Ricin, Bioterrorism Summary

SYMPTOMS

Sudden onset of fever, chest tightness, cough, difficulty breathing, nausea, and arthralgias occurs 4 to 8 hours after inhalation exposure. Airway necrosis and pulmonary capillary leak resulting in pulmonary edema would likely occur within 18-24 hours, followed by severe *respiratory distress* (unable to breathe) and death from *hypoxemia* (not enough oxygen in the blood) in 36-72 hours.

DIAGNOSIS

Sudden lung injury in large numbers of grouped patients suggests exposure to airborne ricin. The rapid time course to severe symptoms and death would be unusual for infectious agents. Serum and respiratory secretions should be submitted for antigen detection (ELISA). Acute and convalescent sera provide retrospective diagnosis. Nonspecific laboratory and radiographic findings include leukocytosis and bilateral interstitial infiltrates.

TREATMENT

Management is supportive and should include treatment for *pulmonary edema* (water in the lungs). *Gastric lavage* (washing out the stomach) and cathartics are indicated for ingestion, but charcoal is of little value for large molecules such as ricin.

PROPHYLAXIS

There is currently no vaccine or prophylactic antitoxin available for human use, although immunization appears promising in animal models. Use of the protective mask is currently the best protection against inhalation.

ISOLATION AND DECONTAMINATION

There are standard precautions for healthcare workers. Ricin is non-volatile, and secondary aerosols are not expected to be a danger to health care providers. Decontaminate with soap and water. Hypochlorite solutions (0.1% sodium hypochlorite or Bleach) can inactivate ricin.

OVERVIEW

Ricin is a potent poison derived from the beans of the castor plant (*Ricinus communis*). Castor beans are found worldwide, and the toxin is fairly easy to extract, therefore, ricin is potentially widely available. When inhaled as a small particle aerosol, this toxin may produce damage within 8 hours and severe respiratory symptoms followed by acute hypoxic respiratory failure in 36-72 hours. When ingested, ricin causes severe gastrointestinal symptoms followed by vascular collapse and death. This toxin may also cause disseminated intravascular coagulation (clotting throughout the body), microcirculatory failure and multiple organ failure if given intravenously in laboratory animals.

HISTORY AND SIGNIFICANCE

Ricin's significance as a potential biological warfare toxin relates in part to its wide availability. Worldwide, one million tons of castor beans are processed annually in the production of castor oil; the waste mash from this process is 5% ricin by weight. The toxin is also quite stable and extremely toxic by several routes of exposure, including the respiratory route. Ricin was apparently used in the assassination of Bulgarian exile Georgi Markov in London in 1978. Markov was attacked with a specially engineered weapon disguised as an umbrella, which implanted a ricin-containing pellet into his body. This technique was used in at least 6 other assassination attempts in the late 1970's and early 1980's. In 1994 and 1995, four men from a tax-protest group known as the “Minnesota Patriots Council,” were convicted of possessing ricin and conspiring to use it (by mixing it with the solvent DMSO) to murder law enforcement officials. In 1995, a Kansas City oncologist, Deborah Green, attempted to murder her husband by contaminating his food with ricin. In 1997, a Wisconsin resident, Thomas Leahy, was arrested and charged with possession with intent to use ricin as a weapon. Ricin has a high terrorist potential due to its ready availability, relative ease of extraction, and notoriety in the press.

TOXIN CHARACTERISTICS

Ricin can be spread as an aerosol, injected into a target, or used to contaminate food or water on a small scale. Ricin is stable under ambient conditions, but is detoxified by heat ($80^{O}C$ for 10 min., or $50^{O}C$ for about an hour at pH 7.8) and chlorine (greater than 99.4% inactivation by 100 mg/L FAC in 20 min.). Low chlorine concentrations, such as 10 mg/L FAC, as well as iodine at up to 16 mg/L, have no effect on ricin. Ricin's toxicity is marginal when compared to other toxins, such as botulinum. An enemy would need to produce it in large quantities to cover a significant area on the battlefield, thus potentially limiting large-scale use of ricin by an adversary.

MECHANISM OF TOXICITY

Ricin is very toxic to cells. In rodents, exposure is characterized by necrosis of upper and lower respiratory epithelium, causing tracheitis, bronchitis, bronchiolitis, and interstitial pneumonia with perivascular and alveolar edema. There is a latent period of 8 hours post-inhalation exposure before histologic lesions are observed in animal models. In rodents, ricin is more toxic by the aerosol route than by other routes of exposure.

CLINICAL FEATURES

- The clinical picture in victims would depend on the route of exposure. After aerosol exposure, signs and symptoms would depend on the dose inhaled. Accidental sublethal aerosol exposures which occurred in humans in the 1940's were characterized by sudden onset of the following symptoms in 4 to 8 hours: fever, chest tightness, cough, dyspnea, nausea, and arthralgias. The onset of profuse sweating some hours later was commonly the sign of termination of most of the symptoms. Although lethal human aerosol exposures have not been described, the severe pathophysiologic changes seen in the animal respiratory tract, including necrosis and severe alveolar flooding, are probably sufficient to cause death from ARDS and respiratory failure. Time to death in experimental animals is dose dependent, occurring 36-72 hours post inhalation exposure. Humans would be expected to develop severe lung inflammation with progressive cough, dyspnea, cyanosis and pulmonary edema.
- By other routes of exposure, ricin is not a direct lung irritant; however, intravascular injection can cause minimal water in the lungs (edema) due to vascular endothelial injury. Ingestion causes necrosis of the gastrointestinal epithelium, local hemorrhage, and hepatic, splenic, and renal necrosis. Intramuscular injection causes severe local necrosis of muscle and regional lymph nodes with moderate visceral organ involvement.

DIAGNOSIS

- An attack with air spread ricin would be primarily diagnosed according to the setting. Sudden lung injury affecting a large number of clustered cases should raise suspicion of an attack with a lung irritant such as ricin, although other pulmonary pathogens could present with similar signs and symptoms. Other biological threats, such as SEB, Q fever, tularemia, plague, and some chemical warfare agents like phosgene, need to be included in the differential diagnosis. Ricin-induced pulmonary edema would be expected to occur much later (1-3 days post exposure) compared to that induced by SEB (about 12 hours post exposure) or phosgene (about 6 hours post exposure). Ricin intoxication would be expected to progress despite treatment with antibiotics, as opposed to an infectious process. There would be no involvement of structures around the heart as seen with inhalation anthrax. Ricin patients would not be expected to level off clinically.
- Specific ELISA and ECL testing on serum and respiratory secretions, or immunohistochemical stains of tissue may be used where available to confirm the diagnosis. Ricin is an extremely immunogenic toxin, and paired acute and convalescent sera should be obtained from survivors for measurement of antibody response. PCR can detect castor bean DNA in most ricin preparations. Additional supportive clinical or diagnostic features after aerosol exposure to ricin may include the following: bilateral infiltrates on chest radiographs, arterial hypoxemia, neutrophilic leukocytosis, and a bronchial aspirate rich in protein compared to plasma which is characteristic of high permeability pulmonary edema.

MEDICAL MANAGEMENT

Management of ricin-intoxicated patients depends on the route of exposure. Patients with pulmonary intoxication are managed by appropriate respiratory support (oxygen, intubation, ventilation, PEEP, and hemodynamic monitoring) and treatment for pulmonary edema, as indicated. Gastrointestinal intoxication is best managed by vigorous gastric lavage, followed by use of cathartics such as magnesium citrate. Superactivated charcoal is of little value for large molecules such as ricin. Volume replacement of GI fluid losses is important. In percutaneous exposures, treatment would be primarily supportive.

PROPHYLAXIS

The protective mask is effective in preventing aerosol exposure. Although a vaccine is not currently available, candidate vaccines are under development which are immunogenic and confer protection against lethal aerosol exposures in animals. Pre-exposure Prophylaxis with such a vaccine is the most promising defense against a biological warfare attack with ricin.

***Most of this information is courtesy of US Government CDC*.** In times of an emergency much of this material may not apply when it comes to specialized care and testing. These are guidelines to help you when that care is not available. Some of this information is very technical and difficult to understand, but hopefully someone will be available for help in treatment and understanding.

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