

Overview

Zoonoses of Occupational Health Importance in Contemporary Laboratory Animal Research

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In contemporary laboratory animal facilities, workplace exposure to zoonotic pathogens, agents transmitted to humans from vertebrate animals or their tissues, is an occupational hazard. The primary (e.g., macaques, pigs, dogs, rabbits, mice, and rats) and secondary species (e.g., sheep, goats, cats, ferrets, and pigeons) of animals commonly used in biomedical research, as classified by the American College of Laboratory Animal Medicine, are established or potential hosts for a large number of zoonotic agents. Diseases included in this review are principally those wherein a risk to biomedical facility personnel has been documented by published reports of human cases in laboratory animal research settings, or under reasonably similar circumstances. Diseases are listed alphabetically, and each section includes information about clinical disease, transmission, occurrence, and prevention in animal reservoir species and humans. Our goal is to provide a resource for veterinarians, health-care professionals, technical staff, and administrators that will assist in the design and on-going evaluation of institutional occupational health and safety programs.

It is a requirement of the Public Health Service and the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), International, that institutions maintain an occupational health and safety program as part of their overall program of animal care and use. The AAALAC and the *Guide for the Care and Use of Laboratory Animals* stipulate that, "Potential hazards—such as animal bites, chemical cleaning agents, allergens, and zoonoses—that are inherent in or intrinsic to animal use should be identified and evaluated" (134). The word zoonosis originates from its Greek origins *zoion* (animal) and *noses* (disease), and is defined as "an infection or infestation shared in nature by man and lower vertebrate animals" (235). The purpose of this overview is to provide a summary of zoonoses that could be transmitted to humans from commonly used vertebrate animals or their tissues in the context of biomedical research programs. Our goal is to provide a resource with reference citations for veterinarians, health-care professionals, technical staff, and administrators that will assist in the design and on-going evaluation of institutional occupational health and safety programs.

Most animals currently maintained in laboratory animal settings are supplied by commercial vendors that have been successful in eliminating all or most zoonotic agents from their

animal colonies (52). However, some research activities still require the use of animal species that are unavailable from pathogen-free sources, whether wild-caught or reared without re-derivation to eliminate zoonotic pathogens. In contemporary settings, a large number of animal species are used in the course of biomedical research, many of which are established or potential hosts for zoonotic agents. We have chosen to focus this review on the animal species in the primary and secondary category listings outlined by the American College of Laboratory Animal Medicine (ACLAM) (3) (Table 1). The species in these categories represent those most likely to be used in biomedical research.

Diseases included in this review are principally those wherein a true risk to biomedical facility personnel has been documented by published reports of human cases in laboratory animal research settings, or under reasonably similar circumstances. However, for some of the agents, the published cases may have occurred decades previously, and hence, the actual risks (within the context of animal sources, research usage, and work practices) may be minimal to non-existent in the modern era. Nonetheless, the likelihood that there could be a resurgence of concern due to changes in any of these risk factors argues that such agents should continue to be regarded as potential hazards.

The clinical and epidemiologic features of each disease discussed are formatted in manner similar to that of a renowned professional reference text on communicable diseases (48). Where appropriate, our summaries have been augmented with information from published reports to underscore issues pertinent to laboratory animal medicine and management. Each disease is listed alphabetically by common name according to the following outline of categories and their definitions. **Disease name** is the most commonly accepted term used in the litera-

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Table 1. Laboratory animal species categories from American College of Laboratory Animal Medicine (ACLAM) Role Delineation Document

Primary	Secondary	Tertiary
Macaque (<i>Macaca</i> spp.)	Squirrel monkey (<i>Saimiri sciureus</i>) Baboon (<i>Papio</i> spp.)	Other nonhuman primates
Mouse (<i>Mus musculus</i>) Rat (<i>Rattus norvegicus</i>)	Gerbil (<i>Meriones</i> spp.) Syrian hamster (<i>Mesocricetus auratus</i>) Guinea pig (<i>Cavia porcellus</i>)	Other rodents
Pig (<i>Sus scrofa</i>)	Sheep (<i>Ovis aries</i>) Goat (<i>Capra hircus</i>)	Other livestock species
Dog (<i>Canis familiaris</i>) Rabbit (<i>Oryctolagus cuniculus</i>)	Cat (<i>Felis domestica</i>) Ferret (<i>Mustela putorius furo</i>)	Other mammals
	Pigeon (<i>Columba livia</i>) Chicken (<i>Gallus domestica</i>)	Other birds
	African clawed frog (<i>Xenopus laevis</i>)	Other amphibians
	Zebrafish (<i>Danio rerio</i>)	Fish
		Reptiles
		Invertebrates

ture. **Agent** is the specific pathogen(s) that cause(s) the disease, followed by the type of organism it represents. The **Laboratory animal reservoir** section includes the vertebrates in which the infective agent resides, and is subdivided into four categories: hosts, disease, detection and control. The **Hosts** are the animal sources of the agent, excluding those beyond the scope of the ACLAM Role Delineation Document. **Disease** describes the clinical manifestations, if any, that are manifested in the laboratory animal hosts. **Detection** describes how the infection may be diagnosed in the hosts. **Control** includes methods by which infection in the host(s) can be prevented, treated, or eradicated. **Mode of transmission** is the means by which the agent spreads from the reservoir host to humans. **Communicability** is a general assessment of the agent's infectivity and the relative ease with which the agent may be transmitted to humans.

The **Humans** section is subdivided into six categories: occurrence, clinical syndromes, incubation period, diagnosis, prevention, and treatment. **Occurrence** provides brief information on documented cases and includes the source of the infection and some characteristics of the affected persons. **Clinical syndromes** describes the principal clinical features of the disease (48), including those reported in documented cases. **Incubation period** is the time between exposure to the agent and the appearance of clinical signs of disease in humans. **Diagnosis** describes the laboratory methods that may be used to detect infection in humans. **Prevention** provides information on measures used to avoid or minimize exposure and disease in humans. **Treatment** provides information on the manner in which the disease may be treated. Diseases are also cross-referenced by species (Table 2).

This report deals exclusively with modes of transmission that are known or conceivable within laboratory animal settings; therefore, zoonoses acquired only by ingestion of contaminated food or animal by-products are not discussed. Several reviews of zoonotic diseases, in a variety of laboratory animal species, some of which have contributed to this work, have been published (66, 86, 87, 109, 209, 219, 255). However, in contrast to these reviews, our review discusses the zoonoses in a standardized format, providing information on key features that is readily accessible, and drawn from human cases that have been reported in laboratory animal research facilities.

Amebiasis

Agent: *Entamoeba histolytica*; protozoa

Laboratory Animal Reservoir:

Hosts: Macaques, baboons, squirrel monkeys, and other non-human primates (92, 188, 190, 230); occasionally dogs and cats.

Disease: Asymptomatic to severe diarrhea (hemorrhagic or catarrhal) with weight loss, depending on strain of organism and invasiveness of the condition; lesions outside of the intestinal tract occasionally develop.

Detection: Microscopic examination of fresh wet fecal smears for trophozoites or cysts. Repeated examinations may be necessary due to periodic fecal shedding. Cysts may be identified by use of zinc sulfate flotation examination of feces (179).

Control: Antimicrobial treatment or culling of carriers; strict sanitation practices.

Mode of transmission: Fecal-oral. Flies and cockroaches can spread cyst forms of the agent.

Communicability: High, due to potential for asymptomatic carriers (humans) that can act as a source of infection for non-human primates.

Humans:

Occurrence: Man is the natural host and is the usual source of infection for animals (190). Clinical cases in laboratory animal settings have not been documented.

Clinical syndromes: Asymptomatic to acute or fulminating dysentery with fever, chills, and hemorrhagic or catarrhal diarrhea; extraintestinal abscesses may develop.

Incubation period: Ranges from two to four weeks, may be longer.

Diagnosis: Examination of fresh stool smears for trophozoites; serologic testing for invasive forms of the disease.

Prevention: Good hygiene; strict sanitation; barrier methods of protection; vermin control programs.

Treatment: Metronidazole, followed by iodoquinol, paromomycin, or diloxanide furoate (48).

B Virus

Agent: *Cercopithecine herpesvirus 1*, *Herpesvirus simiae*, Herpes B; alphaherpesvirus.

Table 2. Zoonoses associated with commonly used laboratory animals

Animal	Disease
African clawed frogs	Chlamydiosis Cryptosporidiosis
Baboons	Amebiasis Balantidiasis Campylobacteriosis Cryptosporidiosis Dermatophytosis Ectoparasitism Giardiasis Leptospirosis Poxvirus Salmonellosis Shigellosis Simian foamy virus Strongyloidiasis Tuberculosis Yellow fever
Cats	Amebiasis Campylobacteriosis Capnocytophagosis Cat Scratch Disease Chlamydiosis Cryptosporidiosis Dermatophytosis Ectoparasitism Giardiasis Leptospirosis Pasteurellosis Q fever Rabies Salmonellosis Toxoplasmosis Tuberculosis
Chickens	Campylobacteriosis Cryptosporidiosis Ectoparasitism Erysipelas Psittacosis Salmonellosis Tuberculosis
Dogs	Amebiasis Brucellosis Campylobacteriosis Capnocytophagosis Cat Scratch Disease Chlamydiosis Cryptosporidiosis Dermatophytosis Echinococcosis Ectoparasitism Giardiasis Leptospirosis Pasteurellosis Q fever Rabies Strongyloidiasis Tuberculosis
Ferrets	Campylobacteriosis Cryptosporidiosis Ectoparasitism Rabies
Gerbils	Ectoparasitism Leptospirosis
Goats	Brucellosis Chlamydiosis Dermatophytosis Ectoparasitism Giardiasis Leptospirosis Orf Q fever Tuberculosis
Guinea pigs	Balantidiasis Chlamydiosis Dermatophytosis Ectoparasitism Lymphocytic choriomeningitis Salmonellosis

Table 2. Zoonoses associated with commonly used laboratory animals (cont.)

Animal	Disease
Hamsters	Campylobacteriosis Ectoparasitism Lymphocytic choriomeningitis Leptospirosis
Macaques	Amebiasis B Virus Balantidiasis Campylobacteriosis Cryptosporidiosis Dermatophytosis Ectoparasitism Giardiasis Leptospirosis Poxvirus Salmonellosis Shigellosis Simian foamy virus Strongyloidiasis Tuberculosis Yellow fever
Mice	Ectoparasitism Hantaviral diseases Leptospirosis Lymphocytic choriomeningitis Rat bite fever Salmonellosis
Pigs	Balantidiasis Brucellosis Campylobacteriosis Cryptosporidiosis Ectoparasitism Erysipelas Giardiasis Leptospirosis Pasteurellosis Salmonellosis Streptococcosis Tuberculosis
Pigeons	Cryptococcosis Ectoparasitism Psittacosis Tuberculosis
Rabbits	Dermatophytosis Ectoparasitism Pasteurellosis Salmonellosis
Rats	Ectoparasitism Hantaviral diseases Leptospirosis Lymphocytic choriomeningitis Rat bite fever Salmonellosis
Sheep	Brucellosis Campylobacteriosis Chlamydiosis Cryptosporidiosis Dermatophytosis Ectoparasitism Giardiasis Leptospirosis Orf Q fever Salmonellosis Tuberculosis
Squirrel monkeys	Amebiasis Balantidiasis Campylobacteriosis Cryptosporidiosis Dermatophytosis Ectoparasitism Giardiasis Leptospirosis Salmonellosis Shigellosis Simian foamy virus Strongyloidiasis Tuberculosis Yellow fever

Laboratory Animal Reservoir:

Host: Macaques (197).

Disease: Most commonly asymptomatic, may cause vesiculo-ulcerative lesions in oral cavity and genitalia; conjunctivitis. Rarely associated with disseminated disease involving other organ systems.

Detection: Serologic testing; virus isolation; polymerase chain reaction (PCR) assay; reverse transcriptase (RT)-PCR assay (203).

Control: Obtain macaques from B virus-negative colonies; ensure husbandry procedures prevent potential for infection; verify absence of identifiable infection through repeated serologic testing. Once infection is established, virus remains latent in sensory ganglia of macaques.

Mode of transmission: Contaminated bites and scratches, splashes to mucous membranes of the face, needlestick injuries, and contamination of broken skin with body fluids of macaques; cuts from contaminated equipment and contact with unfixed tissues or primary cell culture material from macaques. Transmission by the aerosol route is not important. B virus is not considered a blood-borne pathogen.

Communicability: Low frequency but high severity of disease if exposure site left unattended. This is the most important infectious occupational health hazard in the conduct of nonhuman primate research. Direct correlation does not exist between the extent of animal-associated injury and the likelihood of infection in humans. Cases have occurred without any specific exposure that the patient could recall, requiring high vigilance to rule out the possibility of B virus in persons working with macaques who have symptoms consistent with the many different manifestations of the disease. Nonetheless, human cases of B virus are considered extremely rare, despite its high prevalence in the host species and given the large numbers of macaques used in research (131).

Humans:

Occurrence: Cases of B virus infection have been documented on at least 50 occasions and have led to 23 or more deaths (45, 51). One case of human-to-human transmission resulted from self-inoculation of an infectious skin lesion from the forearm of an animal technician to the finger of his spouse (44). Additional human cases of occupationally acquired B virus meningencephalitis may have historically occurred in persons without recognition of this etiopathogenesis, likely due to non-specific symptoms and limited awareness of appropriate reference laboratories available for agent identification.

Clinical syndromes: Ascending encephalomyelitis and death have been observed in cases without the benefit of prompt evaluation and follow-up care. In the absence of such care, the case fatality rate is approximately 80%. Early-stage symptoms include flu-like illness (fever, chills, nausea, vomiting, dizziness), sinusitis, and persistent headaches. On some occasions, fluid-filled vesicles have formed near skin wounds sustained from macaque bites or scratches followed by localized paresthesia. Progression of disease may be manifested with other symptoms attributable to central nervous system infection, such as altered vision, seizures, and respiratory failure (257).

Incubation period: Ranges from one week to three weeks in most cases. Reactivation of latent B-virus infection years after

initial exposure has been suspected in at least one human case, but not confirmed (51).

Diagnosis: Serologic testing; virus isolation; PCR assay.

Prevention: Personal protective equipment (PPE); safe animal handling procedures; prompt and sufficient attention to disinfection of body sites known or thought to be contaminated; prompt evaluation and follow-up care, as indicated, by a medical professional knowledgeable about the disease.

Treatment: Antiviral therapy (acyclovir, valacyclovir, ganciclovir) has been efficacious when instituted sufficiently early in the course of documented human infections (51).

Balantidiasis

Agent: *Balantidium coli*; ciliated protozoa.

Laboratory Animal Reservoir:

Hosts: Pigs, nonhuman primates (macaques, baboons, squirrel monkeys and other nonhuman primates) (92, 154, 188, 190), guinea pigs (110).

Disease: Asymptomatic to watery diarrhea and ulcerative enterocolitis, weight loss; rectal prolapse.

Detection: Examination of fresh wet fecal smears for trophozoites or cysts; histologic examination; autofluorescence microscopy of feces (61).

Control: Sanitation; treatment of infected animals with antimicrobials.

Mode of transmission: Fecal-oral.

Communicability: Humans have a high natural resistance to this parasite, but infection may pose more substantial health hazards in debilitated individuals.

Humans:

Occurrence: In human cases, contact with pigs is the most likely source of infection. Up to 100% of pigs more than four weeks old on one farm were test positive for *B. coli* cysts in their feces (121). *Balantidium coli* can complicate other gastrointestinal tract diseases of humans (142).

Clinical syndromes: Diarrhea, gastroenteritis, tenesmus, nausea, vomiting.

Incubation period: Unknown, possibly a few days.

Diagnosis: Examination of fresh wet smear of stool for trophozoites or cysts.

Prevention: Good hygiene and strict sanitation; barrier methods of protection.

Treatment: Tetracycline, metronidazole (48); supportive care.

Brucellosis

Agent: *Brucella abortus*, *B. canis*, *B. melitensis*, *B. ovis*, *B. suis*; aerobic, gram-negative coccobacilli.

Laboratory Animal Reservoir:

Hosts: *Brucella melitensis*, *B. ovis*, *B. abortus* (occasionally)—sheep, *B. melitensis*—goats, *B. suis*—pigs, *B. canis*—dogs.

Disease: Infection of the genital tract causing infertility, abortion with chronic vaginal discharge; orchitis, prostatitis, epididymitis. Arthritis, lymphadenopathy, uveitis, and diskospondylitis may occur.

Detection: Culture, using selective media, of genital discharges, aborted fetuses, udder secretions, and tissues; PCR assay; rose bengal plate agglutination and complement-fixation (CF) tests are recommended for screening flocks and individu-

als (90); enzyme-linked immunosorbent assay (ELISA).

Control: Vaccination if available (live-agent vaccines superior to inactivated); animal testing and removal programs are frequently used; long-term antimicrobial therapy has been successful in dogs (179).

Mode of transmission: Direct contact of broken skin or conjunctiva with genital secretions, aborted fetuses, fetal fluids, and urine from animals; inhalation of aerosols from tissues (144).

Communicability: High with exposure to infected livestock or their tissues. The disease is uncommon in countries where control programs have largely eradicated the disease in livestock. Rarely, dogs can be infected with various strains of *Brucella* spp., and may serve to disseminate the agent to livestock (179). *Brucella abortus* and *B. melitensis* appear to be the agents of most zoonotic importance, followed by *B. suis*. It is unclear whether *B. ovis* has zoonotic importance. Since brucellosis in dogs is not uncommon, the risk may be low to moderate with *B. canis*.

Humans:

Occurrence: A survey of veterinarians in The Netherlands indicated that four of 89 (5%) had antibodies to *B. abortus* (75). Although two of the veterinarians were cattle practitioners; one was a swine practitioner, and the other worked for government, industry, or academia. In a serologic survey of 43 veterinarians in Florida, none had antibodies to *B. canis*, although six had antibodies to other *Brucella* spp. (125). However, in a seroepidemiologic study in Oklahoma, 53 of 73 (72%) practicing veterinarians had antibodies to *B. canis* (182). An animal technician had serologic evidence of *B. canis* infection (186). A fatal case of brucellosis due to *B. suis* was reported in a pig farmer that had not been exposed to livestock for at least 20 years (200).

Clinical syndromes: Acute or chronic onset with undulating fever, headache, myalgia, arthralgia, weakness; osteoarticular complications, including sacroiliitis; genitourinary infection.

Incubation period: Ranges from five days to five months, average one to two months; may be longer (200).

Diagnosis: Blood culture during the acute phase, using the lysis concentration method (55); serologic diagnosis by enzyme immunoassay (EIA) (55). Specialized serologic techniques are needed to detect *B. canis* antibodies because of cross-reaction with other species within the genus (48).

Prevention: PPE; strict hygienic measures for disposal of placenta, discharges, fluids, and fetuses after abortions; disinfection of contaminated surfaces. Satisfactory vaccines are not available for humans.

Treatment: Combination of rifampin or streptomycin, and doxycycline, for at least six weeks; severe disease may benefit from concurrent steroid administration (48).

Campylobacteriosis

Agent: *Campylobacter coli*, *C. fetus*, *C. hyointestinalis*, *C. jejuni*; microaerophilic, gram-negative, rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Pigs, chickens (256), sheep, dogs (195, 261), cats, ferrets (85, 168), hamsters (91), and nonhuman primates (including macaques, baboons, and squirrel monkeys) (246).

Disease: Asymptomatic to watery or mucohemorrhagic diar-

rhea; abortion and stillbirths due to *C. fetus*; fever, reduced appetite, vomiting. Clinical manifestations may be more severe in young animals (179).

Detection: Culture of feces on selective media; examination of fresh fecal or tissue samples, using dark-field or phase-contrast microscopy; serial serum samples to document increasing antibody titer by ELISA.

Control: Antimicrobials may be helpful; infected animals usually remain carriers despite treatment.

Mode of transmission: Fecal-oral.

Communicability: Low to moderate if proper sanitation measures are followed (77, 243). Prevalence of this organism in laboratory nonhuman primate colonies may be low (254).

Humans:

Occurrence: Cases of enteritis have been associated with exposure to domestic animals (5), sheep (70), and pigs (96). Asymptomatic laboratory-housed coyotes transmitted the agent to animal technicians (88).

Clinical syndromes: Often asymptomatic; abdominal pain, malaise, fever, nausea, vomiting, diarrhea; typhoid-like syndrome or reactive arthritis may develop. Rarely, may observe febrile convulsions, Guillain-Barré syndrome, and meningitis.

Incubation period: Ranges from one day to 10 days, usually two to five days.

Diagnosis: Culture of stool.

Prevention: Good hygiene and sanitation; detection and treatment of infected animals.

Treatment: Supportive care, including rehydration and electrolyte replacement, as needed (48). Select antimicrobial agents (e.g., erythromycin) may be efficacious during initial stages of disease, but isolation and susceptibility testing should be performed prior to administration.

Capnocytophagosis

Agent: *Capnocytophaga canimorsus*, *C. cynodegmi* (formerly *Dysgonic Fermenter-type 2*); aerobic gram-negative rod.

Laboratory Animal Reservoir:

Hosts: Dogs, cats, rodents.

Disease: Asymptomatic in host species.

Detection: Culture, using stringent growth conditions, of saliva and oral mucosa.

Control: Impractical, agent considered to be highly associated within the oral cavity of reservoir hosts.

Mode of transmission: Animal bites or scratches, or contamination with oral secretions.

Communicability: Low if proper animal handling techniques are used. Splenectomy and alcoholism appear to be strong predisposing factors for disease in human cases (34).

Humans:

Occurrence: No known cases have been reported in animal facilities; however, multiple reports of transmission to humans from pets exist. Purpura fulminans was noted following a dog bite (36). Two cases in immunocompetent persons were linked to contact with dogs, involving licks and scratches (271). In one study, 14 individuals developed fever and septicemia after contact with dogs or dog bites (39); in another review, 42 of 52 hu-

man cases were linked to dog or cat bites, scratches or contact (271). Two cases of fever and erythema, one in an asplenic person, were linked to cat bites and scratches (42). Septicemia developed in an immunosuppressed asplenic individual after a cat scratch (166).

Clinical syndromes: Cellulitis, fever, septicemia, purulent meningitis, endocarditis and septic arthritis; can be fatal. Immunosuppressed and splenectomized patients, as well as alcoholics and those with various chronic diseases, appear to be at highest risk.

Incubation period: Ranges from one to five days.

Diagnosis: Identification of bacteria within neutrophils; isolation by culture.

Prevention: PPE, including gloves; proper training in animal handling and restraint; disinfect wounds following injury or exposure.

Treatment: Penicillin G is the antibiotic of choice (48).

Cat Scratch Disease

Agent: *Bartonella henselae*; aerobic, gram-negative bacilli.

Laboratory Animal Reservoir:

Hosts: Cats, occasionally dogs (16).

Disease: Usually asymptomatic; however, may cause reproductive failure in female cats and peliosis hepatis in dogs (152).

Detection: Culture; PCR assay of formalin-fixed, paraffin-embedded tissues (167).

Control: Impractical, agent considered to be highly associated within the reservoir host; control of flea population to reduce transmission between cats.

Mode of transmission: Principally spread by fleas among cats; however, flea-to-human transmission is unlikely. Infection typically occurs after bites or scratches from healthy young cats and occasionally dogs.

Communicability: Low with proper animal handling techniques and protective equipment. This is an emerging pathogen among immunosuppressed individuals in the general population, and warrants appropriate precaution in animal facilities (143). Veterinary care personnel are generally considered to be at higher risk (158).

Humans:

Occurrence: Reports of transmission to humans from pet cats; however, no documented cases in laboratory animal settings. A higher rate of suspected cat-scratch disease was documented among veterinary surgeons (18.6%) and veterinary technicians (8.9%) than in non-veterinary workers (1.3%) (10). Pet dogs transmitted the pathogen to two persons, in the absence of any contact with cats, with resulting fever and lymphadenopathy (189).

Clinical syndromes: Papule at site of lesion within one week after exposure, lymphadenopathy within two weeks, fever, malaise, myalgia, bacillary angiomatosis (particularly in immunosuppressed persons), peliosis hepatis, lymphadenitis, aseptic meningitis with bacteremia; chronic osteomyelitis (208).

Incubation period: Ranges from three to 14 days for development of primary lesion, up to 50 days for development of lymphadenopathy.

Diagnosis: History of clinical signs of disease; immunofluorescent antibody (IFA) test; biopsy of lymph node followed by

Warthin-Starry silver stain to demonstrate the organism histologically; PCR assay.

Prevention: Proper training in cat handling and PPE; disinfect wounds following injury or exposure from cats.

Treatment: Not generally used or indicated in symptomatic persons since disease is often self-limiting; however, rifampin, erythromycin, or doxycycline can be administered to immunocompromised individuals if disease sequelae are more severe (48).

Chlamydiosis

Agent: *Chlamydomphila abortus* (formerly *Chlamydomphila (Chlamydia) psittaci*—non-avian biotypes), *C. pecorum*, *C. pneumoniae*; obligate, intracellular, gram-negative, coccoid, rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: *C. abortus*—sheep and goats (196, 205, 225), dogs (102, 205, 225), cats and guinea pigs (205, 225); *C. pecorum*—sheep and goats (196); *C. pneumoniae*—frogs (*Xenopus* sp.) (211). Three reports in frogs were published before identification of *C. pneumoniae*; the agent was, therefore, only described by genus (129) or as *C. psittaci* (194, 260).

Disease: Asymptomatic; fetal loss (abortion, stillbirth), pneumonia, and enteritis due to *C. abortus* in sheep and goats; keratoconjunctivitis and polyarthritis due to *C. pecorum* in sheep and goats; pneumonia and endocarditis in dogs, keratoconjunctivitis and pneumonitis in cats; conjunctivitis, keratitis, salpingitis in guinea pigs; lethargy, disequilibrium, petechiation, and edema in frogs.

Detection: Histologic examination of tissues; identification of chlamydial inclusions in tissue scrapings; CF with acute and convalescent sera (more useful on a flock than an individual basis) (196).

Control: Antimicrobials (e.g., tetracyclines and erythromycin [orally and topically administered]); test and cull infected animals; vaccination in cats.

Mode of transmission: Contact with animals or their tissues, particularly birth products; inhalation of desiccated excretions or secretions.

Communicability: Moderate with exposure to birth fluids and membranes of sheep and goats. Because pregnant women are particularly susceptible, exposure to sheep and goats, particularly parturient animals, should be avoided (174). Human infection from zoonotic transmission has only been reported for *C. abortus*.

Humans:

Occurrence: Disease occurs sporadically in persons exposed to animals. Numerous case reports of infections in pregnant women exposed to sheep in an abattoir (104), and in farm settings, particularly after exposure to aborting sheep (22, 40, 57, 82, 116, 137, 138, 174, 175, 180, 215) or goats (27, 207, 252). In one case, Q fever occurred concurrently (174).

Clinical syndromes: Flu-like illness, conjunctivitis, pneumonia, encephalitis, myocarditis, thrombophlebitis; febrile illness, and abortion in pregnant women (40, 116, 175).

Incubation period: Ranges from one week to four weeks.

Diagnosis: Detection of increasing IgG antibody titer in paired sera by use of CF or microimmunofluorescent assay (MIA).

Prevention: PPE to prevent inhalation of and direct contact

with the agent; disinfection of contaminated waste and environmental surfaces.

Treatment: Antimicrobials, such as tetracycline or doxycycline.

Cryptococcosis

Agent: *Cryptococcus neoformans*; encapsulated yeast.

Laboratory Animal Reservoir:

Hosts: Pigeons.

Disease: Asymptomatic.

Detection: Culture of feces; identification of the organism in feces by use of light microscopy.

Control: Isolation and quarantine of pigeons arriving to facility; strict sanitation of caging areas.

Mode of transmission: Inhalation of agent from dried pigeon feces or their digestive material (e.g., crop contents); contamination of wounds inflicted by pigeons.

Communicability: Low in well-maintained biomedical research environments. In aviaries or poorly sanitized pigeon houses, there is greater risk for human infection.

Humans:

Occurrence: A survey of 101 subjects, who had fed pigeons or operated pigeon farms for two months to 40 years, indicated that four individuals had serum cryptococcal antigen (241). Cutaneous cryptococcosis has been reported in pigeon fanciers (15, 95), and a case of meningitis was reported in a worker exposed to pigeon feces (259). The disease occurs more commonly in immunocompromised persons (15, 95, 241).

Clinical syndromes: Cutaneous lesions, meningitis.

Incubation period: Unknown, may be months to years.

Diagnosis: Histologic examination and special staining of biopsy specimens from cutaneous lesions; microscopic identification of organism in cerebrospinal fluid (CSF) by use of India ink; latex agglutination test of CSF or sera for cryptococcal antigen; culture of CSF or skin lesion biopsy specimens (48).

Prevention: PPE to prevent inhalation and direct contact with agent; good hygiene after contact with pigeons; disinfection of contaminated environmental surfaces.

Treatment: Antifungal agents (e.g., amphotericin B) (259).

Cryptosporidiosis

Agent: *Cryptosporidium parvum*, *C. canis*, *C. felis*; coccidian protozoa.

Laboratory Animal Reservoir:

Hosts: Cats (120), dogs (80), macaques, baboons, squirrel monkeys, and other nonhuman primates (190), sheep (247), pigs (247), ferrets (168, 212), chickens (247); frogs (99).

Disease: Asymptomatic to intractable diarrhea; respiratory tract disease and airsacculitis in chickens (179); proliferative gastritis in frogs (99). Disease can be severe in immunocompromised animals.

Detection: Microscopic detection of oocysts in fecal smears that have been stained by use of the acid-fast procedure; commercially available assay can be used to detect *C. parvum*-specific antigen in fecal samples (120); identification of cryptosporidia in intestinal biopsy specimens by use of histologic examination (212); detection of IgG antibodies by use of ELISA (120).

Control: Environmental sanitation; treatment with paromomycin (17), although its toxicity has been reported (94).

Mode of transmission: Fecal-oral, possibly airborne (126).

Communicability: Low; risk is higher if contact occurs with neonatal animals, which are more susceptible and can shed high titers of the organism. Infections in dogs and cats are rare (198). Oocysts are immediately infective on shedding.

Humans:

Occurrence: In general, cases are more frequently associated with exposure to livestock than to pet animals. A case-control study of human immunodeficiency virus (HIV)-infected individuals, with and without cryptosporidiosis, in the United States, found no difference in overall pet ownership or cat or bird ownership; dog ownership was of borderline significance, indicating that pets were not a major risk factor (93). Although *C. parvum* is the major species involved in human infection, a study of stool samples from 1,680 patients in England indicated that four were infected with *C. felis* and one with *C. canis* (201); in 80 cases from Peru, two were infected with *C. canis* and one with *C. felis* (266), indicating that human infections with these species occur. A person with acquired immune deficiency syndrome (AIDS) developed chronic diarrhea following exposure to a cat (155).

Clinical syndromes: May be asymptomatic or cause profuse watery diarrhea. The agent can cause protracted illness in immunocompromised persons.

Incubation period: Likely ranges from one day to 12 days, with an average of seven days.

Diagnosis: Microscopic detection of oocysts in stool smears, stained by use of the acid-fast procedure (126); detection of cryptosporidia in intestinal biopsy specimens by use of histologic examination; increase in serum antibody titer by IFA test or ELISA (126).

Prevention: PPE; sanitation; good hygiene.

Treatment: Supportive care; antimicrobials have generally not been beneficial.

Dermatophytosis

Agent: *Trichophyton mentagrophytes*, *T. verrucosum*; *Microsporium canis*; saprophytic fungi.

Laboratory Animal Reservoir:

Hosts: *T. mentagrophytes*, *M. canis*—guinea pigs (206) and rabbits (253); *M. canis*—cats, dogs, and nonhuman primates; *T. verrucosum*—sheep and goats.

Disease: May be asymptomatic, especially in cats. Lesions usually develop on or about the head, typically appearing as patchy areas of alopecia and erythema; crusts are present with an underlying inflammatory reaction. Lesions are pruritic, and may spread to other areas of the body. Secondary bacterial infection may result in abscessation of hair follicles.

Detection: Microscopic examination of hair/skin/fleece scrapings mounted in 10% potassium hydroxide, culture on suitable dermatophyte test media; despite limited sensitivity, affected areas can be examined, using a Wood's UV lamp (for *M. canis* only).

Control: Infection is probably low in barrier-maintained or specific-pathogen-free (SPF) animals; topical treatment with miconazole or clotrimazole; systemic griseofulvin can be used for severe cases, but teratogenic and occasionally hepatotoxic effects are noted; a vaccine for cats is available (179). Sheep should be shorn prior to their introduction into the animal facility.

Mode of transmission: Direct contact with skin lesions in various animal species; spores can be widely disseminated and persist in the environment (253). Chronic asymptomatic carrier animals represent a continuing source for transmission.

Communicability: Unknown, but probably low to moderate.

Humans:

Occurrence: A survey of veterinary staff in two governmental departments in the United Kingdom indicated that ringworm was the most commonly reported zoonosis, with overall prevalence of 24% in 1,625 staff interviewed (54). An animal attendant responsible for handling *T. mentagrophytes*-infected laboratory animals developed a ringworm lesion on his wrist (172). Six persons in Japan were infected after exposure to laboratory rats and guinea pigs (124). Three cases in laboratory animal and research technicians that had contact with guinea pigs were reported (156, 157).

Clinical syndromes: Flat, spreading, ring-shaped lesions in the skin ("ringworm"). The margin is usually reddish, vesicular, or pustular and may be dry and scaly with crusts. As the lesions expand peripherally, the central areas often clear, leaving apparently normal skin.

Incubation period: Ranges from 10 to 14 days.

Diagnosis: Appearance of characteristic lesions; fluorescence of organisms under UV light (for *M. canis* only); culture on appropriate fungal media.

Prevention: PPE, including gloves; sanitation.

Treatment: Thorough bathing with soap and water; daily topical application of fungicide for at least one month; oral fungicides (e.g., griseofulvin, itraconazole, and terbinafine) are effective in treatment of extensive lesions (48).

Echinococcosis

Agent: *Echinococcus granulosus*, *E. multilocularis*, *E. oligarthrus*, and *E. vogeli*; cestodes.

Laboratory Animal Reservoir:

Hosts: *Echinococcus granulosus*, *E. multilocularis*, and *E. vogeli*—dogs (final hosts) and other canids; *E. multilocularis* and *E. oligarthrus*—cats (final hosts) and other felids; *E. granulosus*—ungulates (intermediate hosts); and *E. multilocularis*, *E. oligarthrus* and *E. vogeli*—rodents (intermediate hosts). The cycle of *E. granulosus* involving dogs and sheep is especially important (112, 223).

Disease: Infection by strobilar stage typically asymptomatic in final hosts with all species of *Echinococcus*. Cysts most commonly develop in liver and lungs of intermediate hosts.

Detection: In final hosts, observation of the strobilar stage in feces after anthelmintic treatment. Detection of adult worm products in feces: coproantigen by ELISA (62, 63) or copro-DNA by PCR assay (1, 170). Fecal flotation is unreliable since echinococcal eggs are indistinguishable from eggs of *Taenia* spp. Metacestodes in intermediate hosts usually not discernible before death.

Control: Prevent consumption by dogs of viscera of domestic ungulates and reindeer (*E. granulosus*), and rodents (*E. multilocularis* and *E. vogeli*) that harbor metacestodes. Dogs can be treated with praziquantel every 30 (*E. multilocularis*) or 45 days (*E. granulosus*).

Mode of transmission: Ingestion of eggs shed in the feces of the final hosts (dogs and cats).

Communicability: Low in biomedical research environments.

Humans:

Occurrence: Human cases have not been reported in laboratory animal settings. Cystic echinococcosis, caused by *E. granulosus*, is endemic in nearly all livestock-rearing countries (165). Alveolar echinococcosis, caused by *E. multilocularis*, occurs widely in North America and Eurasia (73). Dogs originating in rural areas may be infected with *E. granulosus* or *E. multilocularis*. Polycystic echinococcosis, caused by *E. vogeli*, and infections with *E. oligarthrus*, occur exclusively in Central and South America (73).

Clinical syndromes: The occurrence of clinical signs of disease depends on the species of *Echinococcus*, cyst location, and size (242). The northern biotype (wolf-deer) of *E. granulosus* usually causes benign infections, whereas the synanthropic biotype (dog-sheep) is more pathogenic. Infection results in cysts, principally in the liver and lungs, but other organs may also be affected. Infection with *E. multilocularis* results principally in hepatomegaly, but spread to lungs and brain may occur late in disease. *Echinococcus vogeli* infection causes disease of the liver, with dissemination to other abdominal organs. Only three cases of *E. oligarthrus* infection have been reported, resulting in postorbital cysts (two cases) and a liver cyst (one case).

Incubation period: Ranges from months to years, depending on the species of *Echinococcus*, parasite-burden, rate of growth of the metacestode, the organ(s) affected, and the duration of infection.

Diagnosis: Depends on the species of *Echinococcus* and clinical signs of disease and symptoms compatible with a growing space-occupying or invasive tumor-like mass. Verify by use of radiography, computed tomography, or ultrasonography; serologic testing (ELISA) (270).

Prevention: PPE; good hygiene.

Treatment: Surgical resection of cysts; treatment with albendazole.

Ectoparasitism

Agents: Mites: *Cheyletiella parasitovorax*, *Liponyssoides sanguineus*, *Notoedres cati*, *Ornithonyssus bacoti*, *Sarcoptes scabiei*, and others. Fleas: *Ctenocephalides canis*, *C. felis*, and others. Ticks: *Dermacentor variabilis*, *Rhipicephalus sanguineus*, and others.

Laboratory Animal Reservoir:

Hosts: Cats, dogs, rabbits, rodents, and other common laboratory animal species may occasionally be infested with these arthropod agents (83, 84, 89, 161, 269).

Disease: Asymptomatic to severe dermatitis with alopecia, skin thickening, and secondary pyoderma; anemia, debility, decreased reproduction, pruritus. Some of these ectoparasites are important vectors of various bacterial, rickettsial, and viral diseases.

Detection: Microscopic or direct examination of skin scrapings or tufts of hair; manual collection from the animals or their bedding.

Control: Prompt elimination of infestation from the animals and their habitats is warranted, using appropriate insecticides (e.g., pyrethrins and permethrins, avermectins); nontoxic measures (e.g., insect growth regulators and silica gels) should be used wherever possible (134); isolation or quarantine of random-source animals; prophylactic topical treatment of animals

on arrival at the facility; thorough cleaning of the environment and ensuring that an appropriate pest prevention and control program has been established (83, 269).

Mode of transmission: Direct or indirect contact, including infestation of food, bedding, shipping containers, and caging equipment used in conjunction with animal care.

Communicability: Low to moderate; most ectoparasites of laboratory animals are host-specific, and their life cycle often cannot be sustained in modern animal care programs (83, 269).

Humans:

Occurrence: There have been several reports of ectoparasitism among animal husbandry and research technicians in laboratory animal care settings (83, 84, 89, 161, 269). Recognition of animal infestations has sometimes initially been prompted by medical complaints from staff members or pet owners (56).

Clinical syndromes: Moderate to severe, but transient pruritic dermatitis, eczema, pyoderma, or painful or irritating bites from some arthropods on any area of the skin; more substantial systemic consequences can result from ectoparasites harboring bacterial, rickettsial, or viral agents of human disease.

Incubation period: Immediately following exposure to arthropods.

Diagnosis: Microscopic or direct examination of skin scrapings or tufts of hair.

Prevention: PPE, including gloves when handling animals that are suspect for ectoparasites.

Treatment: Prescribed antiparasitic medication; cleansing baths; vaccination for ectoparasite-borne disease agents (48).

Erysipelas

Agent: *Erysipelothrix rhusiopathiae*; gram-positive, rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Pigs, chickens.

Disease: Fever, lethargy, septicemia, non-suppurative chronic arthritis, diskospondylitis, and sudden death; diamond-shaped skin lesions, necrosis of ear and tail tips in pigs; septicemia in chickens.

Detection: Culture of blood, tonsils, lymph nodes, or joint fluid; histologic identification of organism in tissues at necropsy.

Control: Antimicrobials; good sanitation of housing environment; routine vaccination program; testing and elimination of carriers.

Mode of transmission: Direct contact with animals, tissues, or feces; piglets can be infected through skin abrasions around the navel ("joint ill"); insect vectors (e.g., *Dermanyssus gallinae*) have been linked to spread of the disease in chicken flocks (49). Recovered animals may be carriers for life (179).

Communicability: Low to moderate in biomedical research environments. Risk of cutaneous infection increases if animal handlers have unprotected cuts or abrasions on hands.

Humans:

Occurrence: One case report described concomitant infection with *E. rhusiopathiae* and orf in a sheep farmer (53). Two animal technicians in a chicken-rearing facility were infected after handling sick and dead birds (191).

Clinical syndromes: Cellulitis, fever, bacteremia, endocarditis, encephalitis, septic arthritis.

Incubation period: Ranges from one day to three days.

Diagnosis: Culture of blood.

Prevention: PPE, including gloves when handling infected animals; good hygiene.

Treatment: Penicillins and, less commonly, tetracyclines (191).

Giardiasis

Agent: *Giardia duodenalis*, *G. intestinalis*, *G. lamblia*; flagellate protozoa.

Laboratory Animal Reservoir:

Hosts: Cats, dogs, nonhuman primates (macaques, baboons, squirrel monkeys) (92), pigs, sheep, goats.

Disease: Usually asymptomatic; may have diarrhea, with weight loss, vomiting, and anorexia (108).

Detection: Isolate cysts by use of zinc sulfate fecal flotation; evaluate using light microscopy (38). Due to intermittent cyst shedding, fecal samples from three consecutive days should be examined.

Control: Sanitation of environment; prompt removal of feces from pens; treatment with antiparasitic agents (e.g., metronidazole and fenbendazole).

Mode of transmission: Fecal-oral.

Communicability: Moderate to high when working with livestock obtained from infected herds. The agent may be shed by asymptomatic animals.

Humans:

Occurrence: Infection is common, and may be transmitted from animals to humans and vice-versa. Organisms infecting humans and ruminants are morphologically and antigenically similar (38).

Clinical syndromes: Asymptomatic to chronic intermittent diarrhea, with anorexia, abdominal cramps, and steatorrhea; arthritis.

Incubation period: Ranges from two to more than 25 days, average of 7 to 10 days.

Diagnosis: Identification of cysts or trophozoites in stool samples; document three negative test results in series (48); ELISA.

Prevention: Sanitation; personal hygiene.

Treatment: Antiparasitic agents (e.g., metronidazole); supportive care.

Hantaviral Diseases

Agent: Hantaan virus; Seoul virus; bunyavirus.

Laboratory Animal Reservoir:

Hosts: Rats and mice, other wild rodents, potentially cats (267).

Disease: Asymptomatic.

Detection: Serologic testing for specific antibodies, using ELISA, IFA test.

Control: Exclude wild rodents from laboratory animal facilities; screen rodents prior to acceptance; test rodent-derived cell lines prior to use, particularly those originating from endemic regions.

Mode of transmission: Virus shed in urine, feces, and saliva of persistently infected rodents for months (159); inhalation of

infective aerosols from rodent excreta; wound contamination, conjunctival exposure, ingestion. Rat cell lines have been implicated as a source of virus (232).

Communicability: Low, probability of transmission increased during winter months due to lower humidity and closure of circulation system to outside air (160). Brief periods of exposure have been sufficient to cause human infections (160).

Humans:

Occurrence: Korean hemorrhagic fever was noted among professional staff (veterinarians and physicians) at a Japanese university that used rats (248). A nationwide survey of research institutions in Japan reported that 126 cases of hemorrhagic fever and renal syndrome (HFRS) occurred between 1970 and 1986 (146). The HFRS also occurred in several laboratory staff workers exposed to rats at a university in Belgium and at a cancer research institute in the United Kingdom (65, 163). Screening of laboratory animal personnel for antibodies to Hantaan virus in Japan, France, the United Kingdom, and Singapore indicated that several persons had experienced subclinical infections (164, 248, 264). The Belgian university conducted a serologic survey of 60 staff members that had contact with laboratory animals, particularly rats, and found that 30 (50%) of them had evidence of subclinical infection with Hantaan virus. At two other institutions that had no cases of HFRS, only one of 34 (3%) personnel with similar exposures to laboratory animals had antibodies against the virus (65).

Clinical syndromes: The HFRS of variable severity (mortality < 5%), with clinical signs of disease related to the strain of virus involved; acute onset of fever, lower back pain, sometimes associated with hemorrhage and nephropathy. Hantavirus pulmonary syndrome (HPS), caused by another species of hantavirus, Sin Nombre virus, is characterized by fever, myalgia, and gastrointestinal dysfunction, frequently followed by fulminant respiratory distress and death (48). The HPS has not been associated with rats of the genus *Rattus* or mice of the genus *Mus* (227).

Incubation period: Ranges from a few days to months, average two to four weeks.

Diagnosis: Serologic testing for specific antibodies, using ELISA and the IFA test; RT-PCR assay is the molecular diagnostic test of choice, although the genomic heterogeneity of hantaviruses can complicate interpretation of results (227).

Prevention: Respiratory tract protection is necessary to prevent inhalation exposure; good hygiene; disinfection of contaminated waste and work surfaces.

Treatment: Intravenous fluid therapy; bed rest; ribavirin given intravenously has been beneficial in some cases (48).

Leptospirosis

Agent: *Leptospira canicola*, *L. hardjo*, *L. icterohaemorrhagiae*, *L. interrogans* serovar *ballum*, *L. pomona*, *L. sejroe*, and other *Leptospira* spp; spirochete bacteria.

Laboratory Animal Reservoir:

Hosts: *Leptospira interrogans* serovar *ballum*—mice; *L. icterohaemorrhagiae*—rats; *L. canicola*, *L. sejroe*—dogs; *L. pomona*, *L. hardjo*—pigs, sheep, goats; cats (30); gerbils, hamsters; rarely, squirrel monkeys, baboons, and other nonhuman primates (81).

Disease: Asymptomatic in mice; fever, hematuria, and hepatic and renal disease in dogs (218, 221); reproductive failure

in sheep and goats (76); icterohemorrhagic disease with abortion in squirrel monkeys (204).

Detection: ELISA and MIA test; increasing IgG antibody titer in paired serum samples; detection of leptospire in urine (using dark-field microscopy) or tissues; PCR assay of urine (113, 114).

Control: Sanitation of facilities and appropriate animal waste control, especially of urine; regular vaccination program; treatment of infected animals with antimicrobials (e.g., penicillins and aminoglycosides in small animals, streptomycin in pigs) (76, 179); isolation or quarantine of sick animals; immunization with a custom-prepared inactivated vaccine was used to control the disease in an endemically infected squirrel monkey colony (204).

Mode of transmission: Oral ingestion; exposure to contaminated urine, placenta, fetal tissues; inhalation. Organisms can also infect hosts through abrasions in the skin or mucosal surfaces.

Communicability: Low to moderate.

Humans:

Occurrence: An animal technician developed jaundice after bloodborne exposure to a dog with jaundice (258). The dog and the technician had antibodies to *L. icterohaemorrhagiae* and *L. canicola*. A seroprevalence study of 35 animal technicians indicated that 32 (91%) had antibodies to several leptospiral serovars, compared with four of 20 (20%) laboratory personnel without animal exposure (192). The animal technicians had *Leptospira* antibody profiles that were similar to those of mice, rats, guinea pigs, and rabbits in their facility, with prevalence by species ranging from 71 to 90%. In a cross-sectional study of university employees working with an infected swine herd, nine of 110 (8%) were serologically confirmed as cases (41).

Clinical syndromes: Mild flu-like illness with fever, headaches, rash, and myalgia; may lead to severe infection with renal, hepatic, or meningeal involvement; myocarditis, pulmonary involvement (119); orchitis; jaundice (Weil's disease).

Incubation period: Ranges from four to 19 days, average of 10 days.

Diagnosis: Serologic testing for specific antibodies, using ELISA or IFA test; isolation of leptospire from blood or CSF within seven to 10 days of infection; isolation from urine within 10 days of infection (48).

Prevention: PPE to prevent exposure of uncovered skin or mucous membranes in contaminated settings; good hygiene.

Treatment: Penicillin, cephalosporins, tetracyclines, erythromycin; more severe infections may require intravenously administered antimicrobials (119).

Lymphocytic Choriomeningitis

Agent: Lymphocytic choriomeningitis virus (LCMV); arenavirus.

Laboratory Animal Reservoir:

Hosts: Mice, rats, hamsters, guinea pigs. Nonhuman primates in zoological settings have experienced outbreaks after the accidental feeding of infected mice (13).

Disease: The pattern of disease in animals depends on age of animals, strain and dose of virus, and route of inoculation (202). Asymptomatic to runting and chronic wasting in mice (202); asymptomatic in guinea pigs and hamsters (179, 202); dyspnea, anorexia, lethargy, jaundice, and mortality in marmosets and

tamarins (13).

Detection: Virus isolation in cell culture.

Control: Exclude wild rodents from laboratory animal facilities; screen rodents prior to acceptance; test rodent-derived cell lines prior to use.

Mode of transmission: Transmission to humans by parenteral inoculation, ingestion, inhalation, and splash contamination of mucous membranes with infective secretions (urine, feces and saliva); other routes include contact with contaminated bedding material and infected ectoparasites (52). Athymic and severe-combined-immunodeficient mice pose a special risk to humans by harboring silent, chronic infections (72). The large number of outbreaks attributed to hamsters suggests that they may be amplifying hosts for the virus. The virus has been isolated from immortalized cell lines (21). Transmission by aerosolization poses a particular hazard for pregnant women (19).

Communicability: Low if appropriate protective measures are taken.

Humans:

Occurrence: A flu-like illness due to LCMV in animal technicians and research personnel exposed to nude mice (72) and hamsters (21, 28, 122, 128, 162, 251) that were inoculated with infected tumor cells was reported. A few cases also had aseptic meningitis (12, 28, 72, 251). Additionally, serologic screening of personnel indicated that 10 to 24% experienced subclinical infection with LCMV (72, 122). Seroconversion to LCMV occurred in two zoo veterinarians following bite wounds from and necropsy examinations of infected marmosets and tamarins (183).

Clinical syndromes: Asymptomatic to nonspecific flu-like illness with headache, fever, and myalgia; may progress to aseptic meningitis. The LCMV has been recognized as a teratogen in humans (18, 19).

Incubation period: Ranges from one week to three weeks.

Diagnosis: Detection of IgM antibody, increase in IgG titer in acute and convalescent serum samples by IFA or serum neutralization tests; virus isolation assays.

Prevention: PPE, including gloves for handling rodents or their tissues; good hygiene.

Treatment: Supportive care.

Orf (Contagious Ecthyma)

Agent: Orf virus; parapoxvirus.

Laboratory Animal Reservoir:

Hosts: Sheep, goats.

Disease: Pustular lesions principally around the lips; also on gums, nostrils, and occasionally, teats and udders; interdigital and coronet lesions can lead to lameness (179); atypical presentation as warts on distal aspect of limbs (229); disease in goats more severe than that in sheep (179). Sheep can be reinfected (105).

Detection: Clinical lesions; detection of IgG antibodies by use of ELISA.

Control: Usually self-limiting; vaccination with live attenuated virus or scarification with a suspension of infective scab material (193).

Mode of transmission: Direct contact with animals; virus highly resistant to desiccation and can persist in scabs and

crusts for years (179); communal equipment used between animals in sheep flocks (184).

Communicability: High when exposed to animals with active lesions. The disease is uncommon in laboratory animal facilities as sheep are generally required to be free of clinical signs of disease prior to acceptance.

Humans:

Occurrence: The disease is common in persons with occupational exposure to sheep. In the United Kingdom, 15 to 29% of farm workers reported having had orf (37, 199). A study of English farm workers indicated an annual incidence of 2.8% (199). Several case reports document human infection due to occupational exposure in agricultural (53, 79, 140, 181, 185, 236) and research settings (184, 185). Cases usually involved handling infected animals without gloves. In a laboratory setting, two researchers were infected after being bitten by an affected lamb during passage of an orogastric tube (184). In one report of a sheep farmer, orf was complicated by erysipelas (53).

Clinical syndromes: Pustular dermatitis, usually on the hands and face.

Incubation period: Ranges from three to six days.

Diagnosis: Clinical signs of disease; detection of IgG antibody, using a cell culture immunofluorescence test (199); histologic examination of skin biopsy specimen (151).

Prevention: PRE, especially gloves; good hygiene.

Treatment: None. Typically, disease is self limiting over three to six weeks; secondary bacterial infections may occur.

Pasteurellosis

Agent: *Pasteurella multocida*; facultative anaerobic gram-negative rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Cats, rabbits, dogs, pigs.

Disease: Asymptomatic in cats and dogs; respiratory signs of variable severity, rhinitis, otitis, subcutaneous and visceral abscesses and genital infections in rabbits. Up to 30 to 90% of healthy rabbits may be carriers in conventional rabbit colonies (179); in pigs, atrophic rhinitis can develop in co-infections with *Bordetella bronchiseptica* (179).

Detection: Culture; IFA test on nasal swab specimens.

Control: Antimicrobials (e.g., enrofloxacin) may only provide temporary remission and alleviation of clinical signs of disease. Vaccines for rabbits have been developed (237, 238).

Mode of transmission: Bite wounds, possibly aerosol.

Communicability: Low, but may be greater among debilitated or immunocompromised persons. *Pasteurella* species are the most common isolates from dog (50%) and cat bites (75%) (240).

Humans:

Occurrence: Infection in a pregnant woman from a cat bite resulted in fatal congenital pneumonia (8). Other reports describe the development of meningitis and pericardial tamponade in one individual (4), and pneumonia in an immunosuppressed person following a cat bite (69). An animal technician developed a local abscess after a bite sustained from a rabbit with rhinitis (29). In pig breeders, culture revealed the presence of *P. multocida* in the oropharynxes of 19 of 49 (39%) examined (14).

Clinical syndromes: Cellulitis, erythema and painful swell-

ing at site of bite; septicemia, peritonitis.

Incubation period: Up to 24 h.

Diagnosis: Culture of bite or scratch wounds.

Prevention: PPE, including gloves; appropriate restraint of animals; sanitation.

Treatment: Ceftriaxone, ciprofloxacin (33), and doxycycline (153) have been used with success.

Poxvirus Diseases

Agent: Monkeypox; orthopoxvirus. Yaba and Tanapox; yatapoxvirus.

Laboratory Animal Reservoir:

Hosts: Monkeypox: principally African nonhuman primates, but other species (e.g., macaques) also susceptible (115). African tree squirrels are thought to be an important reservoir species for monkeypox (148). Yatapoxviruses: macaques and other non-human primates (68). However, nonhuman primates are not considered the primary natural reservoir for either group of viruses (149, 150).

Disease: Monkeypox: variable; vesicular exanthema, papules or masses in subcutaneous, pulmonary, or other tissues, high morbidity; internal and external pock lesions. Yatapoxviruses: variable; multiple lesions of the skin, oral cavity, pulmonary tissues, and other regions that typically regress spontaneously within three to six weeks.

Detection: Virus isolation; PCR assay; serologic testing.

Control: Monkeys with clinical signs of disease should be euthanized.

Mode of transmission: Direct and indirect contact; aerosol transmission.

Communicability: Unknown, but thought to be moderate for both types. Introduction of imported exotic rodents (Gambian giant rats and other species), with subsequent transmission to prairie dogs; a rabbit distributed in the pet trade caused numerous cases of monkeypox among persons in the midwestern region of the United States (47). This is the first outbreak of monkeypox in the western hemisphere (78).

Humans:

Occurrence: Cases of monkeypox among workers in laboratory animal settings have not been reported. Outbreaks of monkeypox have occurred with some regularity in endemic regions of Central and West Africa (133). Transmission of yatapoxviruses to humans from infected monkeys has been documented, including iatrogenic infection from contaminated needles (136).

Clinical syndromes: Monkeypox: fever, headache, respiratory signs, rash, pock lesions resembling smallpox on extremities but occasionally disseminated; pronounced lymphadenopathy in neck and inguinal regions, sometimes resulting in fatality. Yaba- and Tanapoxviruses: fever, slow-growing subcutaneous histiocytic nodules, lymphadenopathy.

Incubation period: Ranges from one week to three weeks.

Diagnosis: Virus isolation; PCR assay; serologic testing, including hemagglutination-inhibition (HI) test, radioimmunoassay (RIA), serum neutralization test, immunoblot assay.

Prevention: PPE, including splash and respiratory protection; appropriate restraint procedures; routine quarantine procedures for monkeys; strict sanitation practices for isolation and disposal of infected monkeys; pre-exposure smallpox vaccina-

tion is highly effective in preventing monkeypox.

Treatment: Monkeypox: following exposure, cidofovir and vaccinia immune globulin can be considered, under guidance of health authorities. Yaba- and Tanapoxviruses: self-limiting, no recommended treatment.

Psittacosis (Ornithosis)

Agent: *Chlamydophila psittaci* (formerly *Chlamydia psittaci*) (avian biotypes); obligate intracellular gram-negative coccoid rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Chickens, pigeons (6, 74).

Disease: Asymptomatic (225); occasionally nasal and ocular discharge, conjunctivitis, lethargy, weight loss (179).

Detection: In live birds, culture of combined choanal and cloacal swab specimens, collected for three to five consecutive days and pooled. In dead birds, culture of liver and spleen. Detection of increasing IgG antibody titer in paired sera by use of modified direct CF test (130).

Control: Quarantine and examination of birds for clinical signs of disease; strict sanitation of avian housing areas; testing and elimination of infected birds; treatment of infected birds with orally administered tetracyclines. Guidelines for control and prevention are published regularly (130).

Mode of transmission: Direct contact with nasal discharges or feces from birds; airborne transmission by inhalation of desiccated feces is common (179).

Communicability: Not a common disease, but poses a substantial risk for immunocompromised persons or pregnant women.

Humans:

Occurrence: The disease occurs sporadically among persons exposed to birds. A survey of avian veterinarians in Australia indicated that 14 of 150 (9%) may have contracted psittacosis (97). In a serosurvey of pigeon fanciers in the United Kingdom, 106 of 271 (39%) had antibodies to *C. psittaci*, compared with six of 100 (6%) farmers (32). Additional cases have been reported in a veterinarian, who also experienced reinfection (97), and a person who experienced acute transverse myelitis after exposure to infected pigeons (262).

Clinical syndromes: Flu-like illness, respiratory tract disease, encephalitis, myocarditis, thrombophlebitis; severe illness and abortion in pregnant women (101).

Incubation period: Ranges from five to 14 days, but longer periods have been reported (130).

Diagnosis: Detection of increasing antibody titer by use of CF in paired serum samples obtained two weeks apart; MIA and PCR assay can be used to distinguish *C. psittaci* from other chlamydial species (130).

Prevention: Respiratory tract protection (e.g., N95 rating or higher) where airborne hazards exist; good sanitation programs.

Treatment: Antimicrobials (e.g., chlortetracycline [52], doxycycline [101]).

Q Fever

Agent: *Coxiella burnetii*; obligate intracellular rickettsia.

Laboratory Animal Reservoir:

Hosts: Sheep and goats (main reservoirs), cats, dogs.

Disease: Usually asymptomatic; in cases of severe infection, abortion and reproductive failure may occur (26).

Detection: Detection of antibodies against phase-I antigen by use of ELISA (more useful on a flock than an individual basis); PCR assay; immunohistochemical staining of tissues.

Control: Serologic testing followed by culling of infected animals; strict sanitation practices, especially during lambing since the organism is found in extremely high concentrations in the placenta and amniotic fluid (177); maintenance of *C. burnetii*-free animal populations; antimicrobials (e.g., tetracycline, chloramphenicol).

Mode of transmission: The agent is acquired by exposure to fetal membranes, birth fluids, and stillborn animals. Airborne dissemination occurs during parturition, and humans are infected by inhalation or direct contact with tissues. *Coxiella burnetii* can also be shed in milk, urine, and feces (177). Ixodid and argasid ticks can be invertebrate reservoirs and vectors of the agent (179).

Communicability: Occupational exposure is highly linked to the risk of acquiring infection from animals (176). In research facilities, if sheep are properly screened for infection, the risk is substantially less.

Humans:

Occurrence: A survey in the United Kingdom indicated that 29 of 87 (33%) abattoir workers, 17 of 61 (28%) veterinarians, and 24 of 193 (13%) farm families had antibodies (249). In contrast, only 11 of 697 (2%) of the general population had antibodies. In a serosurvey of personnel at veterinary schools in California, and Minas Gerais, Brazil, 14 of 138 (10%) and 48 of 219 (22%), respectively, had antibodies (214). Sporadic cases and outbreaks have been reported in several biomedical research institutions (43, 98, 106, 107, 178, 210, 222). Serosurveys in laboratory animal settings have indicated that personnel potentially exposed to sheep have a greater prevalence of antibodies (16 to 18%) than do nonexposed groups (0.3 to 0.6%) (222, 228). However, during outbreaks, a considerably higher number of exposed personnel had antibodies (58, 98, 106, 107, 178). Serosurveys have also uncovered the retrospective occurrence of cases (58, 228).

Clinical syndromes: Acute infection results in headaches, fevers, chills, and sweats; myalgias, pneumonia with or without hilar lymphadenopathy (9), fatigue, chest pain, sore throat, nausea, vomiting and diarrhea. Chronic infection results in granulomatous hepatitis and endocarditis. Spontaneous abortion can occur in pregnant women (23, 169, 174).

Incubation period: Ranges from two to three weeks.

Diagnosis: Detection of increasing IgG antibody titer against phase-II antigen, in paired sera by use of ELISA or IFA test.

Prevention: PPE, including respiratory tract protection where airborne hazards exist; good hygiene; human vaccines have undergone clinical trials (26).

Treatment: Tetracyclines administered orally for 15 to 21 days have been effective (48).

Rabies

Agent: Rabies virus; rhabdovirus.

Laboratory Animal Reservoir:

Hosts: Dogs, cats, ferrets, livestock, and nonhuman primates.

Disease: Initial clinical signs of disease are extremely vari-

able; hydrophobia, aerophobia, agitation, confusion, limb pain, paresthesia, ataxia, paralysis. The various forms of disease range from "furious" to "paralytic," on the basis of areas of the central nervous system affected. Death can occur within two to seven days of illness (179).

Detection: Detection of viral antigen in brain by use of the direct fluorescent antibody test (87); confinement and daily observation of healthy dogs, cats, and ferrets for 10 days after bite injury to humans to observe for behavioral signs suggestive of infection that would warrant necropsy (135). Brain tissues for testing must include the hippocampus, medulla oblongata, and cerebellum, and must be refrigerated (179).

Control: Vaccination of laboratory dogs, cats, and ferrets; quarantine, euthanasia, and diagnostic testing of animals manifesting signs of disease. Guidelines for control and prevention are published regularly (135). Requirements for vaccination vary by geographic region, depending on endemic status of virus, as determined by public health authorities. There is no treatment for clinical disease.

Mode of transmission: Bite of rabid animal or inoculation of infective saliva into fresh wounds or mucous membranes.

Communicability: Low if facility acquires animals with verified vaccination history or with no possible exposure to reservoir species (86).

Humans:

Occurrence: No reported cases among persons in laboratory animal settings.

Clinical syndromes: Headache, fever, malaise, acute viral encephalomyelitis, and death due to respiratory paralysis.

Incubation period: Ranges from three to eight weeks, can be as short as nine days.

Diagnosis: Specific immunofluorescent antibody staining of brain tissue, skin, or mucosal scrapings; virus isolation.

Prevention: Pre-exposure immunization series if increased risk of occupational exposure among persons in endemic regions; immediate and thorough postexposure wound disinfection and prophylaxis by administration of human rabies immune globulin at the site of bite wound, and concurrent administration of rabies vaccine (48, 135). National standards address rabies prevention for persons in the United States (46, 111).

Treatment: Supportive care; no specific treatment guidelines. Prognosis is guarded if clinical signs of disease are progressive.

Rat Bite Fever

Agent: *Streptobacillus moniliformis*, gram-negative rod-shaped bacteria. *Spirillum minus*, gram-negative spiral-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Wild or laboratory rats, mice; rarely, cats and nonhuman primates.

Disease: Asymptomatic in rodents because agents are considered to be highly associated within the oral cavity; endocarditis and arthritis in nonhuman primates (250).

Detection: Isolation of the agents from the oral cavity, nares, or conjunctival sacs on appropriate culture medium. Animal inoculation is used for the isolation of *S. minus* (48); PCR assay (31).

Control: Cesarean-derived rodents are free of the agent; wild

rodent control for indoor and outdoor animal facilities; separation of nonhuman primates from rodents.

Mode of transmission: Most frequently occurs from animal bites. Agent transmitted by urine or secretions of the mouth, nares or conjunctival sacs. Indirect inoculation by contaminated fomites through trauma to unprotected skin.

Communicability: Unknown but probably low.

Humans:

Occurrence: An animal technician developed undulating fever and myalgia following a rat bite (7).

Clinical syndromes: *Streptobacillus moniliformis*: chills, fever, headache, myalgia, weakness; regional lymphadenopathy, joint inflammation. *S. minus*: distinctive rash of red to purple-colored plaques.

Incubation period: *Streptobacillus moniliformis*: fewer than 10 days. *S. minus*: two weeks to two months.

Diagnosis: Culture and isolation from primary lesion, lymph node, blood, or synovial fluid.

Prevention: PPE, including gloves; thoroughly wash bite wounds; proper restraint techniques for handling animals.

Treatment: Penicillin or tetracyclines for seven to 10 days (48). Tetanus prophylaxis should be considered (255).

Salmonellosis

Agent: *Salmonella enterica* serovar Enteritidis (*S. Enteritidis*), *S. enterica* serovar Typhimurium (*S. Typhimurium*), other *Salmonella* spp; facultative anaerobic gram-negative rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Guinea pigs, mice, rats, chickens (256), pigs (265), sheep (265), cats (120, 233); rabbits (179), nonhuman primates (macaques, baboons, squirrel monkeys).

Disease: Asymptomatic to septicemia, diarrhea, gastroenteritis (265); abortion in sheep.

Detection: Culture of feces.

Control: Good programs of sanitation in animal housing areas; strict attention to proper methods of animal waste disposal; purchase of *Salmonella*-free animals (127); broad-spectrum antimicrobials used parenterally to treat septicemia, with further treatment based on antimicrobial susceptibility pattern of agent (179). Prevalence of the agent in laboratory nonhuman primate colonies may be low (254).

Mode of transmission: Fecal-oral.

Communicability: High when exposed to infected animals or birds. To date, human infections have not been associated with cats (198).

Humans:

Occurrence: Case report of *S. Enteritidis* septicemia in a chicken breeder (187).

Clinical syndromes: Gastroenteritis with diarrhea.

Incubation period: Ranges from six to 72 h, usually 12 to 36 h.

Diagnosis: Culture of stool.

Prevention: Good hygiene; appropriate PPE, including gloves.

Treatment: Antimicrobials, such as ciprofloxacin, may be ef-

fective; however, antimicrobial therapy is usually not administered to minimize development of antimicrobial resistance to salmonellae. Provide supportive care, including rehydration and electrolyte replacement (48).

Shigellosis

Agent: *Shigella dysenteriae*, *S. flexneri*, *S. sonnei*; facultative anaerobic gram-negative rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Nonhuman primates (139, 263). These agents do not occur naturally in monkeys but are acquired from humans. Transmission occurs between monkeys, with secondary spread back to humans.

Disease: Diarrhea containing mucus, blood, and mucosal fragments, dehydration, weight loss. Gingivitis, abortion, and air sac infection of macaques also reported (25).

Detection: Culture of feces or rectal swab specimen on selective microbiological media.

Control: Strict sanitation practices and antimicrobial therapy, based on results of susceptibility testing; antimicrobials (e.g., enrofloxacin, amoxicillin, trimethoprim sulfa combinations [263]). Prevalence of *Shigella* spp. in laboratory nonhuman primate colonies may be low (254).

Mode of transmission: Fecal-oral.

Communicability: Low.

Humans:

Occurrence: Laboratory animal technicians developed shigellosis after routine handling of macaques (147).

Clinical syndrome: Varies from mild infection to dysentery or watery diarrhea; fever, nausea, tenesmus; may cause reactive arthropathy (Reiter's syndrome) in persons with HLA-B27 genetic background (132).

Incubation period: Ranges from one day to four days.

Diagnosis: Culture of stool.

Prevention: PPE, good hygiene.

Treatment: Antimicrobials.

Simian Foamy Virus

Agent: Foamy virus; spumavirus.

Laboratory Animal Reservoir:

Hosts: Macaques, baboons, other nonhuman primates. Many species have antibodies to the virus.

Disease: None reported.

Detection: Serologic testing: immunoblot assays, IFA, ELISA; PCR assay; virus isolation.

Control: None known.

Mode of transmission: Unknown; presumably via contaminated saliva and other body fluids (35). May contaminate cell cultures.

Communicability: Low to moderate.

Humans:

Occurrence: In two of 46 (4.3%) persons occupationally exposed to macaques, macaque foamy virus antigens were detected (35, 117); in four of 231 (1.8%) persons occupationally exposed to baboons and African green monkeys, foamy virus antibodies, proviral DNA, and virus were detected (117).

Clinical syndromes: None reported.

Incubation period: Unknown.

Diagnosis: Serologic testing: immunoblot assays, IFA, ELISA; PCR assay; virus isolation.

Prevention: PPE; appropriate animal restraint.

Treatment: None known or required.

Streptococcosis

Agent: *Streptococcus suis* type 2; facultative anaerobic gram-positive coccoid-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: Pigs.

Disease: Asymptomatic to severe disease; septicemia; arthritis, polyserositis, meningitis, endocarditis; pneumonia; abortions; abscessation (234).

Detection: Culture of tonsil swab specimens; detection of IgG antibodies by use of ELISA (50).

Control: Good programs of sanitation.

Mode of transmission: Direct contact with pigs.

Communicability: Low.

Humans:

Occurrence: In The Netherlands, the prevalence of antibodies to *S. suis* among pig farmers was two of 190 (1%) whereas veterinarians had a prevalence of six of 100 (6%) (75). The estimated annual risk of developing *S. suis* meningitis in Dutch abattoir workers and pig breeders was three of 100,000 (11). In New Zealand, 0 of 16 (0%) veterinary students, 11 of 107 (10%) meat inspectors, and 15 of 70 (21%) pig farmers had antibodies (216). The annual incidence of seroconversion in pig farmers was estimated at 28% (216). A comparison of 30 cases in The Netherlands and 30 cases reported in literature indicated that 50 (83%) were employed in the pig industry (11).

Clinical syndromes: Septicemia, meningitis, arthritis, endocarditis, endophthalmitis; deafness and ataxia are frequent sequelae of meningitis (11, 71).

Incubation period: Unknown, probably one day to three days.

Diagnosis: Culture; isolation of viridans streptococci or Group-D *Streptococcus* should arouse suspicion of *S. suis* infection in cases with pig exposure (268).

Prevention: PPE, including gloves; sanitation.

Treatment: Antimicrobials (e.g., penicillin); supportive care.

Strongyloidiasis

Agent: *Strongyloides fulleborni*, *S. stercoralis*; nematodes.

Laboratory Animal Reservoir:

Hosts: Macaques, baboons, and other nonhuman primates (2, 20, 154, 188, 190); dogs.

Disease: With heavy parasite burden, diarrhea, weight loss, anorexia, and vomiting.

Detection: Fecal flotation of concentrated specimens for ova; direct fecal smear for larvae; gross and histologic examination of tissues.

Control: Anthelmintics (e.g., ivermectin); strict sanitation practices.

Mode of transmission: Fecal-oral; direct skin penetration by free-living larvae.

Communicability: Low to moderate.

Humans:

Occurrence: *Strongyloides fulleborni* and other *Strongyloides* spp. of nonhuman primates are easily transmitted to humans in natural settings (123). Transmission in laboratory animal settings has not been reported.

Clinical syndromes: Epigastric pain, nausea, diarrhea, and weakness.

Incubation period: Ranges from three to five weeks.

Diagnosis: Flotation of concentrated stool specimens for ova; direct stool smear for larvae.

Prevention: PPE to prevent skin contact with feces; appropriate animal restraint; good hygiene.

Treatment: Anthelmintics.

Toxoplasmosis

Agent: *Toxoplasma gondii*; intracellular coccidian protozoa.

Laboratory Animal Reservoir:

Hosts: Cats (definitive host); mice, rats, dogs, sheep, goats, pigs, chickens (intermediate hosts).

Disease: Asymptomatic in adult cats, but occasionally vomiting, diarrhea, dyspnea, coughing, anorexia, uveitis, pancreatitis, especially in young or immunocompromised cats; hepatic necrosis in dogs; abortions and stillbirths in sheep, goats, and pigs.

Detection: In cats, fecal examination for oocysts; isolation of tachyzoites (rapidly multiplying form of organism) from CSF or aqueous humor. There are no practical methods to detect the presence of bradyzoites (slowly multiplying form of organism) encysted in tissues (e.g., brain, liver, and skeletal and cardiac muscle) of intermediate hosts. Serologic testing: ELISA, IFA test.

Control: Prevent exposure of cats to potentially contaminated meat by feeding only commercially processed cat food; dispose of cat feces daily before oocysts sporulate and become infective; house cats indoors and apart from other species; antimicrobials (e.g., clindamycin) for dogs and cats; acquisition of cats from *T. gondii*-free sources.

Mode of transmission: Fecal-oral, ingestion of infective oocysts from sources contaminated with cat feces (244); cats shed oocytes only after initial infection, usually for 10 to 20 days (179, 198). Intermediate hosts can become lifelong carriers of infection due to encysted bradyzoites.

Communicability: Low; oocysts shed from cats become infective in one day to five days, and may remain viable in water or soil for more than 12 months.

Humans:

Occurrence: The prevalence of *Toxoplasma* antibodies in veterinarians was similar to that of other occupational groups (24, 103, 224, 239, 245). High prevalence of *Toxoplasma* antibodies among animal technicians has been reported, but was attributed to their exposure outside of occupational settings (224). Comparison of the prevalence of *Toxoplasma* antibodies in employees with exposure to cats at a research institution revealed no increase in risk of infection (67).

Clinical syndromes: Asymptomatic to mild flu-like illness; can develop more severe clinical signs of disease, including fever, lymphadenopathy, pneumonia, chorioretinitis, and rashes. Immunosuppressed individuals can develop focal lesions of en-

cephalitis following reactivation of bradyzoites. Infections in pregnant women can lead to birth defects, chorioretinitis, blindness, and severe neurologic sequelae, with mental retardation in infants.

Incubation period: Ranges from five to 20 days for acute disease; from months to years for chronic disease.

Diagnosis: Clinical signs of disease; detection of increase in titer between acute and convalescent serum samples; isolation of *T. gondii* from blood or body fluids.

Prevention: PPE, including gloves, good hygiene when handling potentially infective material.

Treatment: Not routinely indicated for immunocompetent individuals; antimicrobial therapy (e.g., sulfadiazine and pyrimethamine) for immunosuppressed persons manifesting specific symptoms (48, 179).

Tuberculosis

Agent: *Mycobacterium avium* complex, *M. bovis*, *M. tuberculosis*; acid-fast rod-shaped bacteria.

Laboratory Animal Reservoir:

Hosts: *Mycobacterium avium*, *M. bovis*, *M. tuberculosis*—macaques, baboons, squirrel monkeys, and other nonhuman primates (145, 171, 220, 272); *M. bovis*, *M. tuberculosis*—dogs, cats, pigs; *M. bovis*—sheep, goats; *M. avium*—pigs, chickens, pigeons. These agents do not occur naturally in monkeys, but are acquired from humans or other species (*M. bovis*), or directly from environmental sources, such as soil and water (*M. avium*). Transmission occurs between monkeys, with secondary spread back to humans. *Mycobacterium avium* subsp. *paratuberculosis*, the causative agent of Johne's disease, has been recognized in one species of macaque (173), and is a suspected zoonotic agent (100).

Disease: Asymptomatic to sudden death; pulmonary disease, anorexia, chronic weight loss; peripheral lymphadenopathy, with or without chronic draining tracts to the skin; cutaneous abscesses; nodular lesions may form in multiple organs, including gastrointestinal tract, vertebrae, brain and spinal cord.

Detection: Intradermal tuberculin skin test (Mantoux test); thoracic radiography; gross and histologic examination of tissues; ELISA (64); PCR assay (60, 217). False-negative skin test results may occur due to concurrent disease, early stage disease, or immunosuppression, requiring repeated testing during quarantine and thereafter. Culture usually takes four to eight weeks for confirmation.

Control: Testing and elimination of infected animals; rigorous quarantine programs for arriving animals; continuous tuberculosis surveillance; good sanitation programs.

Mode of transmission: Fecal-oral; inhalation of infective aerosols; fomites.

Communicability: Moderate, depending on the host species.

Humans:

Occurrence: Cases have followed occupational exposure to infected nonhuman primates in research settings (141).

Clinical syndromes: Pulmonary, meningeal, visceral organs, and other body systems involved; chronic cough, fatigue, fever, weight loss, and hemoptysis during advanced stages of pulmonary disease; progressive pulmonary disease may be fatal within five years in approximately 50% of untreated cases. Life-long latent (non-progressive) infections within calcified pulmo-

nary nodules also occur. Crohn's disease is linked to *M. avium* subsp. *paratuberculosis* infection (118).

Incubation period: Ranges from two to 10 weeks for development of primary lesions or skin test-positivity.

Diagnosis: May perform dual Mantoux tests (using avian and human precipitin) due to false-negative reactions for non-tuberculous mycobacteria with the use of only the human Mantoux (59); PCR assay; RT-PCR assay (226); pulmonary radiography; acid-fast stain of sputum samples.

Prevention: PPE, including respiratory tract protection; good hygiene; appropriate animal restraint; separate animal facilities from human work areas; (semi)annual tuberculin testing for facility personnel.

Treatment: Antimicrobials based on established regimens (e.g., combination therapy with isoniazid, rifampin, and pyrazinamide). Drug-resistant strains are increasingly being recognized.

Yellow Fever

Agent: Yellow fever virus; flavivirus

Laboratory Animal Reservoir:

Hosts: Baboons, squirrel monkeys, and other nonhuman primates (231).

Disease: Asymptomatic in baboons and other African species that are well-adapted to the virus through sylvatic maintenance cycles. High mortality in squirrel monkeys and other Central and South American nonhuman primate species, presumably because of the recent introduction of yellow fever virus into that geographic region.

Detection: Serologic testing: ELISA, IFA, and HI, CF, and serum neutralization tests; virus isolation; RT-PCR assay.

Control: African species of nonhuman primates support the sylvatic cycle and effectively eliminate the infection through neutralizing antibodies; appropriate international quarantine and transportation programs with mosquito-proof enclosures for nonhuman primates; eliminate or destroy larval habitat for *Aedes* mosquito vectors.

Mode of transmission: Mosquito-borne.

Communicability: Low in biomedical research settings. Highly communicable in endemic regions of the world, such as areas of West Africa, tropical-belt areas of South America, and select Caribbean islands.

Humans:

Occurrence: Laboratory-acquired cases have resulted from exposure to infected macaques and baboons (213). Human infections may result from accidental exposure to infected medical sharps used during quarantine (213).

Clinical syndromes: Variable severity; rapid onset of fever, chills, headache, backache, nausea, vomiting, and jaundice; symptoms may progress to epistaxis, hemoptysis, melena, liver and renal failure, and death.

Incubation period: Ranges from three to six days.

Diagnosis: Serologic testing: HI, CF, and serum neutralization tests, IFA test, ELISA, RIA; virus isolation; PCR assay.

Prevention: Vaccinate personnel at high risk of exposure.

Treatment: Supportive care; no specific treatment guidelines.

Discussion

The purpose of this overview is to provide an compilation of

laboratory animal-acquired zoonoses of concern in modern biomedical facilities and research establishments. It is intended to be a resource for veterinarians, husbandry staff, research workers, occupational health and safety personnel, and institutional animal care and use committees, all of whom have roles and responsibilities for maintaining a safe and healthy workplace. The scope of this article has been limited to pathogenic agents most likely carried by the principal animal species commonly used in biomedical research settings.

The recognition and diagnosis of zoonotic diseases in animal facility personnel is often challenging, despite the spectrum of known and potential viral, bacterial, protozoal, fungal, and parasitic zoonotic pathogens. The difficulty in identifying and reporting many of these diseases is often due to lack of a unique clinical presentation, which may be indistinguishable from other flu-like illnesses that can occur with some regularity in humans. In general, reports of human cases of zoonotic disease originating from animals used in biomedical research are rare. However, the published reports cited herein likely underestimate the true number of cases that have occurred in the context of laboratory animal research. This under-reporting could be due to a failure to establish a cause for incidents of human disease when they occur, or a failure to associate the human disease with workplace-related animal exposures. Certain zoonotic diseases can cause symptoms and pathologic changes involving several organ systems and, therefore, may result in ambiguous or misleading diagnoses. As well, unsuccessful pathogen identification may be attributable to a lack of appropriate diagnostic tests or culture conditions readily available for certain agents.

Numerous preventive measures exist within contemporary animal research facilities that reduce the likelihood of zoonotic disease transmission to laboratory animal personnel. Most facilities are designed to allow for high rates of single-pass air exchange, controlled animal room air pressure differentials, and dedicated areas for quarantine and barrier-protection of animals. These components are implemented to prevent or control pathogen entry and spread among research animal species and colonies. The provision and use of disposable and washable PPE (gloves and gowns, face masks and shields, eye goggles, and hair bonnets) serves as a secondary barrier between the animal and the worker to further minimize the risk of zoonotic pathogen exposure. Many of these PPE devices are designed for use within the confines of the facility and should be changed as needed to minimize contamination. Institutional occupational health and safety professionals should provide guidance, training sessions, and preventive medical services to personnel, including tuberculosis testing, tetanus toxoid boosters, and selective vaccinations on a routine basis. In addition, laboratory animal veterinarians and veterinary staff provide education in the humane and safe handling of animals and in the adherence to standard operating procedures for workplace safety in the animal facility. These preventive mechanisms, previously outlined, are extremely effective at reducing occupational risks to employees if used appropriately and in conjunction with each other (213).

Beyond the zoonotic diseases described in this review, there is a continuing threat of emerging infectious diseases that have implications to persons working in biomedical research environments. Due to expanding scientific efforts in all aspects of human and animal health, future animal models for human

disease may be discovered in species in which the biology and husbandry are not well described. Veterinarians, veterinary and husbandry technicians, and health providers must be alert to the potential for new diseases of occupational health importance in research animals and in the personnel who work with them. Continued publication of case reports on zoonoses in laboratory animal environments is encouraged to further educate members of the biomedical research community. In conclusion, individuals who oversee animal care and worker safety are encouraged to build upon the foundation provided by this article for continued efforts at disease prevention in environments where laboratory animals are used.

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