

## CHAPTER 8

### AGENT SUMMARY STATEMENTS

#### Bacterial Agents

##### Agent: *Bacillus anthracis*

Numerous cases of laboratory-associated anthrax, occurring primarily at facilities conducting anthrax research, have been reported.<sup>(1)(2)</sup> No laboratory-associated cases of anthrax have been reported in the United States since the late 1950s when human anthrax vaccine was introduced. Any work with *B. anthracis* requires special security considerations due to its potential use for purposes of biological terrorism. Naturally and experimentally infected animals pose a potential risk to laboratory and animal care personnel.

*Laboratory Hazards:* The agent may be present in blood, skin lesion exudates, cerebrospinal fluid, pleural fluid, sputum, and rarely, in urine and feces. Direct and indirect contact of the intact and broken skin with cultures and contaminated laboratory surfaces, accidental parenteral inoculation, and rarely, exposure to infectious aerosols are the primary hazards to laboratory personnel.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities using clinical materials and diagnostic quantities of infectious cultures. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for studies utilizing experimentally infected laboratory rodents. Biosafety Level 3 practices, containment equipment, and facilities are recommended for work involving production quantities or concentrations of cultures, and for activities with a high potential for aerosol production.

*Note:* A licensed vaccine is available through the Centers for Disease Control and Prevention; however, immunization of laboratory personnel is not recommended unless frequent work with clinical specimens or diagnostic cultures is anticipated (e.g., animal disease diagnostic laboratory). In these facilities immunization is recommended for all persons working with the agent, all persons working in the same laboratory room where the cultures are handled, and persons working with infected animals.

*Transfer of Agent:* For a permit to import this agent, contact CDC. Contact the Department of Commerce for a permit to export this agent. Laboratory registration with CDC is required before sending or receiving this select agent. An importation or domestic transfer permit for this agent can be obtained from USDA/APHIS/VS.

**Agent: Bordetella pertussis**

*Bordetella pertussis*, a human respiratory pathogen of worldwide distribution, is the causative agent of whooping cough. The disease is typically a childhood illness; however, the agent has increasingly been associated with adult illness.<sup>(3)(4)(5)</sup> Several outbreaks in health-care workers have been reported in the literature.<sup>(6)(7)</sup> Adolescents and adults with atypical or undiagnosed disease can serve as reservoirs of infection and transmit the organism to infants and children.<sup>(8)</sup> Eight cases of infection with *B. pertussis* in adults have been documented at a large research institution. The individuals involved did not work directly with the organism, but had access to common laboratory spaces where the organism was manipulated. One case of secondary transmission to a family member was documented.<sup>(9)</sup> A similar incident occurred at a large Midwestern university resulting in two documented cases of laboratory-acquired infection and one documented case of secondary transmission.<sup>(10)</sup> Other laboratory-acquired infections with *B. pertussis* have been reported, as well as adult-to-adult transmission in the workplace.<sup>(11) (12)</sup> Laboratory-acquired infections resulting from the manipulation of clinical specimens or isolates have not been reported. The attack rate of this airborne infection is influenced by intimacy and frequency of exposure of susceptible individuals.

*Laboratory Hazards:* The agent may be present in respiratory secretions, but is not found in blood or tissue. Since the natural mode of transmission is by the respiratory route, the greatest potential hazard is aerosol generation during the manipulation of cultures or concentrated suspensions of the organism.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of known or potentially infectious clinical materials or cultures. Animal Biosafety Level 2 should be used for the housing of infected animals. Primary containment devices and equipment (e.g., biological safety cabinets, centrifuge safety cups, or specially designed safety centrifuges) should be used for activities likely to generate potentially infectious aerosols. Biosafety Level 3 practices, procedures, and facilities are appropriate when engaged in large scale production operations.

*Note:* Pertussis vaccines are available but are not currently recommended for use in adults. The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for pertussis vaccination in adults.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

**Agent: Brucella (B. abortus, B. canis, B. melitensis, B. suis)**

Brucellosis continues to be the most commonly reported laboratory-associated bacterial infection.<sup>(13)(14)(15)</sup> *B. abortus*, *B. canis*, *B. melitensis*, and *B. suis* have all caused illness in

laboratory personnel.<sup>(16)(17)(18)</sup> Hypersensitivity to *Brucella* antigens is also a hazard to laboratory personnel. Occasional cases have been attributed to exposure to experimentally and naturally infected animals or their tissues.

*Laboratory Hazards:* The agent may be present in blood, cerebrospinal fluid, semen, and occasionally urine. Most laboratory-associated cases have occurred in research facilities and have involved exposure to *Brucella* organisms grown in large quantities. Cases have also occurred in the clinical laboratory setting from sniffing bacteriological cultures.<sup>(19)</sup> Direct skin contact with cultures or with infectious clinical specimens from animals (e.g., blood, uterine discharges) are commonly implicated in these cases. Aerosols generated during laboratory procedures have caused large outbreaks.<sup>(20)(21)</sup> Mouth pipetting, accidental parenteral inoculations, and sprays into eyes, nose, and mouth have also resulted in infection.

*Recommended Precautions:* Biosafety Level 2 practices are recommended for activities with clinical specimens of human or animal origin containing or potentially containing pathogenic *Brucella* spp. Biosafety Level 3 and Animal Biosafety Level 3 practices, containment equipment, and facilities are recommended, respectively, for all manipulations of cultures of the pathogenic *Brucella* spp. listed in this summary, and for experimental animal studies.

*Note:* While human *Brucella* vaccines have been developed and tested in other countries with limited success, at the time of this publication no human vaccine is available in the United States.<sup>(22)</sup>

*Transfer of Agent:* For a permit to import this agent, contact CDC. Contact the Department of Commerce for a permit to export this agent. Laboratory registration with CDC is required before sending or receiving this select agent. An importation or domestic transfer permit for this agent can be obtained from USDA/APHIS/VS.

Two laboratory-associated cases of melioidosis have been reported: one associated with a massive aerosol and skin exposure;<sup>(23)</sup> the second resulting from an aerosol created during the open-flask sonication of a culture presumed to be *Ps. cepacia*.<sup>(24)</sup>

*Laboratory Hazards:* The agent may be present in sputum, blood, wound exudates and various tissues depending on the infection's site of localization. Direct contact with cultures and infectious materials from humans, animals, or the environment, ingestion, autoinoculation, and exposure to infectious aerosols and droplets are the primary laboratory hazards. The agent has been demonstrated in blood, sputum, and abscess materials and may be present in soil and water samples from endemic areas.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious body fluids, tissues, and cultures. Gloves should be worn when handling infected animals, during their necropsy, and when there is the likelihood of direct skin contact with infectious materials. Additional primary containment and personnel precautions, such as

those described for Biosafety Level 3, may be indicated for activities with a high potential for aerosol or droplet production, and for activities involving production quantities or concentrations of infectious materials. Vaccines are not currently available for use in humans.

*Transfer of Agent:* Contact the Department of Commerce for a permit to export this agent.

**Agent: Campylobacter (*C. jejuni*/*C. coli*, *C. fetus* subsp. *fetus*)**

*C. jejuni*/*C. coli* gastroenteritis is rarely a cause of laboratory-associated illness, although laboratory-acquired cases have been documented.<sup>(25)(26)(27)</sup> Numerous domestic and wild animals, including poultry, pets, farm animals, laboratory animals, and wild birds are known reservoirs and are a potential source of infection for laboratory and animal care personnel. Experimentally infected animals are also a potential source of infection.<sup>(28)</sup>

*Laboratory Hazards:* Pathogenic campylobacters may occur in fecal specimens in large numbers. *C. fetus* subsp. *fetus* may also be present in blood, exudates from abscesses, tissues, and sputa. Ingestion or parenteral inoculation of *C. jejuni* constitute the primary laboratory hazards. The oral ingestion of 500 organisms caused infection in one individual.<sup>(29)</sup> The importance of aerosol exposure is not known.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with cultures or potentially infectious clinical materials. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with naturally or experimentally infected animals. Vaccines are currently not available for use in humans.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

**Agent: Chlamydia psittaci, C. pneumoniae, C. trachomatis**

Psittacosis, lymphogranuloma venereum (LGV), and trachoma infections were at one time among the most commonly reported laboratory-associated bacterial infections.<sup>(30)</sup> In cases reported before 1955,<sup>(31)</sup> the majority of infections were psittacosis, and these had the highest case fatality rate of laboratory-acquired infectious agents. Contact with and exposure to infectious aerosols in the handling, care, or necropsy of naturally or experimentally infected birds are the major sources of laboratory-associated psittacosis. Infected mice and eggs are less important sources of *C. psittaci*. Laboratory animals are not a reported source of human infection with *C. trachomatis*.

*Laboratory Hazards:* *C. psittaci* may be present in the tissues, feces, nasal secretions and blood of infected birds, and in blood, sputum, and tissues of infected humans. *C. trachomatis* may be present in genital, bubo, and conjunctival fluids of infected humans.

Exposure to infectious aerosols and droplets, created during the handling of infected birds and tissues, are the primary hazards to laboratory personnel working with psittacosis. The primary laboratory hazards of *C. trachomatis* are accidental parenteral inoculation and direct and indirect exposure of mucous membranes of the eyes, nose, and mouth to genital, bubo, or conjunctival fluids, cell culture materials, and fluids from infected eggs. Infectious aerosols may also pose a potential source of infection.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities involving the necropsy of infected birds and the diagnostic examination of tissues or cultures known to contain or potentially infected with *C. psittaci* or *C. trachomatis*. Wetting the feathers of infected birds with a detergent-disinfectant prior to necropsy can appreciably reduce the risk of aerosols of infected feces and nasal secretions on the feathers and external surfaces of the bird. Animal Biosafety Level 2 practices, containment equipment, and facilities and respiratory protection are recommended for personnel working with naturally or experimentally infected caged birds. Gloves are recommended for the necropsy of birds and mice, the opening of inoculated eggs, and when there is the likelihood of direct skin contact with infected tissues, bubo fluids, and other clinical materials. Biosafety Level 3 facilities and practices are indicated for activities with high potential for droplet or aerosol production and for activities involving large quantities or concentrations of infectious materials.

*Note:* Vaccines are not currently available for use in humans.

*Transfer of Agent:* Contact the Department of Commerce for a permit to export these agents.

### **Agent: Clostridium botulinum**

While there is only one report<sup>(32)</sup> of botulism associated with the handling of the agent or toxin in the laboratory or working with naturally or experimentally infected animals, the consequences of such intoxications must still be considered quite grave. Work with cultures of *C. botulinum* requires special security considerations due to their potential use for purposes of biological terrorism.

*Laboratory Hazards:* *C. botulinum* or its toxin may be present in a variety of food products, clinical materials (serum, feces), and environmental samples (soil, surface water). Exposure to the toxin of *C. botulinum* is the primary laboratory hazard. The toxin may be absorbed after ingestion or following contact with the skin, eyes, or mucous membranes, including the respiratory tract.<sup>(33)</sup> Accidental parenteral inoculation may also represent a significant exposure to toxin. Broth cultures grown under conditions of optimal toxin production may contain  $2 \times 10^6$  mouse LD<sub>50</sub> per mL.<sup>(34)</sup>

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities with materials known to contain or potentially containing the toxin. A pentavalent (ABCDE) botulism toxoid is available through the Centers for Disease Control and Prevention, as an investigational new drug (IND). This

toxoid is recommended for personnel working with cultures of *C. botulinum* or its toxins. Solutions of sodium hypochlorite (0.1%) or sodium hydroxide (0.1N) readily inactivate the toxin and are recommended for decontaminating work surfaces and spills of cultures or toxin. Additional primary containment and personnel precautions, such as those recommended for Biosafety Level 3, are indicated for activities with a high potential for aerosol or droplet production, and those involving production quantities of toxin. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for diagnostic studies and titration of toxin.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: Clostridium tetani**

Although the risk of infection to laboratory personnel is negligible, five incidents related to exposure of personnel during manipulation of the toxin have been recorded.<sup>(35)</sup>

*Laboratory Hazards:* Accidental parenteral inoculation and ingestion of the toxin are the primary hazards to laboratory personnel. Because it is uncertain if tetanus toxin can be absorbed through mucous membranes, the hazards associated with aerosols and droplets remain unclear.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities involving the manipulation of cultures or toxin. While the risk of laboratory-associated tetanus is low, the administration of an adult diphtheria-tetanus toxoid at 10-year intervals further reduces the risk to laboratory and animal care personnel of toxin exposures and wound contamination, and is therefore highly recommended.<sup>(36)</sup> The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for adult vaccination against *C. tetani*.

*Transfer of Agent:* For a permit to import this agent, contact CDC. Contact the Department of Commerce for a permit to export this agent. Laboratory registration with CDC is required before sending or receiving this select agent.

### **Agent: Corynebacterium diphtheriae**

Laboratory-associated infections with *C. diphtheriae* have been documented. Laboratory animal-associated infections have not been reported.<sup>(37)</sup>

*Laboratory Hazards:* The agent may be present in exudates or secretions of the nose, throat (tonsil), pharynx, larynx, wounds, in blood, and on the skin. Inhalation, accidental parenteral inoculation, and ingestion are the primary laboratory hazards.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infected clinical materials or cultures. Animal Biosafety Level 2 facilities are recommended for studies utilizing infected laboratory animals. While the risk of laboratory-associated diphtheria is low, the administration of an adult diphtheria-tetanus toxoid at 10-year intervals may further reduce the risk of toxin exposures and work with infectious materials to laboratory and animal care personnel.<sup>(38)</sup> The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for vaccination against *C. diphtheriae*.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: Escherichia coli (Cytotoxin-producing (VTEC/SLT) organisms)**

Cytotoxin-producing (VTEC/SLT) strains of *Escherichia coli* (also called enterohemorrhagic strains) are a demonstrated hazard to laboratory personnel in the United States and elsewhere.<sup>(39)(40)(41)</sup> Hemolytic uremic syndrome occurs in a small proportion of patients (usually children) and is responsible for most deaths associated with infections with these organisms. Domestic farm animals (particularly bovines) are significant reservoirs of the organisms. However, experimentally infected small animals are also sources of infection in the laboratory.

*Laboratory Hazards:* Enterohemorrhagic *E. coli* is usually isolated from feces. A variety of foods contaminated with the organisms may serve as vehicles of spread, and include uncooked ground beef and unpasteurized dairy products. It may rarely be found in blood of infected humans or animals. Ingestion is the primary laboratory hazard. The importance of aerosol exposure is not known.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious clinical materials or cultures. Animal Biosafety Level 2 facilities and practices are recommended for activities with experimentally or naturally infected animals. Vaccines are currently not available for use in humans. The reader is advised to consult the current related recommendations of the ACIP published in the CDC *Morbidity and Mortality Weekly Report* (MMWR) for the existence of recommendations for vaccination against enterohemorrhagic strains of *E. coli*.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: *Francisella tularensis***

Tularemia has been a commonly reported laboratory-associated bacterial infection.<sup>(42)</sup> Almost all cases occurred at facilities involved in tularemia research. Occasional cases have been related to work with naturally or experimentally infected animals or their ectoparasites. Although not reported, cases have occurred in clinical laboratories. Work with cultures of *F. tularensis* requires special security considerations due to their potential use for purposes of biological terrorism.

*Laboratory Hazards:* The agent may be present in lesion exudates, respiratory secretions, cerebrospinal fluid, blood, urine, tissues from infected animals, and fluids from infected arthropods. Direct contact of skin or mucous membranes with infectious materials, accidental parenteral inoculation, ingestion, and exposure to aerosols and infectious droplets have resulted in infection. Infection has been more commonly associated with cultures than with clinical materials and infected animals. The human 25% to 50% infectious dose is approximately 10 organisms by the respiratory route.<sup>(43)</sup>

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with clinical materials of human or animal origin containing or potentially containing *Francisella tularensis*. Biosafety Level 3 and Animal Biosafety Level 3 practices, containment equipment, and facilities are recommended, respectively, for all manipulations of cultures and for experimental animal studies.

*Note:* Vaccination for *F. tularensis* is available and should be considered for personnel working with infectious materials or infected rodents. Vaccination is recommended for persons working with the agent or infected animals, and for persons working in or entering the laboratory or animal room where cultures or infected animals are maintained.<sup>(44)</sup> The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for vaccination against *F. tularensis*.

*Transfer of Agent:* For a permit to import this agent, contact CDC. Contact the Department of Commerce for a permit to export this agent. Laboratory registration with CDC is required before sending or receiving this select agent.

### **Agent: *Leptospira interrogans* - all serovars**

Leptospirosis is a well-documented laboratory hazard. Pike reported 67 laboratory-associated infections and 10 deaths,<sup>(48)</sup> and three additional cases have been reported elsewhere.<sup>(49)</sup>

An experimentally infected rabbit was identified as the source of an infection with *L. interrogans* serovar *icterohemorrhagiae*.<sup>(50)</sup> Direct and indirect contact with fluids and tissues of experimentally or naturally infected mammals during handling, care, or necropsy is a potential source of infection. In animals with chronic kidney infections, the agent is shed in the urine in enormous numbers for long periods of time.

*Laboratory Hazards:* The agent may be present in urine, blood, and tissues of infected animals and humans. Ingestion, accidental parenteral inoculation, and direct and indirect contact of skin or mucous membranes with cultures or infected tissues or body fluids--especially urine--are the primary laboratory hazards. The importance of aerosol exposure is not known.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of known or potentially infectious tissues, body fluids, and cultures, and for the housing of infected animals. Gloves are recommended for the handling and necropsy of infected animals, and when there is the likelihood of direct skin contact with infectious materials. Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import these agents, contact CDC. An importation or domestic transfer permit for this agent can be obtained from USDA/APHIS/VS.

### **Agent: *Helicobacter pylori***

Since its discovery in 1982, *Helicobacter pylori* has received increasing attention as an agent of gastritis.<sup>(45)</sup> The main habitat of *H. pylori* is the human gastric mucosa. Human infection with *H. pylori* may be long in duration with few or no symptoms, or may present as an acute gastric illness. Both experimental and accidental laboratory-acquired human infections with *H. pylori* have been reported.<sup>(46)(47)</sup> The agent may be present in gastric or oral secretions and stool. Transmission, while incompletely understood, is thought to be by the fecal-oral or oral-oral route.

*Laboratory Hazards:* The agent may be present in gastric and oral secretions and stool. Ingestion is the primary known laboratory hazard. The importance of aerosol exposures is unknown.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with clinical materials and cultures known to contain or potentially containing the agents. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with experimentally or naturally infected animals. Vaccines are currently not available for use in humans.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: *Listeria monocytogenes***

*Listeria monocytogenes* poses a potential hazard to laboratory personnel. The gram-positive, non-spore-forming, aerobic bacilli are hemolytic and catalase-positive.<sup>(51)</sup> Bacteria have been isolated from soil, dust, human food, animals, and asymptomatic

humans.<sup>(52)(53)</sup> Most cases of listeriosis have arisen from eating contaminated food products, most notably soft cheeses, raw meat, and unwashed raw vegetables.<sup>(54)</sup> Although healthy adults and children can contract a *Listeria* infection, they do not usually become seriously ill. At risk of severe illness are pregnant women, newborns, and persons with impaired immune function.

*Laboratory Hazards:* *Listeria monocytogenes* may be found in feces, CSF, and blood, as well as food and environmental materials.<sup>(55)(56)</sup> Naturally or experimentally infected animals are a source of exposure to laboratory workers and animal care personnel, and other animals. Ingestion is the most likely mode of exposure, but *Listeria* can also cause eye and skin infections following a direct exposure. *Listeria monocytogenes* infections in pregnant women occur most often in the third trimester and may precipitate labor. Transplacental transmission of *L. monocytogenes* poses a grave risk to the fetus and may result in disseminated abscesses contributing to a mortality rate of nearly 100%.<sup>(57)</sup>

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with clinical specimens and cultures known or suspected to contain the agent. Gloves and eye protection should be worn while handling infected cultures. Animal Biosafety Level 2 practices, containment equipment and facilities are recommended for activities with experimentally or naturally infected animals. Vaccines are not currently available for use in humans.<sup>(58)</sup> Pregnant women who work with *Listeria monocytogenes* in the clinical or research laboratory setting should be fully informed of the potential hazards associated with the organism, including potential risks to the fetus.

*Transfer of Agent:* An importation or domestic transfer permit for this agent can be obtained from USDA/APHIS/VS.

### **Agent: Legionella pneumophila; other Legionella-like agents**

A single documented nonfatal laboratory-associated case of legionellosis, due to presumed aerosol or droplet exposure during animal challenge studies with Pontiac Fever agent (*L. pneumophila*), has been recorded.<sup>(59)</sup> Human-to-human spread has not been documented. Experimental infections are readily produced in guinea pigs and embryonate chicken eggs.<sup>(60)</sup> Challenged rabbits develop antibodies but not clinical disease. Mice are refractory to parenteral exposure. Unpublished studies at the Centers for Disease Control and Prevention have shown that animal-to-animal transmission did not occur in a variety of experimentally infected mammalian and avian species.

*Laboratory Hazards:* The agent may be present in pleural fluid, tissue, sputum, and environmental sources (e.g., cooling tower water). Because the natural mode of transmission appears to be airborne, the greatest potential hazard is the generation of aerosols during the manipulation of cultures or of other materials containing high concentrations of infectious microorganisms (e.g., infected yolk sacs and tissues).

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of known or potentially infectious clinical materials or cultures, and for the housing of infected animals. Biosafety Level 3 practices with primary containment devices and equipment (e.g., biological safety cabinets, centrifuge safety cups) are used for activities likely to generate potentially infectious aerosols and for activities involving production quantities of microorganisms.

*Note:* Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: *Mycobacterium leprae***

Inadvertent parenteral human-to-human transmission of leprosy has been reported following an accidental needle stick in a surgeon<sup>(61)</sup> and the use of a presumably contaminated tattoo needle.<sup>(62)</sup> There are no cases reported as a result of working in a laboratory with biopsy or other clinical materials of human or animal origin. While naturally occurring leprosy or leprosy-like diseases have been reported in armadillos<sup>(63)</sup> and in nonhuman primates,<sup>(64)(65)</sup> humans are the only known important reservoir of this disease.

*Laboratory Hazards:* The infectious agent may be present in tissues and exudates from lesions of infected humans and experimentally or naturally infected animals. Direct contact of the skin and mucous membranes with infectious materials and accidental parenteral inoculation are the primary laboratory hazards associated with handling infectious clinical materials.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities with known or potentially infectious clinical materials from infected humans and animals. Extraordinary care should be taken to avoid accidental parenteral inoculation with contaminated sharp instruments. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for animal studies utilizing rodents, armadillos, and nonhuman primates. Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: *Mycobacterium* spp. other than *M. tuberculosis*, *M. bovis* or *M. leprae***

Pike reported 40 cases of nonpulmonary "tuberculosis" thought to be related to accidents or incidents in the laboratory or autopsy room.<sup>(66)</sup> Presumably, these infections were due to mycobacteria other than *M. tuberculosis* or *M. bovis*. A number of mycobacteria that are ubiquitous in nature are associated with diseases other than tuberculosis or leprosy in

humans, domestic animals, and wildlife. Characteristically, these organisms are infectious but not contagious. Clinically, the diseases associated with infections by these "atypical" mycobacteria can be divided into three general categories:

1. **Pulmonary diseases resembling tuberculosis**, which may be associated with infection by *M. kansasii*, *M. avium* complex, and rarely, by *M. xenopi*, *M. malmoense*, *M. asiaticum*, *M. simiae*, and *M. szulgai*.
2. **Lymphadenitis**, which may be associated with infection by *M. scrofulaceum*, *M. avium* complex, and rarely, by *M. fortuitum* and *M. kansasii*.
3. **Skin ulcers and soft tissue wound infections**, which may be associated with infection by *M. ulcerans*, *M. marinum*, *M. fortuitum*, and *M. chelonae*.

*Laboratory Hazards:* The agents may be present in sputa, exudates from lesions, tissues, and in environmental samples (e.g., soil and water). Direct contact of skin or mucous membranes with infectious materials, ingestion, and accidental parenteral inoculation are the primary laboratory hazards associated with clinical materials and cultures. A potential infection hazard to laboratory personnel is also posed by the infectious aerosols created during the manipulation of broth cultures or tissue homogenates of these organisms associated with pulmonary disease.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with clinical materials and cultures of *Mycobacterium* spp. other than *M. tuberculosis* or *M. bovis*. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for animal studies with mycobacteria other than *M. tuberculosis*, *M. bovis*, or *M. leprae*. Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import these agents, contact CDC.

### **Agent: *Mycobacterium tuberculosis*, *M. bovis***

*Mycobacterium tuberculosis* and *M. bovis* (including BCG) infections are a proven hazard to laboratory personnel as well as others who may be exposed to infectious aerosols in the laboratory.<sup>(67)(68)(69)(70)(71)</sup> The incidence of tuberculosis in laboratory personnel working with *M. tuberculosis* has been reported to be three times higher than that of those not working with the agent.<sup>(72)</sup> Naturally or experimentally infected nonhuman primates are a proven source of human infection (e.g., the annual tuberculin conversion rate in personnel working with infected nonhuman primates is about 70/10,000 compared with a rate of less than 3/10,000 in the general population).<sup>(73)</sup> Experimentally infected guinea pigs or mice do not pose the same problem since droplet nuclei are not produced by coughing in these species; however, litter from infected animals may become contaminated and serve as a source of infectious aerosols.

*Laboratory Hazards:* Tubercle bacilli may be present in sputum, gastric lavage fluids, cerebrospinal fluid, urine, and in lesions from a variety of tissues.<sup>(74)</sup> Exposure to laboratory-generated aerosols is the most important hazard encountered. Tubercle bacilli may survive in heat-fixed smears,<sup>(75)</sup> and may be aerosolized in the preparation of frozen sections and during manipulation of liquid cultures. Because of the low infective dose of *M. tuberculosis* for humans (i.e., ID<sub>50</sub> <10 bacilli) and, in some laboratories, a high rate of isolation of acid-fast organisms from clinical specimens (>10%),<sup>(76)</sup> sputa, and other clinical specimens from suspected or known cases of tuberculosis must be considered potentially infectious and handled with appropriate precautions.

*Recommended Precautions:* Biosafety Level 2 practices and procedures, containment equipment, and facilities are required for non-aerosol-producing manipulations of clinical specimens such as preparation of acid-fast smears. All aerosol-generating activities must be conducted in a Class I or II biological safety cabinet. Use of a slide-warming tray, rather than flame-drying, is recommended. Liquification and concentration of sputa for acid-fast staining may also be conducted safely on the open bench by first treating the specimen (in a Class I or II safety cabinet) with an equal volume of 5% sodium hypochlorite solution (undiluted household bleach) and waiting 15 minutes before centrifugation.<sup>(77)(78)</sup>

Biosafety Level 3 practices, containment equipment, and facilities are required for laboratory activities in the propagation and manipulation of cultures of *M. tuberculosis* or *M. bovis*, and for animal studies utilizing nonhuman primates experimentally or naturally infected with *M. tuberculosis* or *M. bovis*. Animal studies utilizing guinea pigs or mice can be conducted at Animal Biosafety Level 2.<sup>(79)</sup>

**Note:** Skin testing with purified protein derivative (PPD) of previously skin-tested-negative laboratory personnel can be used as a surveillance procedure. An attenuated live vaccine (BCG) is available but is not used in the United States for laboratory personnel. The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for current vaccination recommendations.

*Transfer of Agent:* For a permit to import these agents, contact CDC. An importation or domestic transfer permit for *M. Bovis* can be obtained from USDA/APHIS/VS.

### **Agent: Neisseria gonorrhoeae**

Laboratory-associated gonococcal infections have been reported in the United States.<sup>(80)</sup>  
*Laboratory Hazards:* The agent may be present in conjunctival, urethral and cervical exudates, synovial fluid, urine, feces, and cerebrospinal fluid. Accidental parenteral inoculation and direct or indirect contact of mucous membranes with infectious clinical materials are the known primary laboratory hazards. The importance of aerosols is not determined.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of clinical materials or cultures. Gloves should be worn when handling infected laboratory animals and when there is the likelihood of direct skin contact with infectious materials. Additional primary containment and personnel precautions, such as those described for Biosafety Level 3, may be indicated for aerosol or droplet production, and for activities involving production quantities or concentrations of infectious materials. Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: *Neisseria meningitidis***

Meningococcal meningitis is a demonstrated but rare hazard to laboratory workers.<sup>(81)(82)(83)</sup>

*Laboratory Hazards:* The agent may be present in pharyngeal exudates, cerebrospinal fluid, blood, and saliva. Parenteral inoculation, droplet exposure of mucous membranes, infectious aerosol and ingestion are the primary hazards to laboratory personnel.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious body fluids, tissues, and cultures. Additional primary containment and personnel precautions, such as those described for Biosafety Level 3, may be indicated for activities with a high potential for droplet or aerosol production and for activities involving production quantities or concentrations of infectious materials.

*Note:* Vaccines for *N. meningitidis* are available and should be considered for personnel regularly working with infectious materials. The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for vaccination against *N. meningitidis*.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

### **Agent: *Salmonella* - all serotypes except typhi**

Salmonellosis is a documented hazard to laboratory personnel.<sup>(84)(85)(86)</sup> Primary reservoir hosts include a broad spectrum of domestic and wild animals, including birds, mammals, and reptiles, all of which may serve as a source of infection to laboratory personnel.

*Laboratory Hazards:* The agent may be present in feces, blood, urine, and in food, feed, and environmental materials. Ingestion or parenteral inoculation are the primary laboratory hazards. The importance of aerosol exposure is not known. Naturally or experimentally

infected animals are a potential source of infection for laboratory and animal care personnel, and for other animals.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with clinical materials and cultures known to contain or potentially containing the agents. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with experimentally or naturally infected animals. Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import these agents, contact CDC.

### **Agent: Salmonella typhi**

Typhoid fever is a demonstrated hazard to laboratory personnel.<sup>(87)(88)(89)</sup>

*Laboratory Hazards:* The agent may be present in feces, blood, gallbladder (bile), and urine. Humans are the only known reservoir of infection. Ingestion and parenteral inoculation of the organism represent the primary laboratory hazards. The importance of aerosol exposure is not known.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious clinical materials and cultures. Biosafety Level 3 practices and procedures are recommended for activities likely to generate aerosols or for activities involving production quantities of organisms.

Vaccines for *S. typhi* are available and should be considered for personnel regularly working with potentially infectious materials. The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for vaccination against *S. typhi*.

*Transfer of Agent:* Contact the Department of Commerce for a permit to export this agent.

### **Agent: Shigella spp.**

Shigellosis is a demonstrated hazard to laboratory personnel, with dozens of cases reported in the United States and Great Britain alone.<sup>(90)(91)(92)(93)</sup> While outbreaks have occurred in captive nonhuman primates, humans are the only significant reservoir of infection. However, experimentally infected guinea pigs, other rodents, and nonhuman primates are also proven sources of infection.

*Laboratory Hazards:* The agent may be present in feces and, rarely, in the blood of infected humans or animals. Ingestion and parenteral inoculation of the agent are the

primary laboratory hazards. The oral 25%-50% infectious dose of *S. flexneri* for humans is approximately 200 organisms.<sup>(94)</sup> The importance of aerosol exposure is not known.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious clinical materials or cultures. Animal Biosafety Level 2 facilities and practices are recommended for activities with experimentally or naturally infected animals. Vaccines are currently not available for use in humans.

*Transfer of Agent:* Contact the Department of Commerce for a permit to export this agent.

### **Agent: *Treponema pallidum***

Syphilis is a documented hazard to laboratory personnel who handle or collect clinical material from cutaneous lesions. Pike lists 20 cases of laboratory-associated infection.<sup>(95)</sup> Humans are the only known natural reservoir of the agent. Syphilis has been transmitted to laboratory personnel working with a concentrated suspension of *T. pallidum* obtained from an experimental rabbit orchitis.<sup>(96)</sup> Hematogenous transfer of syphilis has occurred from the transfusion of a unit of fresh blood obtained from a patient with secondary syphilis. *T. pallidum* is present in the circulation during primary and secondary syphilis. The minimum number (LD<sub>50</sub>) of *T. pallidum* organisms needed to infect by subcutaneous injection is 23.<sup>(97)</sup> The concentration of *T. pallidum* in patients' blood during early syphilis, however, has not been determined.

No cases of laboratory animal-associated infections are reported; however, rabbit-adapted strains of *T. pallidum* (Nichols and possibly others) retain their virulence for humans.

*Laboratory Hazards:* The agent may be present in materials collected from primary and secondary cutaneous and mucosal lesions and in blood. Accidental parenteral inoculation, contact of mucous membranes or broken skin with infectious clinical materials, and possibly infectious aerosols, are the primary hazards to laboratory personnel.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of blood or lesion materials from humans or infected rabbits. Gloves should be worn when there is a likelihood of direct skin contact with lesion materials. Periodic serological monitoring should be considered in personnel regularly working with infectious materials. Vaccines are not currently available for use in humans.

*Transfer of Agent:* For a permit to import this agent, contact CDC.

**Agent: Vibrionic enteritis (*Vibrio cholerae*, *V. para-haemolyticus*)**

Vibrionic enteritis due to *Vibrio cholerae* or *Vibrio parahaemolyticus* is a documented but rare cause of laboratory-associated illness.<sup>(98)</sup> Naturally and experimentally infected animals are a potential source of infection.

*Laboratory Hazards:* Pathogenic vibrios may occur in feces. Ingestion of *V. cholerae* and ingestion or parenteral inoculation of other vibrios constitute the primary laboratory hazard. The human oral infecting dose of *V. cholerae* in healthy non-achlorhydric individuals is approximately  $10^6$  organisms.<sup>(99)</sup> The importance of aerosol exposure is not known. The risk of infection following oral exposure may be increased in achlorhydric individuals.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with cultures or potentially infectious clinical materials. Animal Biosafety Level 2 practices, containment equipment, and facilities are recommended for activities with naturally or experimentally infected animals. Although cholera vaccines exist, their routine use by laboratory staff has not been recommended. The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for recommendations for vaccination against *V. cholerae*. There are currently no human vaccines against *V. parahaemolyticus*.

*Transfer of Agent:* Contact the Department of Commerce for a permit to export this agent.

**Agent: *Yersinia pestis***

Plague is a proven but rare laboratory hazard; cases have been reported in the United States.<sup>(100)(101)</sup> Work with *Y. pestis* requires special security considerations due to its potential use for purposes of biological terrorism.

*Laboratory Hazards:* The agent may be present in bubo fluid, blood, sputum, cerebrospinal fluid (CSF), feces, and urine from humans, depending on the clinical form and stage of the disease. Primary hazards to laboratory personnel include direct contact with cultures and infectious materials from humans or rodents, infectious aerosols or droplets generated during the manipulation of cultures, and infected tissues. In the necropsy of rodents, primary hazards to laboratory personnel include accidental autoinoculation, ingestion, and bites by infected fleas collected from rodents.

*Recommended Precautions:* Biosafety Level 2 practices, containment equipment, and facilities are recommended for all activities involving the handling of potentially infectious clinical materials and cultures. Special care should be taken to avoid the generation of aerosols from infectious materials, and during the necropsy of naturally or experimentally infected rodents. Gloves should be worn when handling field-collected or infected

laboratory rodents, and when there is the likelihood of direct skin contact with infectious materials. Necropsy of rodents is ideally conducted in a biological safety cabinet. Additional primary containment and personnel precautions, such as those described for Biosafety Level 3, are recommended for activities with high potential for droplet or aerosol production, for work with antibiotic-resistant strains, and for activities involving production quantities or concentrations of infectious materials.

**Note:** Vaccination for *Y. pestis* is available and should be considered for personnel working with infectious materials or infected rodents. The reader is advised to consult the current recommendations of the Advisory Committee on Immunization Practices (ACIP) published in the CDC Morbidity and Mortality Weekly Report (MMWR) for information on vaccination against *Y. pestis*.

**Transfer of Agent:** For a permit to import this agent, contact CDC. Contact the Department of Commerce for a permit to export this agent. Laboratory registration with CDC is required before sending or receiving this select agent.

## References

1. Ellingson, H.V., et al. 1946. Cutaneous anthrax: report of twenty-five cases. JAMA 131:1105-8.
2. Pike, R.M. 1976. Laboratory-associated infections: Summary and analysis of 3,921 cases. Hlth Lab Sci 13:105-114.
3. Linneman, C.C., et al. 1975. Use of pertussis vaccine in an epidemic involving hospital staff. Lancet 2:540.
4. Kurt, T.L., et al. 1972. Spread of pertussis by hospital staff. JAMA 221:264.
5. Morse, S.I. 1968. Pertussis in Adults (editorial). Ann Intern Med. 68:953.
6. Kurt, T.L., et al. 1972. (4)
7. Linneman, C.C., et al. 1975. (3)
8. Nelson, J.D. 1978. The changing epidemiology of pertussis in young infants. The role of adults as reservoirs of infection. Am J Dis Child 132:371.
9. McKinney, R.W., et al. 1985. XXVII Biological Safety Conference, Salk Institute for Biological Studies, La Jolla, CA.
10. Parker, C. 1992. Dept. of Microbiology, University of Missouri, Columbia, Missouri (personal communication).

11. Burstyn, D.G., et al. 1983. Serological response to filamentous hemagglutinin and lymphocytosis-promoting toxin of *Bordetella pertussis*. *Infection and Immunity* 41(3):1150-6.
12. Centers for Disease Control. 1985. Pertussis - Washington, 1984. *MMWR* 34(26):90-400.
13. Miller, C.D., Songer, J.R., and Sullivan, J.F. 1987. A twenty-five year review of laboratory-acquired human infections at the National Animal Disease Center. *Am Ind Hyg Assoc J* 48:271-275.
14. Olle-Goig, J. and Canela-Soler, J.C. 1987. An outbreak of *Brucella melitensis* infection by airborne transmission among laboratory workers. *Am J Publ Hlth* 77:335-338.
15. Pike, R.M. 1976. (2).
16. Morisset, R. and Spink, W.W. 1969. Epidemic canine brucellosis due to a new species, *Brucella canis*. *Lancet* 2:1000-2.
17. Pike, R.M. 1976. (2)
18. Spink, W.W. 1956. *The Nature of Brucellosis*. Minneapolis, The University of Minnesota Press, pp. 106-108.
19. Grammont-Cupillard, M., L. Berthet-Badetti and P. Dellamonica. 1996. *Lancet* 348:1733-1734.
20. Huddleson, I.F. and Munger, M. 1940. A study of an epidemic of brucellosis due to *Brucella melitensis*. *Am J Public Health* 30:944-954.
21. Staszkiwicz, J., C.M. Lewis, J. Coville, M. Zervos and J. Band. 1991. Outbreak of *Brucella melitensis* among microbiology laboratory workers in a community hospital. *J. Clin. Microbiol.* 29:278-290.
22. Nicoletti, P. 1990. Vaccination against Brucella. *Advances in Biotechnological Processes* 13:147-168.
23. Green, R.N. and Tuffnell, P.G. 1968. Laboratory-acquired melioidosis. *Am J Med* 44: 599-605.
24. Schleich, W.F., et al. 1981. Laboratory-acquired infection with *Pseudomona pseudomallie* (melioidosis). *N Eng J Med* 305:1133-1135
25. Oates, J.D. and Hodgin, U.G., Jr. 1981. Laboratory-acquired *Campylobacter* enteritis. *South Med J* 74:83.

26. Penner, J.L., et al. 1983. Application of serotyping and chromosomal restriction endonuclease digest analysis in investigating a laboratory-acquired case of *Campylobacter jejuni* enteritis. J Clin Microbiol 18:1427-1428.
27. Prescott, J.F. and Karmali, M.A. 1978. Attempts to transmit *Campylobacter enteritis* to dogs and cats (letter). Can Med Assoc J 119:1001-1002.
28. Prescott, J.F. and Karmali, M.A. 1978. (25)
29. Robinson, D.A. 1981. Infective dose of *Campylobacter jejuni* in milk. Brit Med J 282:1584.
30. Miller, C.D., Songer, J.R., and Sullivan, J.F. 1987. (13)
31. Pike, R.M. 1976. (2)
32. Sterne, M. and Wertzell, L.M. 1950. A new method of large-scale production of high-titer botulinum formol-toxoid types C and D. J Immunol 65:175-183.
33. Holzer, E. 1962. Botulism caused by inhalation. Med Klin 41:1735-1740.
34. Sterne, M. and Wertzell, L.M. 1950. (30)
35. Pike, R.M. 1976. (2)
36. Centers for Disease Control. 1981. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Diphtheria, Tetanus, and Pertussis. MMWR 30(32):392-396.
37. Pike, R.M. 1976. (2)
38. Centers for Disease Control. 1981. (34)
39. Anonymous. 1994. Laboratory acquired infection with *Escherichia coli* O157. Communicable Disease Weekly 4(7):29.
40. Rao, G.G, B.P. Saunders and R.G. Masterton. 1996. Laboratory-acquired verotoxin producing *Escherichia coli* (VTEC) infection. J. Hospital Infection 33(3):228-230.
41. Burnens, A.P., R. Zbinden, L. Kaempfer, I. Heinzer and J. Nicolet. 1993. A case of laboratory-acquired infection with *Escherichia coli* O157:H7. Zentralblatt für Bakteriologie 279:512-517.
42. Pike, R.M. 1976. (2)

43. Burke, D.S. 1977. Immunization against tularemia: Analysis of the effectiveness of live *Francisella tularensis* vaccine in prevention of laboratory-acquired tularemia. *J Infect Dis* 135:55-60.
44. Burke, D.S. 1977 (41)
45. Marshall, B. J., and J.R. Warren, 1984. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* i:1311-1315.
46. Marshall, B.J., J.A. Armstrong, D.B. McGeachie and R.J. Glancy. Attempt to fulfill Koch's postulates for pyloric *Campylobacter*. 1985. *Med. J. Aust.* 142:436-439.
47. Matysiak-Budnik, T., F. Briet, M. Heyman and F. Megraud. 1995. Laboratory-acquired *Helicobacter pylori* infection. *Lancet* 346:1489-1490.
48. Pike, R.M. 1976. (2)
49. Miller, C.D., Songer, J.R., and Sullivan, J.F. 1987. (13)
50. Richardson, J.H. 1973. Provisional summary of 109 laboratory-associated infections at the Centers for Disease Control, 1947-1973. Presented at the 16th Annual Biosafety Conference, Ames, Iowa.
51. Schuchat, A., Swaminathan, B., Broome, C.V. 1991 Epidemiology of Human Listeriosis. *Clin. Microbiol. Rev.* 4:169-83.
52. Armstrong, D. *Listeria Monocytogenes*. In: Principles and Practices of Infectious Diseases, Mandell, G.L., Bennett, J.E., Dolin, R., Eds. (Churchill Livingstone, New York, 1995) pp. 1880-1.
53. Schuchat, A., Swaminathan, B., Broome, C.V. 1991. (49)
54. Centers for Disease Control and Prevention. 1992. Update: Foodborne Listeriosis - United States, 1988-1990. *MMWR*. 41:251-7.
55. Armstrong, D. 1995. (50)
56. Schuchat, A., Swaminathan, B., Broome, C.V. 1991. (49)
57. Armstrong, D. 1995. (50)
58. Gellin, B.G. and Broome, C.V. 1989. Listeriosis. *JAMA*. 261:1313-20.
59. Centers for Disease Control. 1976. Unpublished data. Center for Infectious Diseases. U.S. Department of Health, Education and Welfare, Public Health Service.

60. McDade, J.E. and Shepard, C.C. 1979. Virulent to avirulent conversion of Legionnaire's disease bacterium (*Legionella pneumophila*) - Its effect on isolation techniques. J Infect Dis 139:707-711.
61. Marchoux, P.E. 1934. Un cas d'inoculation accidentelle du bacille de Hanson en pays non lepreux. Int J Lepr 2:1-7.
62. Parritt, R.J. and Olsen, R.E. 1947. Two simultaneous cases of leprosy developing in tattoos. Am J Pathol 23:805-817.
63. Walsh, G.P., et al. 1975. Leprosy-like disease occurring naturally in armadillos. J Reticuloendothel Soc 18:347-351.
64. Donham, K.J. and Leininger, J.R. 1977. Spontaneous leprosy-like disease in a chimpanzee. J Infect Dis 136:132-136.
65. Meyers, W.M., et al. 1980. Naturally acquired leprosy in a mangabey monkey (*Cercocebus* sp.) Int J Lepr 48:495-496.
66. Pike, R.M. 1976. (2)
67. Grist, N.R. and Emslie, J.A.N. 1985. Infections in British clinical laboratories, 1982-3. J Clin Pathol 38:721-725.
68. Miller, C.D., Songer, J.R., and Sullivan, J.F. 1987. (13)
69. Müller, H.E. 1988. Laboratory-acquired mycobacterial infection. Lancet 2:331.
70. Pike, R.M. 1976 (2)
71. Pike, R.M., Sulkin, S.E., and Schulze, M.L. 1965. Continuing importance of laboratory-acquired infections. Am J Public Health 55:190-199.
72. Reid, D.D. 1957. Incidence of tuberculosis among workers in medical laboratories. Brit Med J 2:10-14.
73. Kaufmann, A.F. and Anderson, D.C. 1978. Tuberculosis control in nonhuman primates. In: Montali, R.J. (ed.). *Mycobacterial Infections of Zoo Animals*. Washington, D.C.: Smithsonian Institution Press, 227-234.
74. Anonymous. 1980. Tuberculosis infection associated with tissue processing. Cal Morbid 30.
75. Allen, B.W. 1981. Survival of tubercle bacilli in heat-fixed sputum smears. J Clin Pathol 34:719-722.

76. Good, R.C. and Snider, D.E., Jr. 1982. Isolation of nontuberculosis mycobacteria in the U.S., 1980. *J Infect Dis* 146:829-833.
77. Smithwick, R.W. and Stratigos, C.B. 1978. Preparation of acid-fast microscopy smears for proficiency testing and quality control. *J Clin Microbiol* 8:110-111.
78. 78. Oliver, J. and Reusser, T.R. 1942. Rapid method for the concentration of tubercle bacilli. *Am Rev Tuberc* 45:450-452.
79. Richmond, J.Y., Knudsen, R.C., and Good, R.C. 1996. Biosafety in the clinical mycobacteriology laboratory. *Clin Mycobac* 16(3):527-550.
80. Diena, B.B., et al. 1976. Gonococcal conjunctivitis: accidental infection. *Can Med Assoc J* 115:609,612.
81. Bacteriologist dies of meningitis. 1936. *JAMA* 106:129.
82. Centers for Disease Control. 1991. Laboratory-acquired meningococemia - California and Massachusetts. *MMWR* 40(3):46-47,55.
83. Pike, R.M. 1979. Laboratory-associated infections: incidence, fatalities, causes and prevention. *Ann Rev Microbiol* 33:41-66.
84. Grist, N.R. and Emslie, J.A.N. 1987. Infections in British clinical laboratories, 1984-5. *J Clin Pathol* 40:826-829.
85. Miller, C.D., Songer, J.R., and Sullivan, J.F. 1987. (13)
86. Pike, R.M. 1976. (2)
87. Blaser, M.J., et al. 1980. *Salmonella typhi*: the laboratory as a reservoir of infection. *J Infect Dis* 142:934-938.
88. Grist, N.R. and Emslie, J.A.N. 1987. (84)
89. Pike, R.M. 1979. (85)
90. Grist, N.R. and Emslie, J.A.N. 1985. (65)
91. Grist, N.R. and Emslie, J.A.N. 1987. (84)
92. Jacobson, J.T., Orlob, R.B., Clayton, J.L. 1985. Infections acquired in clinical laboratories in Utah. *J Clin Microbiol* 21:486-489.
93. Pike, R.M. 1976. (2)

94. Wedum, A.G., Barkley, W.E., and Hellman, A. 1972. Handling of infectious agents. *J Am Vet Med Assoc* 161:1557-1567.
95. Pike, R.M. 1976. (2)
96. Fitzgerald, J.J., Johnson, R.C., and Smith, M. 1976. Accidental laboratory infection with *Treponema pallidum*, Nichols strain. *J Am Vener Dis Assoc* 3:76-78.
97. Magnuson, H.J., et al. 1956. Inoculation syphilis in human volunteers. *Medicine* 35:33-82.
98. Pike, R.M. 1979. (85)
99. Levine, M.M., et al. 1983. New knowledge on pathogenesis of bacterial enteric infections as applied to vaccine development. *Microbiol Reviews* 47:510-550.
100. Burmeister, R.W., Tigertt, W.D., and Overholt, E.L. 1962. Laboratory-acquired pneumonic plague. *Ann Intern Med* 56:789-800.
101. Pike, R.M. 1976. (2)