

SUMMARY
Centers for Disease Control and Prevention
Clinician Outreach and Communication Activity
Clinician Briefing
Ricin as a Biologic Agent
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BACKGROUND

- Ricin is a potent toxalbumin present in the castor bean plant, which grows in warm climates throughout the world. Castor beans are a commercial source of castor oil which is extracted from the castor bean and used for a number of different purposes. Castor oil does not contain any ricin toxin.
- Ricin exerts its toxicity by inhibiting protein synthesis in eukaryotic cells, which may ultimately lead to cell death.
- Ricin can be produced in three forms: liquid, crystalline, or dry powder. It is water-soluble, odorless, tasteless, and stable under ambient conditions.
- Ricin exposure can occur through ingestion, inhalation, dermal or ocular contact, or injection. Inhalation and parenteral exposure are the most lethal routes of administration.
- Experience with ricin poisoning is very limited and is based on animal studies, one homicide, three suicides, many cases of ingestion of macerated castor beans, and occupational exposure to castor bean dust, pulp, and oil.
- Ricin would need to be dispersed in particles smaller than five microns to be used as an effective terrorist or military weapon by the inhalational route. It is very difficult to prepare particles of this size. Ricin could also be used as a terrorist weapon through the contamination of food, beverages, or potentially some consumer products.

CLINICAL PRESENTATION OF RICIN POISONING

Ingestion

The ingestion and mastication of three to six castor beans is the estimated fatal dose in adults. The fatal dose in children is not known but is likely less.

Mild Toxicity Symptoms

- Nausea, vomiting, diarrhea, and/or abdominal cramping.
- Oropharyngeal irritation may also occur following ingestion.
- Symptoms typically resolve within 24 hours, and bloody diarrhea and systemic signs, such as hypotension, hemolysis, and renal failure, are not present.
- The onset of gastrointestinal symptoms after ingestion typically occurs in less than ten hours. Delayed presentation of gastrointestinal symptoms beyond ten hours of ingestion is extremely unlikely.

Moderate to Severe Toxicity Symptoms

- Moderate to severe poisoning may include gastrointestinal symptoms, such as persistent vomiting and voluminous diarrhea – either bloody or non-bloody. The latter may lead to significant fluid loss resulting in dehydration and hypovolemic shock, which would manifest as tachycardia, hypotension, decreased urine output, and possibly altered mental status, such as confusion or disorientation.
- In severe poisoning, hepatic and renal failure – as well as death – are possible within 36 to 72 hours of exposure. The most common findings on animal autopsy are multifocal ulcerations and hemorrhages of gastric and small intestinal mucosa, necrosis of mesenteric lymph nodes, hepatic necrosis, splenitis, and nephritis.

Inhalational Exposure

- Data on inhalational exposure to ricin in humans is extremely limited, and systemic toxicity as a result of ricin inhalation has not been described in humans. Animal studies suggest that inhalation is one of the most lethal forms of ricin poisoning.
- Unintentional sublethal aerosol exposures to ricin occurred in humans in the 1940s and were characterized by onset of the following symptoms within four to eight hours: fever, chest tightness, cough, difficulty breathing, nausea, and arthralgias, followed by diaphoresis. However, there was no reported progression of illness in these cases.
- In a nonhuman primate study, inhalational toxicity was manifested by a dose-dependent, preclinical period of eight to twenty-four hours followed by anorexia and decreased activity. On autopsy, the lungs were edematous, with accompanying necrosis and hemorrhage.
- Inhalational exposure to ricin in animals may include the development of pulmonary edema and hemorrhage, hypotension, respiratory failure, and death within 36 to 72 hours. Although there is no human data, humans can probably be expected to follow a similarly rapid course of illness progression, although dose, size of the ricin particle, and duration of exposure will affect degree of poisoning.
- An allergic syndrome has been reported in workers exposed to castor bean dust in or around castor oil processing plants. It is characterized by nasal and throat congestion, eye irritation, hives and skin irritation, chest tightness, and in some severe cases, wheezing.

- Particles smaller than 5 microns have been used for aerosol dispersion in animal studies. Ricin is not considered persistent in the environment, but particles of this size may stay suspended in undisturbed air for many hours, and resuspension of settled ricin from disturbed surfaces may occur.

Intravenous Exposure

Experience with human exposure by injection is limited to only a few cases some of which are discussed below:

- A 20-year-old man was admitted to the hospital 36 hours after injecting castor bean extract subcutaneously. He complained of nausea, weakness, dizziness, and myalgias. He developed anuria and hypotension, followed by hepatorenal and cardiorespiratory failure, and died 18 hours following admission.
- A 36-year-old chemist extracted ricin from a castor bean and self-administered intramuscular injections for the purpose of scientific curiosity. He developed fever, nausea, anorexia, mild elevation of liver function tests, and tissue damage at the site of injection. Symptoms persisted for approximately eight to ten days and then improved, at which point he was discharged from the hospital.
- The Bulgarian dissident, Georgi Markov, is thought to have been assassinated with an extremely small amount of ricin, however, the ricin was never actually confirmed. His symptoms included immediate pain at the injection site, weakness within five hours, and fever and vomiting within 24 hours. His clinical course worsened to include shock, multiorgan failure, and death over the next three days.
- Ricin, coupled to cancer cell-specific antibodies, was administered intravenously to cancer patients in very low doses in one large clinical trial evaluating ricin as a chemotherapeutic agent. Flu-like symptoms with fatigue and myalgias were common reported side effects and only lasted a few days.

DIFFERENTIAL DIAGNOSIS

- Route of exposure will affect clinical and differential diagnosis as early inhalational ricin poisoning will have primarily respiratory signs and symptoms, whereas ingested ricin will probably present early with gastrointestinal symptoms.
 - Differential diagnosis of inhalational ricin poisoning: consider staphylococcal enterotoxin B; exposure to pyrolysis byproducts of organoflourines such as Teflon or Kevlar, nitrogen oxides, phosgene, influenza, anthrax, Q-fever, and pneumonic plague. These are just some examples of other diagnoses to consider and not an all-inclusive list.
 - Differential diagnosis of ricin poisoning by ingestion: consider enteric pathogens such as salmonella or shigella, mushrooms, caustics, iron or other metals, arsenic, colchicine. These are just some examples of other diagnoses to consider and not an all-inclusive list.
- The current, very limited body of knowledge suggests that significant ricin poisoning through inhalation, ingestion, and parenteral exposure would consist of a relatively rapid, progressive worsening of symptoms over approximately four to 36 hours.

- Early ricin poisoning through ingestion may resemble a typical gastroenteritis or through inhalation, a simple respiratory illness. This may make it initially very difficult to discern true poisoning from other common and less virulent illnesses such as an upper respiratory tract infection or gastroenteritis.
- The confirmation of ricin poisoning requires clinical manifestations of illness with laboratory detection of ricin in either biologic fluids or environmental samples from the area where the patient was exposed.
- There are currently no clinically validated assays for the detection of ricin in biologic fluids readily available. Further clinical tests for ricinine, an alkaloidal component of the castor bean plant, are being developed, but also have not been tested for clinical use. The potential uses of these tests for either ricin or ricinine in human samples would primarily be for purposes of confirming exposure or assessing the prevalence of exposure rather than diagnostic use.
- The Centers for Disease Control and Prevention and member public health laboratories in the Laboratory Response Network are able to detect ricin in environmental samples. However, testing will most likely not be immediately available to assist in clinical decision making. Environmental testing may document the potential for exposure or affirm the exposure circumstance.
- There are no additional laboratory tests readily available to the physician, such as a cell blood count, serum electrolyte panel, or radiograph, that are pathognomonic for ricin poisoning. The presence of leukocytosis and/or abnormal liver and renal function tests may suggest ricin-associated illness in the correct clinical context but are not very specific.
- Suspicion and clinical diagnosis of ricin poisoning should occur when clinically compatible illness is present in conjunction with a highly suspected or known exposure, a credible threat, or an applicable epidemiologic clue.

DECONTAMINATION

Gross Decontamination

Only limited data or experience exist regarding approaches to decontamination of victims following a ricin release. Therefore, what follows is based largely on inference from limited information and our best judgment, using a prudent public health approach. The primary goal is to make the victim as clean as possible after life threatening issues have been addressed.

- In the event of a recognized release or exposure, patients suspected to be contaminated with ricin should receive gross decontamination to the extent possible prior to arrival in the emergency department.
- Decontamination at the scene of the release is generally preferable unless the medical condition of a victim dictates immediate transport to the hospital.
- Gross decontamination consists of
 - Cutting away or otherwise removing all suspected contaminated clothing, including jewelry and watches
 - Washing off any obvious contamination with soap and copious amounts of water.

- Showering with liquid soap and warm water is widely considered the most effective and preferred method for removing remaining hazardous substances from a victim's skin.
- For the comfort of the victims and to improve cooperation, during decontamination, water should be at a comfortable temperature if at all possible, and attention should be given to privacy considerations and to security of personal belongings. The procedure should be explained to the victim so that he or she can understand what is occurring.
- There is no need to perform skin decontamination for patients exposed to ricin through ingestion only.
- Environmental surfaces or equipment, such as in the ambulance, can be cleaned with soap and water or a 0.1% sodium hypochlorite solution.
- Used clothing removed from the victim should be double bagged and labeled as contaminated and then secured in a safe location until it can be safely disposed of.
- Nondisposable personal protective equipment, such as gloves, face shields, and goggles, should be decontaminated by thoroughly rinsing with soap and water, soaking in a 0.1% sodium hypochlorite solution for 15 minutes, and then rinsing with water and allowing to air dry.
- Personal protective equipment for first responders, including those who are decontaminating victims at the scene, is generally determined by the incident commander based on a hazard assessment and site conditions, including the mechanism of dispersal and whether or not dispersal is continuing.
- Preventing droplets from contacting broken skin or mucosal membranes, for example, the mouth or eyes, is important when decontaminating someone or cleaning up bodily fluids that may contain toxin.
- Airborne dispersal of ricin during decontamination is an unlikely hazard.
- Healthcare personnel decontaminating victims who arrive at the hospital without having been adequately decontaminated on scene should use personal protective equipment consisting of a full chemical resistant suit with gloves, surgical mask, and eye/face protection such as face shield and goggles.
- After completing decontamination tasks, personnel should carefully remove all PPE and shower.
- Because victims should have received gross decontamination prior to arriving at the hospital or at the hospital prior to entering the emergency department, the quantity of contaminant that health care workers treating these patients may encounter should be dramatically less than what originally may have been deposited on them. Simply removing contaminated clothing can reduce the contaminant associated with the victim by up to 90%.

Precautions for Healthcare Workers Treating Victims Who Have Been Grossly Decontaminated

- Although the risk for exposure to ricin is likely to be very low after gross decontamination, it is still prudent to follow standard precautions when coming into contact with the patient or his or her personal effects.
- Healthcare workers should follow standard precautions:
 - Wear scrubs or preferably a disposable gown and a lab coat
 - Wear disposable nitrile gloves
 - Wear a surgical mask and safety glasses/goggles or face shield to prevent inadvertently contaminating mucous membrane
 - Follow good hand hygiene practices after caring for patients

TREATMENT

- Treatment of ricin poisoning is supportive; there is no known antidote.
- Ricin is not dialyzable.
- Healthcare providers should continue to use standard precautions when caring for patients with suspected or known ricin-associated illness. This includes care given after skin decontamination and when dealing with patient belongings and secretions.

Treating Ricin Ingestion

- Perform gastrointestinal decontamination.
- Consider gastric lavage if presentation is early – generally less than one hour after exposure – if the patient is not vomiting and if no general contraindications are present.
- If ingested ricin was in the form of a powder, liquid, or similar substance, consider gastric lavage with a nasogastric tube.
- Administer a single dose of activated charcoal if the patient has not begun to vomit and if the airway is secure.
- Current medical literature suggests that ricin poisoning by the oral route significantly contributes to gastrointestinal losses of fluid and hypotension. Hypotension will interrupt normal perfusion of tissues and cause further organ dysfunction. Therefore, intravenous fluid administration and blood pressure support through the use of intravenous vasopressor agents should be used to counter fluid loss and hypotension.

Treating Inhalation and Parenteral Exposure

Treatment is still mainly supportive in nature.

- Inhalational and parenteral poisoning is of much greater severity than oral poisoning, based mostly on animal data.
- Inhalational poisoning will most likely require earlier and greater respiratory support. This may include supplemental oxygen, pulmonary toilet, and mechanical ventilation with positive end expiratory pressure to maintain oxygenation if needed.
- Parenteral poisoning should be treated in a similar fashion as needed.

- Further care should be supportive in nature and may consist of procedures such as hemodialysis for renal failure.
- Individualized management guidelines should always be obtained by calling your regional poison control center, at 1-800-222-1222, or consulting your local medical toxicologist.

RECOGNIZING RICIN POISONING

- Certain epidemiologic clues may suggest the covert release of a chemical agent or a biological toxin such as ricin:
 - an unusual increase in the number of patients seeking care for potential chemical or biological toxin related illness;
 - unexplained death among otherwise healthy or young people;
 - detection of unexplained odors on presenting patients;
 - clusters of illness in people who have common characteristics, such as drinking water from the same source;
 - rapid onset of symptoms after an exposure to a potentially contaminated source;
 - unexplained death of plants, fish or animals;
 - presence of a particular syndrome known to be associated with a chemical agent or biological toxin.
- Patients who have clinical findings consistent with ricin-associated poisoning and have a highly suspected or known exposure to ricin or who present in the context of a credible threat, should be decontaminated as needed, treated as described above and admitted to a hospital for observation of illness progression.
- Although most available evidence suggests a relatively rapid progression of symptoms in significant toxicity approximately 4 to 36 hours following exposure, experience with ricin poisoning is very limited. A subsequent period of observation cannot be definitively specified.
- Persons who have had an exposure to a highly suspected or known ricin-containing compound and who are asymptomatic should also be observed for development of ricin-associated illness.
- Exposures in asymptomatic patients may vary considerably, and the specific situation of each patient will help determine ultimate disposition. For instance, a patient who was on the opposite side of the room when a sealed container of ricin was discovered may not reflect a true exposure. Regardless, any patient that is sent home after a complete evaluation should be instructed to return to the hospital immediately for development of any signs or symptoms consistent with ricin-associated illness.
- If someone has clinical findings consistent with ricin poisoning in the context of an epidemiologic clue suggestive of a possible chemical or biological toxin-associated illness, but with no suspected or known ricin exposure, nor in conjunction with a credible threat, disposition should be determined after the proper public health authorities have been notified. This includes the regional poison control center, as well as local and state health departments.

- If there is no highly suspected or known exposure, no credible threat, and no applicable epidemiological clue, then disposition is left to the clinician's judgment.

REPORTING

- The regional poison control center and the local and/or state public health agencies, should be contacted in all cases of illness consistent with ricin poisoning in the presence of one or more of the following:
 - A suspected or known exposure to ricin
 - A credible threat of a ricin release
 - An applicable epidemiological clue suggesting a chemical or biological toxin release
- The following cases should be reported to local and state health agencies as well as the regional poison control center:
 - Suspected or known cases of ricin exposure
 - Any case of ricin-associated illness
 - Clinical illness consistent with ricin poisoning in conjunction with a credible threat
 - Clinical illness consistent with ricin poisoning in conjunction with an applicable epidemiological clue
- To contact your regional poison control center, dial the national toll-free hotline, 1-800-222-1222, which connects the caller automatically to the closest poison center in the United States.

Note: Please refer to the following for additional information:

- *Slides and text of the December 30, 2004, CDC Webcast/satellite broadcast entitled Recognition, Management and Surveillance of Ricin-Associated Illness*
<http://www.phppo.cdc.gov/phtn/webcast/ricin/default.asp>
- *Investigation of a Ricin-Containing Envelope at a Postal Facility --- South Carolina, 2003 MMWR November 21, 2003 / 52(46);1129-1131.*
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5246a5.htm>