imbalance in eukaryotic cells. This new understanding of this aspect of the bacterium may lead to new formulations for prevention and treatment.

**Tricothecenes**

One of the tricothecenes, T-2 mycotoxin, gained notoriety during the Vietnam-America war, when it was used in a chemical attack and became better known as 'yellow rain'. The tricothecenes are comprised of about 150 structurally related compounds and are produced by several genera of fungi including *Fusarium*, *Myrothecium* and *Stachybotrys* (4). The naturally occurring mycotoxins in foods and feeds produced by *Fusarium* species include: deoxynivalenol (DON), also known as vomitoxin, T-2 toxin (yellow rain), nivalenol and diacetoxyscirpenol. The alimentary toxic aleukia which occurred in Russia in the early 1940s is thought to have been caused by T-2 toxin, but this has never been proven. T-2 toxin will produce an almost identical disease in animals. *Stachybotrys*-contaminated hay will induce a disease syndrome in cattle and horses and has been incriminated in a disease in humans. Tricothecene mycotoxins produce several disease syndromes in domestic animals. Tricothecenes have been found in corn, wheat, commercial cattle feed and mixed feeds. As a group, these mycotoxins can induce digestive disorders, haemorrhage, oedema, oral lesions, dermatitis and leucopaenia, all of which are radiomimetic-like effects (3).

Manifestations are the result of the inhibition of protein synthesis in rapidly proliferating tissues. Regardless of the route of exposure, intoxication has haematopoietic and immunosuppressive effects, central nervous effects, and vascular effects leading to hypotension and shock. Local route-specific effects may include: oral exposure with lesions to the upper gastrointestinal tract; local cutaneous necrosis and inflammation (dermal exposure); and corneal injury (ocular exposure) (9).

Clinical signs in human beings are recognisable after a variable latent period. The effects are seen between 2 and 5 minutes with ocular exposure, less than 1 hour after exposure via the respiratory route, between 1 and 3 hours following oral exposure and effects following dermal exposure may not be evident for 6 to 12 hours. Clinical signs in human beings include airway effects such as nose and throat pain, nasal discharge, itching, sneezing, coughing, dyspnoea, wheezing, chest pain and haemoptysis. Effects involving the skin include skin pain, pruritus, redness, vesicles, necrosis and sloughing of the epidermis. Prostration, weakness, ataxia, collapse, shock and death may follow severe intoxications. Clearly, this toxin affects many organ systems through the varied routes of dermal exposure, inhalation or ingestion. Some of these same signs may be evident in animals. Furthermore, it is possible for the slightly oily substance to transfer from the hair of animals to people. Animals and people can die from this exposure.

Decontamination may be effected by washing exposed areas of people and animals with soap and water. Penetration through the epidermal tissue is fairly rapid. However, decontamination will stop or decrease further exposure.
Intoxication caused by some of this family of toxins manifests as feed refusal in animals, especially in swine. Vomiting and dermal necrosis are also common. Goats standing in feed pans have suffered dermal necrosis, primarily on feet and legs, from contact with the toxin in the feed. Other animals have been similarly affected by tricothecenes. In the event of widespread use of T-2 mycotoxin, such as occurred in Southeast Asia, it is likely animal deaths would occur in multiple species including cattle, pigs, sheep and goats, chickens and ducks.

Botulism is a disease caused by one or more of the seven toxins which may be produced by various strains of Clostridium botulinum, a spore-forming, obligate anaerobic bacillus, commonly found in the soil and very easily isolated (22). The clostridial neurotoxins are the most toxic substances known, and only tetanus toxin from C. tetani and Shigella neurotoxins appear to have potencies of the same order of magnitude (5, 18).

Botulinum toxins have a history of being used or prepared for use in biological warfare, for example, in the 1930s the Japanese biological warfare group (Unit 731) fed C. botulinum cultures to prisoners in Manchuria, and the biological weapons programme in the USA, which was ended in 1970, produced botulinum toxin and botulinum toxoid in the 1940s in response to suspected German toxin weapons (22). Botulism is characterised by an acute, afebrile, symmetric, descending flaccid paralysis that always begins in the bulbar musculature in humans, but it causes a progressive, symmetric, ascending paralysis in dogs (5, 21). Botulinum toxin remains a potential terrorist weapon delivered either by contaminating food and/or feed stuffs or in an aerosol form. The likelihood of botulinum toxin contaminating municipal water supplies is highly unlikely because the toxin is rapidly inactivated by standard potable water treatments, and large amounts of toxin would be required (5). There are some doubts whether botulinum toxin could be weaponised because of constraints in concentrating and stabilising the toxin for aerosol dispersion (22). A deliberate release of a point-source aerosol botulinum toxin in an urban environment could, in theory, incapacitate or kill approximately 10% of the exposed human population (22). At a minimum, the same percent morbidity and mortality could be expected of an exposed animal population. In such an event the locations of affected and unaffected animals, along with parallel information on the human population, theoretically could be used to determine the area of exposure and therefore provide information on the mode of dispersal and potentially the volume released.

The seven distinct botulinum toxins (A-G) are defined by their antigenicity (22). In addition to C. botulinum, other clostridial strains may produce the toxins. The toxin is a dichain polypeptide weighing approximately 150 kD, which consists of a 100-kD ‘heavy’ chain and a 50-kD ‘light’ chain. Botulinum toxin in solution is colourless, odourless, and as far as is known, tasteless. It is inactivated by heat (> 85°C for 5 min) (22). The seven types of botulinum toxin do not necessarily cause disease in all mammals. Types C and D normally occur in domestic animals and wildlife, and type G is a soil isolate from South America. Primates are susceptible to aerosol samples of all three (22, 34). Types A, B, E, and F have been isolated in food poisoning cases in humans. Humans may be exposed to naturally occurring botulinum toxin by consuming poorly preserved food; small animals, dogs and cats may

**Staphylococcal enterotoxin B**

**Staphylococcus aureus** produces a number of exotoxins, one of which is staphylococcal enterotoxin B (SEB). The toxins are excreted from the organism but exert their effects within the intestine; they are enterotoxins. The SEB is a pyrogenic toxin associated with food poisoning in humans. Clinical signs are markedly different if the toxin is ingested rather than inhaled.

Staphylococcal enterotoxins belong to a group of potent immune stimulants known as bacterial superantigens. There is a direct stimulation of a large population of T-helper cells by bypassing the usual antigen processing presentation. There is an intense inflammatory response that injures host tissue. The subsequent released cytokines are thought to mediate many of the toxic effects of SEB.

Clinical features are manifest after a latent period of 3 h to 12 h after inhalation or 4 h to 10 h after ingestion. Oral exposure results in predominantly gastrointestinal signs including vomiting and diarrhoea. Inhalation exposures produce predominantly respiratory signs, such as cough, dyspnoea, and possibly chest pain. Gastrointestinal symptoms may accompany respiratory exposure due to inadvertent swallowing of the toxin after normal mucociliary clearance. Fever may last for up to five days. The cough may persist for four weeks. Human patients are essentially incapacitated. Companion animals are likely to be affected in much the same manner as human beings. Livestock may be affected similarly when exposed by the inhalation route, and colic may be seen in horses exposed through ingestion (12).

Differential diagnoses would include influenza, the adenoviruses and mycoplasma diseases. However, treatment is supportive in most of these.

**Botulinum toxins**

The previously mentioned toxins are very much of a concern with large impacts when used inappropriately. However, the toxic dose of botulism is extremely small and as such, more time in this chapter will be devoted to this particular toxin.
be exposed by ingesting carrion, spoiled meat and compost piles; and herbivorous animals may become infected by ingesting decomposing animal carcasses (17, 21, 23, 34).

The LD₅₀ (intravenous [IV] and intraperitoneal [IP]) of the various botulinum toxins range from 0.1 ng/kg to 40 ng/kg (1 ng = 0.000001 mg) (13). The cattle IV median lethal dose (MLD) is 0.388 ng/kg (23). It is estimated that the lethal oral dose of botulinum toxin is 500 to 700 times greater than the lethal parenteral dose and 77 to 100 times greater than the lethal inhalational dose (22). The estimated human parenteral lethal dose is 1.3 ng/kg to 2.4 ng/kg, and the parenteral minimum lethal dose in animals is estimated to be 1.0 ng/kg. The human inhalational lethal dose is approximately 0.01 ng/kg, and the oral lethal dose is 1.0 ng/kg (5). Most avian species, including domesticated and wild fowl, are affected by botulinum toxin (13, 28). Based on a limited sample of birds, the American turkey vulture (Cathartes aura septentrionalis) appears to be resistant to the effects of botulinum toxin (5, 22, 28).

Botulinum toxins may be absorbed via any mucosal surface, but most commonly they are absorbed through the gastrointestinal tract following oral exposure (22). In the case of inhalational exposure, botulinum toxins may be absorbed through the lungs as has been shown experimentally in primates and in humans following a laboratory mishap (19, 34). The evidence of this toxin's ability to affect the lungs led to it being developed as a weapon. Botulinum toxins may be absorbed through devitalised wounds containing anaerobic tissue. The toxins do not penetrate through intact skin. The botulinum toxins are distributed by the blood to the various tissues, but they do not penetrate the blood-brain barrier. The biotransformation mechanisms, distribution kinetics, and excretion of the botulinum toxins are unknown (3).

Botulinum toxin binds to the presynaptic membrane at the neuromuscular synapse, but the structure of the receptor(s) is (are) unknown. The receptor-bound toxin is internalised by a mechanism known as receptor-mediated endocytosis, and the vesicles are transported within the cell (22). The light (50 kD) chain is cleaved from the heavy chain, leaves the vesicle, and prevents the synaptic vesicle containing acetylcholine from fusing with the neuronal membrane. This action prevents the release of the acetylcholine and results in a flaccid paralysis where the muscles are unable to contract (5).

With naturally occurring botulism, there may be a history of unsupervised animals with access to carrion, garbage, and compost piles (21). In the case of inhalational exposures, presenting animals may be the first indication of a terrorist action in the area. The chief complaint is a progressive rear end weakness or paresis starting 12 h to 6 days post-exposure. Possible signs include progressive, symmetric paresis and/or paralysis beginning in the pelvic limbs, and ascending to include the thoracic limbs. Cranial nerve signs include mydriasis, slow pupillary light response, decreased jaw tone, decreased palpebral and gag responses, and weak vocalisation. Keratitis and conjunctivitis may occur because of weak palpebral reflexes. The respiratory pattern is characterised by diaphragmatic respirations with limited costal respirations. Bradycardia, constipation, and urinary retention are very common. As in humans, there is no loss of mental awareness or pain perception. Interestingly, in dogs the tail wag is usually still present (21). Megaesophagus and aspiration pneumonia may be complicating factors (32).

There are no common laboratory abnormalities typical of botulism (21). The occurrence of secondary bacterial infections may cause white blood cell abnormalities, and depending upon the time sequence, an increased packed-cell volume may be seen if dehydration is occurring (30). An electromyogram may or may not be beneficial. Because megaesophagus commonly occurs, thoracic radiographs are indicated.

The definitive diagnosis depends upon toxin identification. In the case of oral exposures, most diagnostic laboratories require at least 4 ml of serum and 50 g of vomitus, faeces, or ingested food samples. It is best to call the laboratory that is doing the testing in advance and find out what samples are most appropriate and how to properly preserve them. In the case of inhalational exposure with botulinum toxins, the toxins cannot be identified in body fluids other than nasal secretions. Therefore the best diagnostic sample for immunological identification is from nasal mucosal swabs obtained within 24 h of exposure (22).

Treatment in cases of botulism normally includes supportive therapy consisting of maintaining hydration and nutritional support (21, 30). If the animal is hypoxaemic, oxygen therapy, including a tracheostomy and intermittent positive pressure ventilation, may be indicated. In animals able to swallow, hand feeding and watering may be used (30). If the animal is unable to swallow, enteral feeding via a nasogastric tube, esophagostomy tube, or gastrostomy tube, will be indicated (30).

Soft bedding with frequent repositioning will be required to prevent decubital ulcers and prevent atelectasis leading to the development of pneumonia. Animals with megaesophagus may develop aspiration pneumonia. Additional nursing care may include eye ointment to prevent keratitis, warm water enemas, and periodic expressing of the urinary bladder (21).

A licensed antitoxin is available, but is of no value for toxins already internalised into the neurons (22).
available, 5 ml of the antitoxin should be administered IV or intramuscularly (IM) once as early as possible, but within five days of exposure (21). The antitoxin is made from horse serum; therefore the clinician should administer a test dose of the antitoxin intradermally before administering the antitoxin to determine any hypersensitivity. The clinician should be ready to treat an allergic reaction.

The prognosis for clinically affected animals is guarded to poor.

No specific gross or histological changes have been reported.

Differential diagnoses should include tick paralysis, coonhound paralysis, myasthenia gravis, the dumb form of rabies, coral snake bite, chronic ionophore poisoning, macadamia nut ingestion, and chronic low-dose exposure to some organophosphate (OP) insecticides (21, 32). Some animals are extremely sensitive to OP insecticides.

In the case of tick paralysis, there will be a history of finding either Dermacentor variabilis or D. andersoni in the USA or Ixodes holocyclus in Australia (21, 32). There are no cranial nerve abnormalities as are present in botulism toxiosis. The clinical signs rapidly abate following tick removal and/or removing the ticks with organophosphate insecticide solutions along with appropriate nursing care. Organophosphate insecticide may be among the acracides used to rid the animal of the ticks.

Animals with coonhound paralysis generally have a slower onset of signs (seven to nine days) (21, 32). There is usually pronounced muscle atrophy present, and cranial nerve signs are either mild or absent.

In animals with myasthenia gravis, the signs are episodic and most commonly related to exercise (21, 32). Edrophonium causes an improvement of clinical signs and may be treated with supportive care and/or anticholinesterase drugs. A large number of these animals may have a spontaneous recovery (32).

Animals with the dumb form of rabies sometimes exhibit muscular weakness (21). Immunisation status should be confirmed and the possibility of exposure to rabid animals explored. Appropriate safeguards must be instituted until a diagnosis is made.

Coral snake venom will cause an ascending flaccid paralysis and depression in dogs and cats (27). The onset of the clinical signs may be delayed for 10 h to 18 h. This is in contrast to the 12-h to 6-day delay of onset of signs in botulism. A history of exposure and/or the presence of bite wounds should assist in the diagnosis (21).

Dogs and especially cats may develop a general neuromuscular weakness syndrome following a chronic low-dose exposure to some organophosphate insecticides (2, 16). This syndrome has been characterised as the ‘intermediate’ syndrome (16). Many of these animals respond to appropriate doses of atropine and pralidoxime (2-PAM) and occasionally the oral or intramuscular administration of diphenhydramine (4 mg/kg, IM or PO), b.i.d. for several days (2, 16). Acetylcholinesterase levels may be depressed at the time of presentation.

Ricin has previously been used as an agent of assassination. Ricin is still a threat to humans and animals.

Ricin is a naturally occurring toxin isolated from the castor bean plant (Ricinus communis) (7). The ricin concentration in the plant is approximately 1% to 5% by weight. Approximately 1 million tons of castor beans are processed annually in the production of castor oil for lubrication and medicinal purposes (11).

Ricin is a large glycoprotein, which is a water soluble, white powder in pure form, stable under ambient temperature conditions, but heat labile (7). Heating the compound to 80°C for 10 min or 50°C for 50 min. effectivly inactives the protein. Ricin has a molecular weight of 66 kDa, which is slightly smaller than albumin, and consists of two chains, A and B (14). Two haemagglutinins are associated with ricin, but their significance is unknown (11).

Ricin is easily obtained in small or large quantities throughout the world. Criminal use is commonly in domestic murders. It is a potential terrorist weapon, but not likely as a chemical warfare agent because large quantities would be required in an aerosol form (31). It can be used to contaminate food or small bodies of water, but aerosolisation would be required in most potential terrorist or weapons of mass destruction activities (11). Ricin has been used for assassination and suicidal activities in humans (26). Toxicities have been associated with accidental ingestions of castor beans in humans, dogs, and horses (1, 6, 7, 25, 29, 33). Ricin occurs as a residual product from the plant material after oil extraction. The material remaining after oil extraction requires additional purification before use (1, 7, 33) as a feed. The residual ‘cake’ is used in some parts of the world for fertilizer and cattle feed, but the latter is used only after heat treatment (7, 33). Castor oil does not contain ricin and is used for lubricants and as an irritant laxative (14, 33).

The toxic or lethal dose of ricin depends upon the species exposed and the route of exposure (14). There is greater than a 100-fold difference between the susceptibility of
various species (6). The oral lethal dose of seed material (assuming 1% to 5% ricin concentration) has been reported for the following species:

- chicken = 14 g/kg (140 mg to 170 mg of ricin/kg);
- swine = 1.3 g/kg (13 mg ricin/kg to 65 mg ricin/kg);
- rabbit = 0.9 g/kg (9 mg ricin/kg to 45 mg ricin/kg) (20);
- horse = 0.1 g/kg (1 mg ricin/kg to 5 mg ricin/kg) (7, 14).

The reported toxic oral doses of pure ricin are:

- mice = 20 mg/kg (LD₅₀) (10);
- horse = 1 to 5 mg/kg;
- dog = unknown, but probably similar to mice (10);
- humans = it is speculated that the lethal dose is 1.0 mg/kg, but some authors question if ricin is that toxic to humans (7, 14).

The intravenous toxic doses of ricin have been reported as:

- mice = 5 μg/kg (LD₅₀), with the minimum lethal dose varying from 0.7 μg/kg to 2.7 μg/kg (10);
- human = unknown, but 1 μg/kg to 10 μg/kg is the suggested toxic dose;
- dog = the MLD is 1.6 μg/kg to 1.75 μg/kg (7, 10, 14).

The inhalation toxic doses are:

- mice = 3 μg/kg to 5 μg/kg (LD₅₀) (10);
- monkeys = 21 μg/kg to 42 μg/kg is the reported lethal dose (14, 35).

The IP LD₅₀ in mice is 22 μg/kg (10, 14). Subcutaneous or intramuscular toxicity of ricin ranges from 24 μg/kg (LD₅₀) in mice, 33 μg/kg to 50 μg/kg in rats (lethal dose [10, 15]), and 70 μg/kg is apparently a lethal dose in humans, but an individual receiving an estimated 140 μg/kg survived with hospitalisation (7, 14).

Ricin is a large protein molecule, which is poorly absorbed from the gastrointestinal tract (14). After an oral exposure, most of the ricin is found in the large intestine 24 h after ingestion, illustrating the limited systemic uptake of the protein (7). Based on mouse toxicity (LD₅₀) data, approximately 0.025% of the ingested ricin is absorbed following oral administration, but other work has shown that up to 0.27% of the ingested ricin may be absorbed (20, 24). Once absorbed, ricin is most likely distributed throughout the extracellular fluid space in the body (7, 14, 32). Ricin appears to be readily absorbed via the inhalation route, but dermal absorption is unlikely to occur through intact skin (7, 14). Intravenously administered ricin distributes primarily to the spleen, kidneys, heart, and liver, and intramuscularly administered ricin distributes to draining lymph nodes (7).

The B chain of ricin binds to galactoside-containing proteins on cell surfaces, which allows for the internalisation of the A chain by triggering an endocytotic uptake (7, 14). This is the probable cause of the 8-h to 24-h latent period associated with ricin and/or castor bean intoxication because the transport may be slow in some instances (14). The A chain binds with the 28S RNA subunit of eukaryotic cells, killing the cell through the inhibition of protein synthesis (14). Ricin has also been shown to disturb calcium homeostasis in the heart, leading to myocardial necrosis and cardiac haemorrhage. Ricin may target Kupffer cells, which give rise to the hepatotoxicity that is often reported (7, 25). It has been speculated that the lesions seen in ricin and/or castor bean intoxications may be due to effects on endothelial cells, causing fluid and protein leakage along with tissue oedema (7). Inhaled ricin binds to ciliated bronchial lining cells, alveolar macrophages, and alveolar lining cells (14). It is of note that castor beans and leaves also contain a pyridine compound, ricinin, which may cause neuromuscular weakness as a result of an interference with acetylcholine binding at nicotinic receptor sites (8).

The clinical signs associated with ricin exposure vary with the dose and route of exposure. With respiratory and/or inhalation exposures, there may be a preclinical dose-dependent delay of 8 h to 24 h (reported in rats and primates) before the onset of the clinical syndrome (10, 14). Anorexia subsequently develops, and there is a progressive decrease in physical activity, probably caused by developing hypoxaemia and the generalised toxic cellular effects of ricin (14). Respiratory distress starts developing, and there are increased inflammatory cell counts and increased protein from bronchiolar lavage at 12 h post-exposure. At 18 h post-exposure, alveolar flooding and pulmonary oedema develop, and at 30 h post-exposure, severe arterial hypoxaemia and acidosis are present. In humans a primary allergic syndrome has been reported in workers exposed to castor bean dust, but this type of syndrome has not been reported in animals (7, 14). Post-mortem airway and pulmonary lesions associated with inhalation exposure to ricin include marked to severe fibrinopurulent pneumonia, diffuse necrosis and acute inflammation of airways, alveolar flooding and peribronchial vascular oedema, acute tracheitis, and marked to severe purulent mediastinal lymphadenitis. The lung lesions are sufficiently severe to cause death. Adrenalitis and hepatic lesions may or may not be present.

Oral exposures to castor beans have been reported in dogs and humans (1, 25, 29). It should be noted that the beans must be broken or masticated for the ricin to be released.
There may be a latent period of 8 h to 24 h following oral exposures to either ricin or castor beans. The gastrointestinal signs which may develop include vomiting (with or without blood), depression, diarrhoea (with or without blood), abdominal pain, and anorexia (1, 25, 29).

In humans there have been cases of intramuscular exposure to ricin and castor beans (14, 26). The initial signs have included localised pain and muscular weakness within 5 h of exposure. At 15 h to 24 h after exposure, high body temperatures, nausea and vomiting, tachycardia with normal blood pressures, swollen regional lymph nodes, induration at the injection site, and a leucophilia (26,000/mm^3) have developed in these individuals. At 48 h after exposure, hypotension, tachycardia, and vascular collapse developed in these individuals. At 72 h, anuria, vomiting blood, complete atrioventricular conduction block, and a white blood cell count of 33,200/mm^3 developed in these individuals. Death occurred very rapidly in spite of heroic resuscitation efforts.

The development of abnormal organ-specific biochemical values may not occur for 12 h to 24 h after exposure. The minimum database to be developed in cases of suspected exposure to ricin or castor beans should include serum alanine transaminase, serum aspartate transaminase, blood urea nitrogen, serum creatinine, CBC, PCV, and total serum solids.

Analytical methods exist for ricin, but they are not readily available at veterinary diagnostic toxicology laboratories.

Lesions caused by ingested ricin or castor beans include: liver necrosis, spleen necrosis, kidney necrosis, along with haemorrhagic gastroenteritis (14, 33). The lesions reported following intramuscular ricin exposure in humans included: severe local lymphoid necrosis, gastrointestinal haemorrhage, hepatic necrosis, diffuse splenitis, and mild to moderate pulmonary oedema. Similar lesions have been reported in experimental animals (11, 20).

The differential diagnoses could be many, depending upon the locale. Those which should be included are garbage poisoning, any other intoxications resulting in gastrointestinal distress (e.g. zinc phosphide, *Abrus precatorius* [precatory bean], inorganic arsenic, lead, mercury, thallium and DON), and numerous bacterial, viral, neoplastic, and inflammatory gastrointestinal insults.

### Saxitoxin and dinoflagellate toxins

Saxitoxin is an extremely toxic water soluble substance produced by certain algae, principally dinoflagellates, which include *Alexandrium tamarense*, *Gymnodinium catenatum* and *Pyrodinium bahamense*. Many of the dinoflagellates produce the toxin associated with red tide (a phenomenon whereby water turns a dark reddish hue due to a sudden rise in algae population and the resultant high density of pigmented cells). The red tide toxins are most often associated with skin and respiratory irritation, and gastrointestinal distress if sufficient amounts of contaminated water are swallowed. Human intoxications have generally been related to the ingestion of infected molluscs. Paralytic shellfish poisoning is fairly well characterised. However, saxitoxin becomes a lethal weapon of concern when it is aerosolised. The inhalation LD$_{50}$ of saxitoxin is 10 µg/kg of body weight. Approximately 2 mg inhaled is sufficient to kill a 70 kg person. Saxitoxin is a neurotoxin and causes respiratory paralysis. The most likely route of exposure is by inhalation or by toxic projectile.

Saxitoxin is a potent sodium channel blocker and like botulinum toxin has some medicinal uses, but although there are some medicinal uses for sodium channel blockers, saxitoxin is now regulated in the USA according to the terrorism prevention act which makes the possession of saxitoxin illegal. Although it may be obtained for medical and research reasons, it is not easily acquired through official channels. American Type Culture sold it with some degree of regularity before the terrorism prevention act. Earlier in the toxin’s history it was only obtainable through the dinoflagellates. However, it can now be chemically synthesised and manufactured. Consequently, it becomes a very likely weapon of the terrorist.
Sampling

In most cases of intoxications, samples of feed, feed commodities, and other feedstuffs, such as hay or silage should be collected. Samples of water and any algae should be collected. Prompt refrigeration of the water samples may be necessary to preserve the algae and its toxin while the samples are being transported to the laboratory.

Biological samples, such as blood or serum, urine, and/or vomitus may be useful in determining the toxin. In some circumstances, hair samples with the suspect toxin may be useful in identifying the toxin.

Most veterinary diagnostic laboratories will be helpful in answering questions as well as providing a diagnosis, if one is not readily apparent. Furthermore, the diagnostic laboratory is a great source of information in an emergency.

Conclusions

Coordination between veterinarians and physicians is critical. This cannot be over-emphasised. Outbreaks in people and animals may occur virtually simultaneously. While the diagnostic cause in either animals or people may be readily apparent, communication with the other sector may be critical in determining and confirming the diagnosis. The coordination of information may be beneficial in identifying the perpetrators of crimes as well.

Clinical signs of intoxications in animals and humans can be quite similar. Companion animals may be a source of exposure to humans. If the toxin remains on the hair coat of the animals, when their owners rub, comb or brush the hair surface that is holding a dermal contaminant, then the owners may be exposed. Similarly, humans can expose animals by feeding them table scraps. The concordance and discordance of species affected is of extreme importance in determining the source of exposure and the probable nature of the event, whether it was normal but unfortunate, or intended. Communication between veterinarians and public health authorities is necessary as clinical signs of intoxications are very similar between people and animals. The public health authorities are well versed in communicating with the public about any necessary precautions that should be taken. Public health officials are frequently one of the first sources of information the public will turn to when seeking answers.

Veterinary and human medical authorities and law enforcement personnel should have pre-existing agreements to jointly assist the other departments in solving crimes and diagnostic mysteries. These three groups of agencies are the most likely to receive telephone calls from the public in the event of a terrorist release of one of these toxins, which are capable of causing sudden, multiple deaths in humans and animals.

Toxines constituant une menace pour les animaux et l’homme

T. Garland & E.M. Bailey

Résumé

Dans le passé, les vétérinaires ont diagnostiqué des intoxications accidentelles et identifié des actions terroristes possibles avant qu’elles soient portées à l’attention des autorités de santé publique. Nombreuses sont les toxines qui représentent une menace pour l’homme et les animaux ; les auteurs en passent en revue plusieurs, à savoir l’agent de la fièvre charbonneuse, les mycotoxines de tricothécènes, l’entérotoxine staphylococcique B, les toxines botuliniques, la ricine, les saxitoxines et les toxines produites par les dinoflagellés. En examinant les voies d’exposition, les signes cliniques et les diagnostics différentiels, les auteurs montrent que les vétérinaires sont particulièrement bien placés pour détecter les zoonoses, l’exposition aux toxines et les actes de bioterrorisme. Les
Toxinas importantes por sus efectos en personas y animales

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Resumen
Históricamente, los veterinarios han diagnosticado casos de envenenamiento accidental y detectado posibles actos terroristas antes de que se ocupen de ellos las autoridades de salud pública. Hay muchas toxinas que son peligrosas tanto para personas como para animales, y los autores se detienen en varias de ellas: ántrax, tricotecenes, enterotoxina estafilocócica B, toxinas botulínicas, ricina, saxitoxina y toxinas de dinoflagelados. Explicando las vías de exposición, la sintomatología clínica y el diagnóstico diferencial, los autores demuestran que los veterinarios se encuentran en posición idónea para reconocer enfermedades zoonóticas, casos de exposición a toxinas o actos de bioterrorismo. La labor de los veterinarios protege el aprovisionamiento alimentario y contribuye a la salud humana, y los autores subrayan la importancia que revisten a este respecto la coordinación y comunicación entre veterinarios y médicos. Compartir información es fundamental no sólo para confirmar diagnósticos sino también, en caso de ataque intencional con toxinas, para ayudar a identificar a los autores del crimen.

Palabras clave
References


