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INHALATION ANTHRAX

Philip S. Brachman

DEFINITION

Anthrax is a zoonotic disease caused by *Bacillus anthracis,* which in humans has three primary forms: cutaneous, inhalation, and gastrointestinal. In the United States, over 95% of reported cases have been the cutaneous form and 5% the inhalation form; no adequately documented cases of the gastrointestinal form have been reported (2). Since 1955 approximately 80% of the cases have been industry related and 20% agriculture related.

Inhalation anthrax is an acute disease of humans resulting from the inhalation of *B. anthracis* spores with the subsequent development of hemorrhagic mediastinitis, toxemia, and septicemia; it is usually fatal. Cases are either directly or indirectly related to an industry which processes *B. anthracis* contaminated animal products (3). The disease has been called wool-sorters' disease because historically it was usually an occupational disease involving workers who sorted wool and less frequently goat hair (10). However, workers who became ill were, for the most part, sorting imported goat hair when they became infected. At times the disease is referred to as pulmonary anthrax. This implies that the disease is primarily a disease of the lungs and this is incorrect. There can be secondary involvement of the lungs, but the primary involvement is of the mediastinal lymphatic system.

CAUSATIVE AGENT

The disease is caused by *B. anthracis*, a gram-positive, spore-forming bacillus that grows well on ordinary laboratory media (i.e., 5% human blood agar), has distinctive growth characteristics, and can be further identified by susceptibility to *B. anthracis* bacteriophage and fluorescent-antibody staining. Characteristically, the organism forms spores which are moderately resistant to destruction; the ability of these spores to remain viable for many years in soil and the industrial environment is an important factor in the epidemiology of anthrax.

OCCUPATIONS AT HIGH RISK

Inhalation anthrax has occurred among individuals employed in industries in which aerosols contaminated with *B. anthracis* are generated by the processing of imported goat hair, wool, and hair from various other animals (including horses and alpacas), as well as hides, skins, and dried bones. In the United States, goat hair imported from Asian countries has caused the most cases of inhalation anthrax. The most frequent use of goat hair is in preparation of thread which is woven into a hair cloth interlining used in clothing. Goat hair may also be processed into a felt material used as underpadding in the carpet industry, as insulation material in the plumbing industry, and as polishing wools, saddle pads, and washers. Jobs most frequently associated with inhalation anthrax have been those that expose workers to the early stages of the goat hair processing cycle—specifically persons who either sort goat hair or work in the picking, blending, carding, or combing departments. The fine hair from Angora goats which may be contaminated with *B. anthracis* is used to knit sweaters; the contaminated wools are usually the coarser wools used in the preparation of carpet yarn. Hides and skins are processed in the tanning industry for leather goods. Dried animal bones are processed into gelatin, fertilizer, glue, or chemicals. Disease may also develop as a result of laboratory exposure.

EPIDEMIOLOGY

Among the 17 cases of inhalation anthrax reported since 1900, the source of *B. anthracis* in 9 is presumed to have been imported goat hair. Three cases had tanneries as their source; two of these three cases had contact with the same tannery in which imported goat skins were pro-

cessed. One person is presumed to have been infected through contact with imported wool, one with rugs, and one from exposure in a bacteriology laboratory in which *B. anthracis* had been handled. For two persons, the source is unknown, though one, a housewife, lived near a goat hair processing plant and approximately two miles from the tannery mentioned above that been associated with two cases.

In the reported cases in which goat hair was the source of infection, the hair originated in one of several Asian countries in which anthrax was endemic among goats. Hair (or wool) is either pulled from the carcasses of goats that have died of anthrax or is clipped from living animals and becomes infected in the environment either from the soil or as a result of being washed in water with other hair that is already contaminated. Additionally, the mixing of hair from many animals into bales allows contamination to spread to previously noninfected hair. One report associates contamination with the presence of dried animal blood on the hair fibers.

Aerosols generated by processing the contaminated, raw animal fibers are heaviest in the early production stages and result from blending various goat hairs and other animal and synthetic fibers by hand as well as by mechanical agitation of the fibers (8). As the material is processed, the degree of contamination with *B. anthracis* decreases because of the loss of much of the material extraneous to the hair fiber and the continual dilution of goat hair fibers with other animal or synthetic fibers. By the time the thread has been produced, the degree of contamination with *B. anthracis* is very low. The spun thread is then used in weaving the final product, the haircloth interlining. If insulation material, felt, or saddle pads are the final products, the level of contamination with *B. anthracis* is influenced by the dilution of the goat hair fibers with other fibers.

Contamination can be evaluated by bacteriologic examination of the raw or processed materials by using common laboratory materials and culture procedures (2). A culture survey of the environment of a mill—done with saline moistened swabs and floor sweepings—can be useful in demonstrating the degree of environmental contamination (quantitative and qualitative) which usually parallels the contamination level of the animal product being processed in that specific area of the plant. The gradual decrease in *B. anthracis* contamination of the fiber, and of the environment as the fiber is processed, parallels the gradually decreasing risk of infection with *B. anthracis*.

Only one epidemic of inhalation anthrax has been reported in the United States, and it occurred in 1957 in a goat hair processing mill in Manchester, New Hampshire. A total of nine cases of anthrax resulted; five cases were inhalation anthrax and four of these were fatal (7). The remaining four cases were cutaneous infections. This mill processed goat hair imported primarily from Pakistan. The employees who developed inhalation anthrax worked in carding (2), combing (2), and weaving (1) departments. In order to investigate the levels of airborne contamination that naturally occur in these mills, 91 primates (cynomolgus monkeys) were exposed to the air in a goat hair processing mill similar to the New Hampshire mill (5). The monkeys had a 10%-25% mortality rate caused by inhalation anthrax from a calculated inhaled dose of 1,000-5,500 *B. anthracis* organisms over 3-5 days. Gross and microscopic examination of their tissues revealed findings similar to that for humans who developed inhalation anthrax after industrial exposure to similar *B. anthracis*-containing aerosols.

The predominance of cases associated with goat hair may reflect differences in the degree of contamination in the imported hair as compared to wool or hides, or differences in the methods of processing the raw materials with resulting qualitative or quantitative differences in the derivative aerosols. Variations in exposure risk among various industrial groups may also reflect the number of persons exposed to these materials.

While the majority of cases have occurred in individuals heavily exposed to industrial aerosols, several cases have had minimal exposure. One case was diagnosed in an individual who walked by the open door of the receiving area of a tannery in which contaminated hides were being handled (6). Subsequent to his death, environmental sampling in the receiving area of the tannery demonstrated the presence of *B. anthracis*. It has been hypothesized that as he walked by the tannery, he inhaled an aerosol containing *B. anthracis* that was generated in the receiving area of the tannery. This man had Boeck's sarcoidosis and was on low doses of steroids at the time of his fatal illness. Another

case of inhalation anthrax had been associated with this particular tannery six years earlier.

An unusual case of inhalation anthrax occurred in a home craftsman who was handling imported goat hair yarn which subsequently was shown to be contaminated with *B. anthracis* (14). Evidently, while handling the yarn, he inhaled an infecting dose of *B. anthracis*.

The possibility of subclinical infections has been discussed in a paper describing serologic studies among employees exposed to *B. anthracis* in a goat hair processing mill (11). The authors verified the presence of what was interpreted as significant titers to *B. anthracis* among employees who had no history of a clinical anthrax infection; therefore, they suggested the employees may have had subclinical infections.

POPULATION AT RISK AND PREVALENCE OF DISEASE

The population at risk includes workers in industries that process imported animal products, including goat hair, wool, hides, skins, and dried bones. The products are imported primarily from Asian, Middle Eastern, and African countries. There are no estimates of the risk of inhalation anthrax alone according to the country of origin of the raw materials or the amount of raw material processed. However, a few studies have been reported describing these associations for cutaneous anthrax alone or cutaneous and inhalation anthrax together. Wolff and Heimann rated imported animals by risk of cutaneous anthrax according to the source (country) of the animal materials (15). They reported that goat hair and skins and carpet wools originating from most parts of Asia and those from Northern Africa and Southern Europe were most likely contaminated with *B. anthracis*. In England, it was estimated that before 1914 about one case of anthrax occurred for every one million pounds of imported East India goat hair processed in English mills (16). There are probably fewer than 5,000 industrial workers currently exposed to these potentially contaminated materials. The number of individuals exposed has been gradually decreasing over the past years because of the increased use of synthetic materials and a reduced demand for goat hair and woolen products. Additionally, improved working conditions and the use of an anthrax vaccine primarily among goat hair workers has also helped reduce the risk of anthrax (4).

Only 17 cases of inhalation anthrax have been reported in the United States since 1900 with 11 of these having occurred since 1955.

PATHOLOGY

Airborne particles of $<5\ \mu$ bearing *B. anthracis* are inhaled, passed through the respiratory tract, and deposited in the terminal respiratory alveoli where they are phagocytized by alveolar microphages and transported across the pulmonary membrane to the hilar and tracheobronchial lymph nodes. In this location, the spores germinate, multiply, and produce a potent toxin with resultant toxemia. Bacteremia can develop when bacilli are deposited in multiple organs throughout the body. A characteristic hemorrhagic, edematous, necrotic mediastinitis develops; this may compress the vascular and respiratory structures and cause significant respiratory distress (1). Widespread capillary thrombosis, particularly in the lung and kidney, is an important factor that leads to death. This thrombosis is secondary to endothelial damage produced by the anthrax toxin (9).

CLINICAL DESCRIPTION

Symptoms

The incubation period is from one to five days. The disease is biphasic, with the initial phase consisting of nonspecific symptoms of a mild upper respiratory tract infection, including malaise, myalgia, fatigue, mild fever, nonproductive cough, and, infrequently, a sensation of precordial oppression (12). After two to four days the patient may show signs of improvement. This is followed within 24 to 48 hours by the sudden development of severe respiratory distress with dyspnea, cyanosis, stridor, profuse diaphoresis, and shock. Death usually occurs within 24 hours after onset of the acute phase.

Signs

Physician examination during the initial phase may reveal rhonchi over the lungs without other significant findings. The patient may have a slight fever ranging from 99-100°F. With onset of the acute phase of the disease, temperature, and respiratory and pulse rates all become significantly elevated, and blood pressure falls. It may be possible to demonstrate subcutaneous edema of the chest and neck. Moist, crepitant, pulmonary rales may be heard, and evidence of pleural effusion may be present. Septicemia and

meningitis (frequently hemorrhagic) may occur.

Natural History

Without appropriate therapy, the patient almost invariably dies. Early treatment with large doses of antibiotics and supportive therapy can reverse the natural course of the disease.

Appropriate Laboratory Investigations

During the initial phase no distinctive laboratory findings are present; during the acute phase the white count may increase and show a shift to the left. Radiographic examination of the chest may reveal widening of the mediastinum and the presence of pleural effusion. Under usual circumstances, inhalation anthrax does not present as a primary pneumonia, but secondary anthrax or other bacterial pneumonia may be present. Septicemia may be present. If meningitis complicates the illness, cerebrospinal fluid (CSF) may contain numerous neutrophils ($\geq$12,000/mm^3); the protein content will be elevated; and a hemorrhagic component will almost always be present with red blood cell counts $\leq$100,000/mm^3. *B. anthracis* is usually demonstrable in the CSF. If pleural fluid is present, it may contain *B. anthracis* organisms.

Treatment

The therapy of inhalation anthrax is based upon empirical knowledge and extrapolation from animal studies. Massive doses of penicillin G by intravenous injection, 50 mg (80,000 units)/kg body weight, as an initial dose given in the first hour, followed by an intravenous maintenance dose of 200 mg (320,000 units) kg/24 h should be used. Streptomycin (7-15 mg/kg body weight/ day as a maintenance dose given intravenously to assure adequate blood levels) may also be used. An alternate therapeutic regime is erythromycin 1-4 g/day via continuous intravenous drip. Specific antitoxin has been reported to be of some value; however, currently there is no domestic source of this material. Supportive therapy such as volume expanders, vasopressors, and oxygen should be given as necessary. If there is mechanical respiratory distress, tracheal intubation should be performed. If hospitalized, the patient should be maintained under strict isolation.

Prognosis

Untreated patients do not usually survive; even with treatment, the fatality rate is close to 100%. There has been only one survivor among the 17 reported cases of inhalation anthrax in the American literature since 1900.

DIAGNOSTIC CRITERIA

Inhalation anthrax may be considered in the differential diagnosis of respiratory disease for a person with a history of exposure to possibly contaminated aerosols. The intial phase of the disease is nondescript and can resemble any mild upper respiratory tract infection such as a "cold" or "flu." Unless there is an epidemic, it is doubtful that a diagnosis of inhalation anthrax would be made during the intial phase. The acute phase, with sudden onset and short duration, is characterized by severe toxicity, respiratory distress, and widening of the mediastinum. It may be possible to identify *B. anthracis* in blood, cerebrospinal fluid, or pleural fluid, although these tests may not be of diagnostic help before death.

METHODS OF PREVENTION

The disease in humans could be prevented if the disease in animals were eradicated. Although an effective animal vaccine is available, it is not administered on a regular basis in the countries supplying much of the high-risk animal products. Implementation of improved animal husbandry procedures is difficult to accomplish because of lack of financial and personnel resources; thus, control should be directed toward the worker. Use of the human anthrax vaccine should be mandatory for workers exposed to contaminated materials. The vaccine has been proven to protect against cutaneous anthrax and appears to be equally effective against inhalation anthrax. However, statistical validity has not been demonstrated for protection against inhalation anthrax because of the small number of cases that occurred during the vaccine field trial. Experiments using nonhuman primates have demonstrated the effectiveness of vaccine in preventing inhalation anthrax.

It should be noted that the Occupational Safety and Health Administration (OSHA) has cited at least one company for failure to administer anthrax vaccine to its employees. OSHA recommends the use of the vaccine for employees who have any contact with contaminated animal products.

As demonstrated in England, decontamination of imported raw materials with formaldehyde significantly reduces the risk of anthrax

among employees who work with the animal fibers (13). Additionally, irradition of contaminated materials has been successfully used in Australia. Also, ethylene oxide has been suggested as an effective decontamination agent.

A meaningful environmental housekeeping program with good control procedures can help reduce the risk of infection. Special attention should be given to an effective ventilation system so that workers are not exposed to contaminated air. Respirators should be worn as this helps reduce the risk of inhaling infective aerosols, but this is not a popular procedure. Workers should be educated about the risk of inhalation anthrax and how to prevent exposure to the organism.

RESEARCH NEEDS

The current methods available for decontaminating raw animal products are expensive and difficult to perform. An easier, less expensive method of decontamination would be advantageous. Patients with fatal inhalation anthrax infection have generalized capillary thrombosis—a phenomenon that should be investigated, and the therapeutic use of anticoagulants or other anticlotting substances should be evaluated. Additionally, the therapeutic use of antitoxin should be evaluated.

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