SCREENING

Martin J. Sepulveda

Desirable features of a detection program for early cancer include a high prevalence of detectable pre-clinical disease in the target population and a treatment regime for screen-detected cancer stage that is more effective than therapy at later stages. Moreover, screening procedures should exhibit high degrees of sensitivity and specificity. Screening must be considered a composite of the actual testing program as well as the consequences resulting from the outcome of each screening procedure. As such, early cancer detection programs are associated with many direct and indirect costs, such as screening, definitive diagnosis, treatment, follow-up and lost earnings, which ought to be reasonable in relation to total health expenditures and anticipated health benefits (3).

Changes in morbidity and mortality are potential indices for the assessment of benefit from screening. Of these, mortality is preferred owing to its objectivity and easy measurement. Case survival is frequently used to assess benefit from screening, but it is an unacceptable evaluation measure if uncorrected for the specific biases to which it is susceptible. Increased case survival may reflect advancement of diagnosis by screening (lead time bias) or bias toward slower-growing, less malignant tumors (length bias) rather than a true postponement of death (4)(2)(10). Selection and observation biases are additional nonrandom factors which may influence any index of benefit assessment.

Clinical trials in lung cancer screening have employed chest roentgenograms, alone or in combination with sputum cytology. These have shown the chest radiograph to be more sensitive than sputum cytologic examination. Its sensitivity, nonetheless, is low (24-82%) as it is only capable of detecting lesions at least one centimeter large (7)(11). In constrast, sputum cytology may be slightly more specific than the chest x-ray. There appears to be little overlap, however, between these tests in lung cancer screening. Chest radiographs are of greater benefit in the detection of peripheral tumors and sputum cytology tends to identify radiographically occult central or hilar malignancies (7)(6)(5)(9).

Studies employing one or both of these tests at variable intervals have established that: first, more lung cancers are discovered in screened versus nonscreened groups; second, screen-detected neoplasms exhibit a greater shift toward early stage tumors; and third, case survival tends to be greater among those with screen-detected malignancies (7)(6)(12)(9). A screen-discovered, early lesion with increased case survival, however, does not necessarily equal a cancer cured or a death postponed. The desired outcome of lung cancer screening is usually the demonstration of a reduction in mortality. To date no clinical trial, including the ongoing National Cancer Institute randomized studies, has shown that screening for lung cancer accomplishes this goal. While detection programs have not been adequately examined in high risk occupational groups, one can expect that such a population will only exhibit an increased prevalence of detectable pre-clinical disease rather than provide a different outcome. Caution must be exercised, therefore, in the commitment of increasingly scarce resources to large scale routine screening for lung cancer—given present knowledge.

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SECTION IX
INFECTIOUS DISEASE

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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HISTOPLASMOSIS

Jeffrey D. Band

DEFINITION

Histoplasmosis is a systemic fungal infection caused by *Histoplasma capsulatum*, a soil fungus. The organism is almost always acquired by the respiratory route, and the primary focus of infection is in the lungs. In more than 95% of individuals, infection is either inapparent, subclinical, or mild and is usually detected at a later time by x-ray findings of scattered areas of residual pulmonary calcification or the presence of a reactive histoplasmin skin test. In some infected persons, however, a variety of clinical manifestations may result, ranging from overwhelming acute pneumonia to chronic progressive pulmonary disease, or disseminated disease involving many organ systems.

ETIOLOGY

The etiologic agent of histoplasmosis is the dimorphic fungus, *H. capsulatum*. The organism has been found in widespread geographic areas throughout the world. In nature, the fungus exists in a mycelial form which elaborates numerous infectious spores. Once deposited in man, the spores transform into yeast forms.

OCCUPATIONS AND INDUSTRIES IN WHICH EXPOSURE MAY OCCUR

The natural habitat of *H. capsulatum* is the soil (7). It is widely distributed within the temperate zones of the world, but is most heavily concentrated in the central United States. In areas of the Mississippi, Missouri, and Ohio river valleys, more than 90% of all residents have evidence of having been infected with the organism at some time (10). Certain organic nutrients (e.g., fowl and bat excrement), which are found in high concentrations in some areas, favor fungal proliferation (4)(16)(17)(20)(21). In these habitats, the organism grows abundantly where the decaying guano is mixed with soil. Persons whose occupations or other activities involve close contact with the soil, in particular soil enriched with avian and bat feces, are at high risk of acquiring infection. These include:

- Farmers — especially when cleaning chicken coops, pigeon roosts, and bat-infested lofts.
- Construction workers and workers involved with earth-moving operations.
- Workers involved with road construction, tree clearing, or landscaping.
- Workers involved in the cleaning or dismantling of contaminated buildings.

EPIDEMIOLOGY OF HISTOPLASMOSIS

Certain environmental conditions appear to favor the growth of *H. capsulatum* in soil. Furcolow found that the organism grows best in environments that are warm (mean temperature of 68 to 90 °F), moist (annual precipitation of 35 to 50 inches), and humid (relative humidity of 67% to 87% or more), and that red-yellow podzolic soil and the presence of limestone in soil are associated with the proliferation and isolation of the fungus (9). In addition, soil enriched with high nitrogen content, generally associated with the guano of birds and bats, supports with growth of the fungus.

The distribution of the fungus has been defined by determining histoplasmin skin reactivity in humans and animals in various regions. Numerous investigators have done extensive skin testing in the United States. States along the Mississippi, Ohio, and Missouri river valleys have been shown to be highly endemic and include Arkansas, Kentucky, Missouri, Tennessee, Illinois, Indiana, Ohio, Oklahoma, Alabama, Kansas, Louisiana, Maryland, Mississippi, Texas, and West Virginia (1)(5). Focal areas of high endemicity occur in numerous other states. The infecting agent is an airborne spore. In endemic areas, small numbers of these spores are con-

stantly circulating in the air (10). The chief vector for dissemination of the spores is, therefore, the wind; in dusty weather increased numbers of spores may become airborne and infect individuals. In addition, since higher concentrations of organisms are generally found in areas containing fowl and bat excrement, working, cleaning, or visiting these areas contaminated with avian and bat excrement may lead to the development of infection. A number of outbreaks have been triggered by contaminated dust raised in vigorous cleanup operations of avian or bat feces-laden soil, buildings, or trees. Chicken houses, starling roosts, pigeon roosts, and hollow trees are highly infectious (11)(15) (19). Within specific geographic areas, farm dwellers generally have the largest percentage of histoplasmin positivity, followed by other rural dwellers and lastly city dwellers; however, in some areas nearly everyone is positive.

Histoplasmosis affects all ages and in endemic areas primary infection develops early and equally in both sexes. Disseminated disease tends to occur in the extremes of age, and chronic pulmonary disease usually affects middle-aged men.

Although a wide variety of animals may acquire histoplasmosis, there is no evidence of animal-to-human spread, nor is there evidence of human-to-human spread.

ESTIMATION OF POPULATION AT RISK AND PREVALENCE OF DISEASE

It is difficult to estimate the occupational groups at risk of exposure to *H. capsulatum.* In some areas of the central United States, almost all residents are infected regardless of occupation, and in most cases they are infected during childhood (10). In 4 states the overall percentage of positive skin test reactors for both rural and urban areas exceeds 50%—Arkansas (58%), Kentucky (67%), Missouri (53%), and Tennessee (65%). In the adjacent states of Illinois (73%), Indiana (68%), Ohio (50%), and Oklahoma (60%), more than half of the individuals in farm areas who were tested had positive skin reactions to histoplasmin (1)(5)(6)(12) (13). Previous estimates of the incidence of histoplasmosis in the United States have been as high as 500,000 infections per year (3). Fraser et al. projected that 23.1 persons per 1,000,000 population in the United States are hospitalized each year with histoplasmosis (15,000 persons annually) (8). For 1976, the overall case-fatality rate was 2.9%. Therefore, it has been estimated that approximately 150 persons die from histoplasmosis each year. Based on large skin test surveys, it has been estimated that as many as 15%-20% of Americans have evidence of *H. capsulatum* infection (1)(5)(6)(12)(13)(14).

PATHOLOGY AND PATHOGENESIS

Infection is acquired by inhalation of fungal spores and deposition of the spores in the lungs. Individuals exposed for the first time (primary infection) initially have poor defense mechanisms to fight the infection, and organisms commonly spread via the lymphatic system and blood-stream to distant sites. However, as previously stated, most primary infections result in only mild or unnoticed respiratory infections and are self-limited. Organisms may multiply within reticuloendothelial cells of the liver, lymph nodes, lung, spleen, adrenal glands, intestine, and bone marrow until sufficient numbers and types of inflammatory cells are delivered to contain the organism. The lesions heal by fibrous encapsulation and eventually calcify. Within the nodule, however, the organisms can remain viable but may be held in check by the body's host defenses. In certain clinical settings, the organisms may cause significant pulmonary or systemic disorders later. Successful recovery from the infection confers some immunity against infection.

CLINICAL DESCRIPTION AND DIAGNOSTIC CRITERIA

The signs and symptoms of histoplasmosis range from those of a slight, self-limited infection to fatal disseminated disease, depending upon the quantity of inoculum and certain host factors such as age, prior exposure, and underlying diseases. Infection in healthy persons is usually asymptomatic or presents as a mild febrile respiratory illness. If the exposure is particularly heavy, a more severe influenza-like syndrome or pulmonary infection develops which may or may not be self-limited. Individuals previously exposed to histoplasmosis rarely become ill upon re-exposure unless the inoculum is quite high; even then the respiratory illness is usually less severe and the incubation period shorter than that for previously unexposed individuals. In general the incubation periods, varies from a few days to 3 weeks, depending upon the size of the inoculum and prior exposure. Clinical dissemination rare-

ly occurs except in individuals at the extremes of age or those otherwise immunologically compromised by an underlying malignancy, disorder of the reticuloendothelial system, or corticosteroids or other immunosuppressant therapy. Chronic progressive pulmonary histoplasmosis is uncommon unless significant cavitation occurs or the patient has pre-existing pulmonary disease. Excessive fibrosis of lung tissue and lymph nodes occasionally results in progressive pulmonary disease.

Diagnosis

A firm diagnosis of histoplasmosis is made by either the isolation of the organism from appropriate clinical specimens or the histopathologic demonstration of the organism in tissue specimens. However, the organism rarely can be demonstrated or isolated except in the presence of disseminated disease or chronic pulmonary histoplasmosis. Therefore, indirect clues to the presence of histoplasmosis must be used. These include 1) history of exposure in an endemic area, 2) positive serologic tests, 3) positive skin tests, and 4) development of miliary calcifications in lung and spleen. Unfortunately, serologic and skin tests are sometimes negative for persons with culturally proved histoplasmosis, and test specificity has not been fully established. Numerous other disease entities may resemble histoplasmosis such as the acute nonbacterial pneumonias, hypersensitivity pneumonitis, tuberculosis, brucellosis, sarcoidosis, and lymphorcticular malignancies.

Therapy

Specific anti-fungal therapy for histoplasmosis is indicated for severely ill patients with acute pulmonary histoplasmosis, in patients with disseminated histoplasmosis, or chronic progressive cavitary pulmonary disease. The drug of choice is amphotericin B.

Prognosis

Over 95% of individuals who have been infected with *H. capsulatum* can recall no clinically distinctive illness and remain free of complications of the disease. However, primary acute disease can be serious and indeed fatal. Progressive disseminated disease, untreated, is uniformly fatal. Untreated, the chronic cavitary form of histoplasmosis results in progressive pulmonary disability and death in 50% of affected individuals within 5 years. Primary acute histoplasmosis rarely evolves directly into chronic cavitary or disseminated disease.

METHODS OF PREVENTION

Short of avoiding contact with known areas that harbor the organism, prevention of infection is difficult because of its widespread distribution. However, if work needs to be done in areas of known or suspected positivity, prewetting the ground may prevent some airborne dissemination. Only workers who are healthy and have known skin test positivity and normal chest x-rays should engage in the work process, and they should wear protective clothing and masks. Chemical decontamination with 3% formaldehyde has been shown to be an effective short-term fungicidal agent and may be useful, in addition to wetting the ground before work, in preventing outbreaks among workers (18)(22). There is no effective vaccine to prevent histoplasmosis.

RESEARCH NEEDS

Additional study is needed on the chemical, physical, and biologic factors influencing the growth of *H. capsulatum* in soil. Improved means of controlling large aggregations of birds and roosts should be sought. Safer and easier methods to decontaminate soil or other contaminated foci should be explored. Further work is necessary to develop an effective and safe vaccine to prevent disease in individuals at high risk for developing complications of the disease. Lastly, improvement is needed in the serologic diagnosis of histoplasmosis, and other less toxic agents for treatment need to be developed.

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BRUCELLOSIS

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DEFINITION

Brucellosis is an infectious disease caused by microorganisms of the genus *Brucella*. It usually affects domestic animals but can be transmitted to humans. Domestic animal diseases that are of public health concern are caused by *Brucella abortus, Br. suis,* and *Br. melitensis. Br. abortus* most commonly infects cattle, causing abortion late in pregnancy and a subsequent high infertility rate. Brucellosis in swine is most often caused by *Br. suis* and is a chronic disease manifested by sterility or abortion in sows, high piglet mortality rates, and orchitis in boars. *Br. melitensis* is the most common cause of brucellosis in goats, causing abortion late in pregnancy. *Br. canis,* affecting mainly dogs, has been associated with only a limited number of human infections and appears to be a less important human public health concern than the other three species.

Brucellosis in humans can be caused by any of the *Brucella* species and is an illness characterized by fever, chills, sweating, malaise, weakness, headache, myalgia, anorexia, and loss of weight.

ETIOLOGY

The etiological agents of Brucellosis are *Brucella abortus, Br. suis* and *Br. melitensis.* These Brucella microorganisms are pleomorphic, short, and slender coccobacilli. They stain gram-negative; bipolar staining is sometimes present. Differential characteristics of Brucella species based on physiological requirements and gas formation, growth in the presence of dyes, oxidative metabolic activities, lysis by phagocytes, and agglutination in monospecific antisera help identify individual species. No exotoxins are formed, but the cell has enterobacterial endotoxins.

OCCUPATIONS AND INDUSTRIES INVOLVED

As an occupational disease, brucellosis occurs in livestock producers, veterinarians, and rendering plant and abattoir employees. The incidence of the disease in the United States is steadily declining, with only about 200 cases currently being reported annually. Approximately half of the cases, primarily those in abattoir workers, are acquired from exposure in an industrial setting (Table IX-1)(5).

EPIDEMIOLOGY

In the United States, the reported incidence of brucellosis has declined from a peak of 6,321 cases in 1947 to its current plateau of 200 cases per year. Pasteurizing dairy products and attempting to eradicate the disease from livestock have been primarily responsible for the falling incidence of human brucellosis. Proportionately more abattoir employees than members of the general population continue to acquire brucellosis; of 2,126 cases from 1968 to 1977 for which information was available, 1,215 (57%) were in abattoir workers.

One investigation of brucellosis infection rates and route of infection in a swine abattoir (EPI 74-2-3, consultation on abattoir-associated brucellosis, Smithfield, Virginia, issued March 1974) revealed a 9% rate of seropositivity, and a greater correlation between exposure to airborne organisms in air from the kill department (Figure IX-1) than to conjunctival or skin contact with hog tissues or tissue fluids. Employees engaged in slaughtering and processing operations performed before deep tissues were exposed (Stage I Operations); in processing operations involving exposure to fresh raw tissue (Stage II Operations); or in other tasks requiring prolonged

Table IX-1

MOST PROBABLE SOURCE OF BRUCELLOSIS
BY OCCUPATIONAL GROUP OF PATIENTS, UNITED STATES, 1965-1974

	Occupational Group			
	Meat-Processing Industry	Livestock Industry	Other and Unknown	Total
Source				
Domestic Animals				
Swine	702	54	39	795
Cattle	121	179	52	352
Swine or Cattle	186	60	45	291
Sheep or Goats	7	5	6	18
Unspecified Farm Animals	57	4	2	63
Dogs	0	0	6	6
Wild Animals				
Caribou or Moose	0	0	12	12
Feral Swine	0	0	7	7
Deer	0	0	2	2
Unpasteurized Dairy Products				
Domestic	0	7	57	64
Foreign	0	2	125	127
Accidents				
Strain 19 vaccine	0	31	0	31
Laboratory	0	0	34	34
Unknown	0	12	233	245
Total	1,073	354	620	2,047
Percentage of Total	52.4	17.3	30.3	

exposure to the kill department (Mixed Operations), had the highest rates of seropositivity (Table IX-2).

In their review, Buchanan et al. noted all the major outbreaks of brucellosis that occurred in the period 1960-1972 were associated with swine slaughter (3). However, a resurgence of bovine brucellosis beginning in 1971-1972 made cattle the primary source of abattoir-acquired brucellosis by 1976.

POPULATION AT RISK

Of abattoir employees, kill department workers are at greatest risk of acquiring brucellosis. Although kill department workers constitute less than 20% of the approximately 150,000 abattoir workers in the United States, those with kill floor exposure have approximately 75% of the Brucella infections reported for abattoir employees. The multiple types of exposure to potentially contaminated animal tissues experienced by most kill department workers prevent the identification of the single "most" significant route.

PATHOLOGY

After they invade the body, brucellae localize in the bone marrow, lymph nodes, liver, and spleen. There they induce reticuloendothelial hyperplasia and the formation of small miliary granulomata. These have many similarities to the granulomata of sarcoidosis and miliary tubercu-

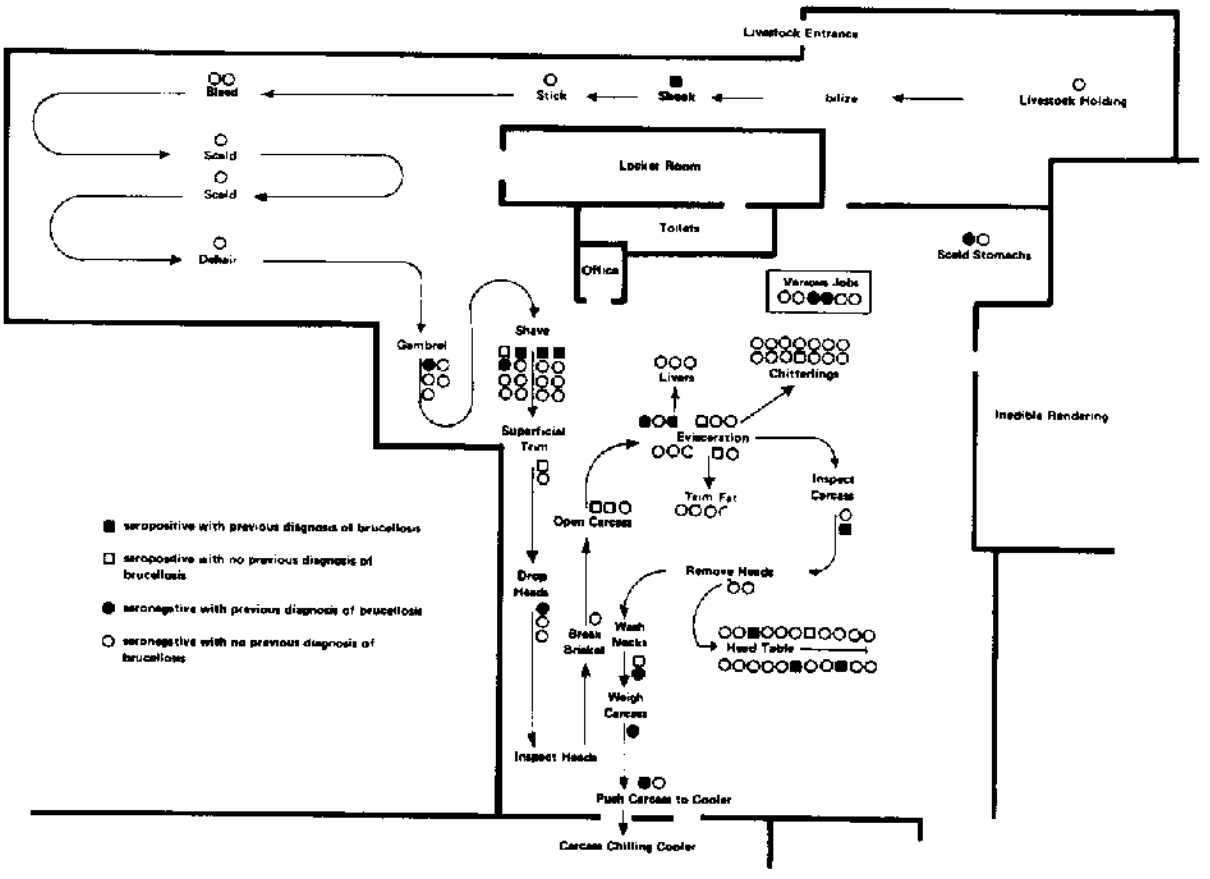

Figure IX-1. Hog Kill Department Employees by Work Location, Brucella Seropositivity and Previous History of Brucellosis, Smithfield, Virginia Packing Plant.

losis and consist of collections of macrophages and reticuloendothelial cells surrounded by a zone of mononuclear cells with some fibroblasts. Often there are giant cells. Rarely the center of the lesion may undergo necrosis with an associated polymorph infiltration, but typical caseation as seen in tuberculosis does not occur.

CLINICAL DESCRIPTION

Commonly reported symptoms of brucellosis include malaise, chills, sweating, weakness, body aches, headache, and anorexia. Clinical signs seen at physical examination include fever (either constant or intermittent), lymphadenopathy, and splenomegaly. Untreated, the illness may last for many months and can cause complications such as spondylitis, osteomyelitis, or endocarditis. Even with antibiotic therapy the patient may be ill for a month or more. Brucellosis is rarely fatal.

The treatment of choice for humans with brucellosis is tetracycline, 2 g daily by mouth for 21 days, with or without streptomycin, 1 g daily intramuscularly for 14 days. Buchanan et al. observed that patients treated with tetracycline and streptomycin had a lower rate of relapse than those treated with tetracycline alone or in combination with other drugs (2).

DIAGNOSTIC CRITERIA

Brucellosis can be definitively diagnosed by isolating the causative organism in culture. Blood is added to tryptase broth and incubated in an atmosphere containing 25% CO_2. The enrichment culture should be subcultured at four-day intervals and, if subcultures are negative, carried for a period of not less than three weeks. For subculture, agar plates of liver infusion or tryptase agar should be inoculated. Individuals suspected of being infected by *Brucella* microorganisms should have appropriate blood samples taken from cultures. Attempts to isolate the organism should be repeated several times before therapy is instituted since bacteremia may be intermittent. For patients with chronic brucellosis, cultures of blood, bone marrow, and other tissues may be productive.

Table IX-2

SEROPOSITIVITY BY WORK DEPARTMENT
SMITHFIELD, VIRGINIA — SEPTEMBER 1973

	Centrifugation Agglutination Test Titer>1:160			
	All Employees Surveyed		Excluding Employees in Departments Other Than Kill Who Previously Worked in the Kill Department	
Stage I Operation				
Kill Dept.	6/31	(19.4%)	6/31	(19.4%)
Stage II Operations				
Kill Dept.	11/81	(13.6%)	11/81	(13.6%)
Lard Rendering Dept.	2/7	(28.6%)	2/6	(33.3%)
Inedible Rendering Dept.	0/8	(0.0%)	0/8	(0.0%)
Total Stage II	13/96	(13.5%)	13/95	(13.7%)
Stage III Operations				
Cut Dept.	4/51	(7.8%)	4/41	(9.8%)
Conversion Dept.	0/5	(0.8%)	0/3	(0.0%)
Ham Boning Dept.	0/19	(0.0%)	0/14	(0.0%)
Bacon Slicing Dept.	0/21	(0.0%)	0/18	(0.0%)
Cure-Pump-Hang Dept.	0/11	(0.0%)	0/10	(0.0%)
Smoked Meat Packing Dept.	2/17	(11.8%)	0/14	(0.0%)
Sausage Packing Dept.	0/19	(0.0%)	0/14	(0.0%)
Sausage Chopping Dept.	0/4	(0.0%)	0/4	(0.0%)
Sausage Stuffing Dept.	0/6	(0.0%)	0/5	(0.0%)
Fresh Sausage Dept.	1/14	(7.1%)	0/10	(0.0%)
Total Stage III	7/167	(4.2%)	4/133	(3.0%)
Mixed Operations				
Maintenance Dept.	5/24	(20.8%)	3/20	(15.0%)
Miscellaneous Dept.	2/11	(18.2%)	1/7	(14.3%)
Total Mixed	7/35	(20.0%)	4/27	(14.8%)
NonProcessing Operations				
Delivery Dept.	0/28	(0.0%)	0/28	(0.0%)
Sanitation Dept.	0/4	(0.0%)	0/3	(0.0%)
Total NonProcessing	0/32	(0.0%)	0/31	(0.0%)
GRAND TOTAL	33/361	(9.1%)	27/317	(8.5%)

Brucellosis is commonly diagnosed serologically. The standard tube agglutination (STA) test is the most sensitive and widely used serologic test in the United States. Although this procedure involves using *Br. abortus* as antigen, it can be used to detect infections caused by *Br. melitensis*, and *Br. suis*, because all three have common antigenic determinants. *Br. canis* infection, however, can only be detected by using the specific antigen.

The 2-mercaptoethanol (2-ME) degradation test is used as an adjunct to the STA test. 2-ME, added to patient's serum before an agglutination test is performed, dissociates the IgM molecules so that any residual agglutination is caused by IgG antibodies. It has been found that the level of IgG remains elevated in persons with chronic brucellosis and disappears in those who are adequately treated. Thus the 2-ME test is particularly useful when low STA titers could indicate either current or past infection.

Both cholera vaccination and tularemia can falsely elevate STA titers (usually only minimally). The etiology of the elevated STA titer can be resolved by evaluating a clinical history or results of specific serological absorption studies.

Individuals suspected of having brucellosis, but whose culture and serologic results are negative pose a significant diagnostic problem. Of the several possible reasons for negative serologic results, the most important are 1) the prozone phenomenon, 2) the presence of blocking antibody in patient serum, 3) *Br. canis* infection in an individual whose sample was analyzed with an STA test in which *Br. canis* was not used as antigen, and 4) the disease is not brucellosis.

The problems of the prozone phenomenon and blocking antibody can be countered with specialized serologic techniques. Since prozone occurs only at lower serum dilutions, serial dilutions of serum samples should all be evaluated before the test is reported to be negative.

The presence of a blocking antibody is more difficult to prove than the prozone phenomenon, but it can be documented by using the Coombs test or centrifuging the reaction tubes before incubation.

PREVENTION

Although eye and skin protection should lower the risk of industrially related brucellosis, protective clothing and equipment commonly worn in abattoirs have apparently not been very effective. Metal mesh gloves protect against more serious cuts, but minor scratches and abrasions provide equally effective portals of entry for *Brucella* organisms. Rubber gloves should provide protection against contact exposure, but the gloves generally used do not cover wrists and forearms, and blood and other potentially infectious materials can enter the gloves through their open end and through accidental perforations. Where the conjunctival route of infection is important, ordinary eyeglasses have not been shown to provide protection.

Other than reducing unnecessary exposure to potentially infectious aerosols generated in the kill room, little can be done on a practical basis to prevent airborne or other transmission of brucellosis to abattoir workers. However, early diagnosis and appropriate therapy will reduce the duration and severity of the illness as well as the frequency of complications.

Only essential personnel should enter the kill room, which should be under negative air pressure in relation to other work areas. Employees should be instructed on how brucellosis is acquired, its symptoms, and the need for prompt diagnosis and therapy. Brucellosis should be routinely considered in the differential diagnosis of febrile illnesses in abattoir workers.

RESEARCH NEEDS

Surveillance of brucellosis and the epidemiologic study of specific problems dealing with abattoir-associated brucellosis should be continued. This is especially important where recommended control measures are of potential rather than proven benefit. Efforts to develop a safe and effective human brucellosis vaccine need to be continued, and vaccine use would probably be highly cost beneficial when administered to targeted populations such as abattoir or laboratory workers.

Further clinical studies dealing with safe and effective treatment of brucellosis are needed. New antibiotics such as trimethoprim-sulfonamide combinations must be thoroughly evaluated before they can be confidently recommended for treating patients with brucellosis.

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TUBERCULOSIS AS AN OCCUPATIONAL DISEASE

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DEFINITION

Tuberculosis is a communicable disease of man and animals caused by the bacterium *Mycobacterium tuberculosis* and, less frequently, *M. bovis.* Lesions most often occur in the lungs but may be found in any part of the body.

CAUSATIVE AGENTS

Species of *Mycobacterium* are characterized by unusual "acid fast" staining properties, slow growth, relative resistance to chemical disinfectants, and the ability to survive for decades within cells in the infected animal. Several species are known to cause human illness, but the virulence and communicability of *M. tuberculosis* make it by far the most significant human pathogen. With the exception of a comment in Research Needs, the information in this section pertains to *M. tuberculosis.*

LIST OF OCCUPATIONS AND INDUSTRIES INVOLVED

Tuberculosis is a contagious disease and can spread among individuals of any occupation. The few published studies of tuberculosis as an occupational hazard suggest that physicians, nurses, medical laboratory workers, and miners are at increased risk of tuberculosis (1)(3)(4). Other occupations presumably at increased risk are migrant workers, overseas personnel in any occupation, zoo employees, prison guards, and social workers and others who work with the impoverished and the derelict.

EPIDEMIOLOGY

Infection is almost always acquired via inhalation of contaminated microscopic particles generated by coughing, sneezing, speaking, or singing. Therefore, persons most likely to become infected are those with a prolonged exposure in a confined area to an infectious person.

In 1981, 27,373 cases of tuberculosis were reported in the United States for an annual incidence of 11.9 per 100,000 persons. The incidence is higher in older age groups, in nonwhite persons, and in males. The incidence is also high among immigrants, alcoholics, and prisoners, but sufficient data are not available to calculate specific rates.

Unfortunately, few studies of tuberculosis incidence among various occupations have been reported. Therefore, only general and somewhat unsatisfactory comments can be made about tuberculosis as an occupational hazard.

Doctors, nurses, and medical laboratory workers are at greater risk than the population as a whole because they care for persons with tuberculosis. Barrett-Connor recently estimated the infection rate of physicians was about twice that of the general population (1). Harrington calculated the disease rate of medical laboratory workers in England was above five times that of the general population (see Table IX-3) (3). Individuals who work with elderly persons, nonwhite persons, immigrants, alcoholics, or prisoners presumably are at increased (but unquantitated) risk of infection.

Miners and others who work in poorly ventilated areas are more likely to be infected by a fellow worker who has tuberculosis than are persons who work in well ventilated areas. Studies among different groups of miners show that the tuberculosis mortality rate ranges from approximately 1.5 times expected for coal miners to approximately 10 times expected for cummingtonite-grunerite miners (see Table IX-3)(4)(5).

ESTIMATE OF POPULATION AT RISK AND PREVALENCE OF DISEASE

Table IX-3 shows that between 1,099 and 4,784 persons have tuberculosis disease because they work in a medical or mining occupation. Un-

Table IX-3

ESTIMATED NUMBER OF PERSONS WITH TUBERCULOSIS ATTRIBUTABLE TO OCCUPATIONAL EXPOSURE, 1977

Occupation	Number of Persons (1)	Relative Rick of Tuberculosis	Estimated Incidence (4)	Estimated Attributable Incidence	Estimated Prevalence (5)	Estimated Attributable Prevalence
Medicine	3,853,000	2-5(2)	1,071-2,678	536-2,142	2,142-5,356	1,071-4,284
Mining	200,000	1½-10(3)	42-278	14-250	84-556	28-500
Social Workers	444,000					
Prison Guards						
Zoo employees						
Migrant Workers	130,000					
Overseas employees						

(1) U.S. Bureau of Census, 1978.
(2) Barrett-Conner, 1979; Harrington 1976.
(3) McDonald, 1978; Rockette, 1977.
(4) Based on United States incidence in 1977 of 13.9 per 100,000.
(5) Assumes average duration of illness is 2 years.

fortunately, sufficient data are not available to estimate the risk to persons in other occupations.

PATHOLOGY

Most tuberculous infections follow inhalation of the bacteria. Less frequently, infections occur after ingestion of direct inoculation through the skin. The bacilli multiply at the site of initial implantation and, if not contained by host defenses, are carried through the lymphatics to local and then more distant lymph nodes.

Usually the bacilli are contained by the host defenses. In some cases, however, either shortly after infection or after a prolonged dormancy, the organisms continue to multiply causing the systemic signs and symptoms of chronic infection with progressive destruction of the organ primarily involved (most often the lungs).

Workers exposed to silica are more likely to have tuberculosis because silica interferes with the function of the pulmonary macrophages (6). We do not know if other chemicals or minerals predispose to tuberculosis for similar reasons.

CLINICAL DESCRIPTION

Symptoms

Pulmonary tuberculosis is manifested by constitutional symptoms of loss of appetite, weight loss, fatigue, fever, night sweats, malaise, and organ-specific symptoms of cough (often productive of sputum and/or blood) and chest pain. Tuberculosis of other organs (such as kidneys or bones) causes the constitutional symptoms listed above plus symptoms specific to the organ involved.

Signs

Pulmonary tuberculosis, depending on its severity and duration, may be associated with nonspecific signs of chronic infection such as anemia. Pulmonary tuberculosis also may produce a variety of signs related to the respiratory tract such as rapid breathing and abnormal physical signs on percussion and auscultation of the chest. The chest x-ray is usually abnormal and often characteristic, but never diagnostic of tuberculosis. The lesions are usually patchy, in the apices of the lungs, and often cavitary.

The signs of tuberculosis of other organs include the (already mentioned) nonspecific signs plus signs specific to the organ involved. For example, tuberculous meningitis may cause cranial nerve damage, blindness, deafness, and disorders of consciousness from confusion to coma. Examination of the cerebral spinal fluid usually shows an increased cell count, increased protein concentration, and decreased glucose concentration. *Mycobacterium tuberculosis* may be demonstrated by appropriate stain or culture.

The Natural History of Disease

Most infections with *M. tuberculosis* are subclinical or unrecognized; the only evidence of infection is a positive tuberculin skin test. Progressive disease occurs in about 5% of persons within the first year after infection and in another 5% later in life. Therefore, once in-

fected, the risk of progressive disease exists for life. Unless treated with antituberculous chemotherapy, about 50% of persons who develop clinical illness die, frequently after months to years of progressive debilitation. Modern chemotherapy, however, if administered promptly and properly (see Treatment), will cure most patients.

Appropriate Laboratory Studies

The single most important laboratory study is the examination of secretions—usually sputum — or tissue for the infecting organism. Special media and procedures are required to culture *M. tuberculosis*. For persons with pulmonary tuberculosis, chest x-ray also is important.

Treatment

Antimicrobial drugs can cure tuberculosis. However the capability of the slowly growing *M. tuberculosis* to lie dormant within the host's cells necessitates prolonged drug treatment. Currently recommended therapy is 9-18 months of daily treatment with 2 or more drugs. Prolonged bedrest and surgery, formerly the mainstays of therapy, now have a very limited role in the treatment of tuberculosis.

Prognosis

Promptly and properly administered chemotherapy confers an excellent prognosis. Although treatment is prolonged, most patients recover with minimal residua. Unfortunately, the long duration of treatment often results in erratic or incomplete ingestion of medicines. Inadequate chemotherapy may result in recurrent episodes of disease, progressive disability, and death.

DIAGNOSTIC CRITERIA

The diagnosis of tuberculosis is confirmed by the growth of *M. tuberculosis* from culture of sputum, CSF, urine, lymph nodes, or other infected tissue. If the organism cannot be grown, the diagnosis of tuberculosis should be made if the patient has a positive tuberculin skin test, the signs and symptoms are compatible with tuberculosis, a thorough evaluation uncovers no other cause for the illness, and the response to therapy is appropriate.

The most common diseases mimicking tuberculosis are systemic fungal infections, other mycobacterial infections, sarcoidosis, cancer, and the pneumoconioses.

METHODS OF PREVENTION

Transmission of tuberculosis can be prevented by the rapid identification and treatment of persons with disease and by the identification and treatment of those persons infected but not yet diseased (i.e., persons with only a positive skin test).

RESEARCH NEEDS

1. More information is needed about the incidence of tuberculosis in occupational groups, particularly those presumed to be at risk of infection.
2. Although a synergism between silicosis and tuberculosis is established, little information exists about possible synergism between tuberculosis and other mineral and chemical exposures.
3. The probable salubrious effect of more active participation of employers in the maintenance of chemotherapy among infected employees should be explored. Patients with tuberculosis can work and the workplace may be a good place to encourage regular drug usage to prevent relapse, progressive disease, and possible transmission. (Denial of employment to a noninfectious person who is on medication, because of fear of spread to fellow employees, is counter-productive and should not be tolerated.)
4. Cost-effective methods to identify contagious persons earlier in the course of illness need imaginative research.
5. Information is needed about the incidence of other Mycobacterial infections among various occupational groups.

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PSITTACOSIS

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DEFINITION

Psittacosis is an acute infectious disease of humans characterized by fever, pneumonia, cough, weakness, fatigue, chills, headaches, myalgia, and occasionally myocarditis and encephalitis.

ETIOLOGIC AGENT

The etiologic agent, *Chlamydia psittaci* is one of several microorganisms that comprise the single genus *Chlamydia*. Once considered to be viruses because they reproduced only within host cells, several properties clearly relate *chlamydia* to bacteria: 1) the presence of both DNA and RNA, 2) division by binary fission, 3) cell walls like those of free-living gram negative bacteria, and 4) susceptibility to antibiotics. *Chlamydia psittaci*, has its reservoir in various domestic and wild birds. The disease has been called psittacosis when it affects psittacine species (i.e., parrots and related birds) and ornithosis when it affects other avian species. Although these terms have been used interchangeably, perhaps the more general term "chlamydiosis" would be preferable.

OCCUPATIONS AND INDUSTRIES INVOLVED

Psittacosis is an occupational health hazard for a large and growing number of individuals employed in quarantine facilities, pet shops, breeding aviaries, veterinary clinics, diagnostic laboratories, and avian distribution networks including wholesale aviaries and air or surface freight companies. Psittacosis (ornithosis) in turkey flocks causes many sporadic human cases in the poultry processing industry. The total number of persons at risk of occupationally related psittacosis is uncertain but probably exceeds 20,000. Approximately 70 cases of psittacosis have been reported annually in the past decade, with about one-third being occupationally acquired or associated. In the period 1975-1977, 48 (20%) of 236 reported cases were associated with the patients' occupations: 22 with the pet bird industry and 26 with the poultry processing industry (Table IX-4) (2).

EPIDEMIOLOGY

Although psittacosis was rarely reported in the United States before 1929, in November of that year, cases of psittacosis began to be reported from various sections of the country. Within the next 6 months, nearly 200 cases (33 fatal) of psittacosis were reported. After these cases were shown to be associated with exposure to parrots imported for the 1929 Christmas trade, the commercial importation of parrots was prohibited in January 1930. Investigations in the period 1935-1950 revealed that psittacosis affected many or all avian species. When available effective antibiotic therapy had lowered the mortality rate, restrictions on importation and interstate shipment of psittacine birds were relaxed. Currently, psittacine birds are imported into domestically located quarantine stations supervised by the U.S. Department of Agriculture (USDA). Although the quarantined birds must be treated with chlortetracycline, adequate blood levels of antibiotics are not always achieved, as evidenced by the fact that psittacosis has been diagnosed in psittacine birds recently released from quarantine. Some employees and government inspectors at quarantine facilities have also had psittacosis.

In the past decade, 8 epidemics involving 142 cases have occurred at 7 turkey processing plants in Texas, Missouri, and Nebraska (Figure IX-2). In an investigation of one outbreak, inhalation of infectious aerosols was clearly implicated as the primary route of exposure (1). Employees in the kill and pick evisceration departments were at the greatest risk.

Although direct contact or inhalation of

Table IX-4

HUMAN PSITTACOSIS CASES BY TYPE OF EXPOSURE AND MOST PROBABLE SOURCE OF INFECTION, UNITED STATES, 1975-1977

SOURCE	*Non-Bird Owner*	*Pet Bird Owner*	*Bird Fancier*	*Pigeon Fancier*	*Pet Shop Employee*	*Other Commercial Trade*	*Poultry Production*	*Poultry Processing*	*Miscellaneous*	*Unknown*	*Total*	*Percentage of Total*
Budgerigars	2	28	3			1			1	1	36	15.2
Cockatiels	1	12	1								14	5.9
Other Psittacine sp.	3	19	3		7	1					33	14.0
Unspecified Psittacine sp.	3	3	2		5	2					15	6.4
Psittacine/Non-Psittacine	3	6	6		6				2		23	9.7
Canaries/Finches	1	3									4	1.7
Domestic Pigeons	4	1	1	17						1	24	10.2
Wild Pigeons	7	2							4	2	15	6.4
Miscellaneous Wild Birds	3	1									4	1.7
Turkeys							1	26	2		29	12.3
Chickens	1						3				4	1.7
Turkeys/Other Birds							1		1		2	0.8
Other Miscellaneous	4	1							2		7	3.0
Unknown	11									15	26	11.0
Total	43	76	16	17	18	4	5	26	12	19	236	100.0

aerosolized tissues has been implicated in disease transmission in turkey processing plants, infection can also be spread by aerosolized bird feces. Person-to-person transmission has been reported only rarely and probably is not important in the epidemiology of the disease.

ESTIMATE OF POPULATION AT RISK AND PREVALENCE OF DISEASE

See Table IX-4 above.

PATHOLOGY

Postmortem examination of persons who have died from psittacosis generally reveals focal or lobar consolidation of the lungs. The alveoli may be filled with exudate and alveolar septal cell hyperplasia may be marked; bronchioles are rarely involved. Splenomegaly is common, and normal splenic architecture may be altered by reticuloendotheliae hyperplasia and focal necrosis. Hepatic focal necrosis is also common. Cardiac involvement in psittacosis cases has been associated with hemorrhagic areas in the endocardium of the valves and evidence of pericarditis and myocarditis.

CLINICAL DESCRIPTION

Although psittacosis is primarily a respiratory disease, it can cause a wide variety of clinical manifestations. Generally, about 10 days (range 4 to 15 or more days) after infection occurs, the clinical illness begins abruptly with fever, chills, weakness, fatigue, myalgia, anorexia, nausea, vomiting, diaphoresis, dyspnea, headache, back-

PSITTACOSIS IN HUMANS, UNITED STATES, 1965-1977

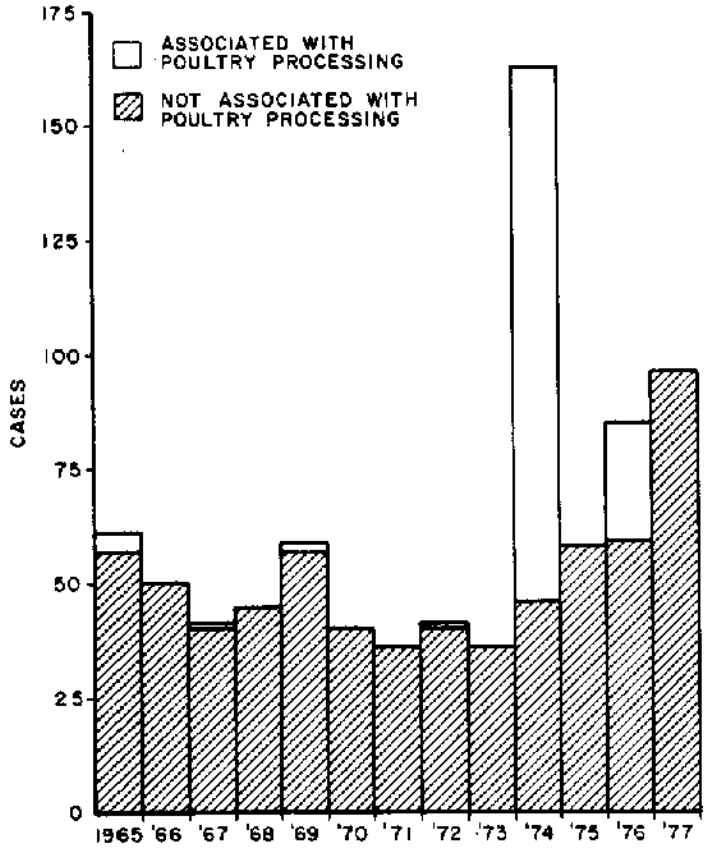

Figure IX-2. Psittacosis in humans, United States, 1965-1977

ache, and photophobia. Prominent clinical signs include pneumonia, weight loss, pleuritic chest pain, hepatomegaly, splenomegaly, and meningismus. Other than a nonproductive cough, signs and symptoms of pneumonia are often minimal, however, chest x-rays commonly reveal a surprising degree of pulmonary involvement. The patchy infiltrates caused by psittacosis frequently resemble those caused by a number of viral agents.

Psittacosis is a systemic disease and can involve multiple organs. Hepatitis, endocarditis, myocarditis, thrombophlebitis, meningoencephalitis, pericardial effusion, disseminated intravascular coagulation, and myositis have all been reported.

Tetracyclines are the drug of choice for treating patients with psittacosis. Chloramphenicol, erythromycin, gentamicin, penicillin, and ampicillin have also been used, but reports of their therapeutic efficacy are largely anecdotal. The dosage and duration for adequate tetracycline therapy are still in dispute. Some authorities recommend 2 grams daily by mouth for 7 days after defervescence (5); others recommend 1 gram daily by mouth for 21 days (7). Most authorities agree that inadequate therapy leads to a risk of relapse.

Although there is generally a dramatic response to tetracycline, the patient may continue to tire easily even after adequate therapy. The case-fatality rate of reported cases in the United States is approximately 1%.

DIAGNOSTIC CRITERIA

A diagnosis of psittacosis is based upon a history of exposure to birds, evidence of infection in the suspected avian source, signs and

symptoms, and laboratory findings.

The laboratory diagnosis of psittacosis relies on serologic test results or cultural isolation of *Chlamydia psittaci*. If possible, the etiologic agent should be isolated before antibiotics are given. Clinical specimens for culture include blood clots and throat washings, which should be shipped to the laboratory frozen on dry ice. Commonly used test systems involve inoculating patient specimens into tissue culture, mice, and eggs. Typical inclusions are then demonstrated with the Gimenez modification of Macchiavello's technique. Laboratory personnel should take special precautions in handling *Chlamydia psittaci* specimens; they are highly infectious.

The complement fixation test is the most widely used serologic procedure for diagnosing psittacosis. A fourfold change in titer (to at least 32) between 2 serum samples collected 2 or more weeks apart, and tested concurrently, is generally accepted as evidence of current infection. Inasmuch as a chlamydial group antigen is used in the serologic test for psittacosis, a history of other chlamydial infections such as lymphogranuloma venereum must be taken into account when results are interpreted.

PREVENTION

No effective vaccine has been developed for psittacosis. Whether naturally acquired infection confers immunity to humans is still not known; infected birds do not become immune.

Controlling exposure to psittacosis for employees in the pet bird trade would probably require banning the importation of psittacine birds, or tightly controlling individual bird identification, importation, and interstate shipment. Adequate controls may not be cost effective. The USDA has intermittently sponsored a program of screening and tetracycline treatment of turkeys to be slaughtered—in attempts to minimize the public health problem associated with poultry processing.

RESEARCH NEEDS

Improved techniques for the treatment of psittacosis in infected birds are needed because currently recommended tetracycline feeding procedures are not reliable. In the case of psittacine birds other than parakeets, the procedures are complicated and may cause adverse side effects in the birds.

Serologic methods with a high degree of sensitivity and specificity are needed for accurate diagnosis. Current complement fixation tests do not clearly differentiate psittacosis from other human chlamydial infections. Other chlamydial diseases are more common than psittascosis, and preexistent antibodies due to these diseases may lead to misdiagnosis of respiratory diseases due to nonchlamydial organisms such as psittacosis. In addition, the clinical spectrum of the various chlamydial diseases overlap, further complicating accurate diagnosis.

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