Occupational Health for Personnel Handling Laboratory Animals
Hazards Associated With The Use Of Laboratory Animals*

Working with laboratory animals, or tissues from laboratory animals, is associated with potential health hazards to humans. These hazards include 1) bites, scratches, and kicks; 2) allergic reactions; and 3) possible zoonotic diseases. The key to minimizing these hazards is awareness and proper training. An on-line program titled "Occupational Health and Safety for Personnel with Laboratory Animal Contact" is mandatory for all personnel with animal contact at Wright State University. This course MUST be satisfactorily completed prior to access to the Laboratory Animal Resources facility. The course addresses the risks associated with contact with laboratory animals and requires the completion of a short test at course conclusion to successfully register. The course is accessible at **http://www.wright.edu/lar/LARsafety.htm**.

Physical Hazards

Animal Bites, Scratches, Kicks, etc.

Animal bites, scratches, and kicks are ubiquitous hazards whenever working with animals, either in the laboratory, or in other locations. Most of these injuries, however, are easily preventable with proper training in animal handling procedures and by proper procedures. Knowledge of animal behavior is important in predicting and responding to the animal's reaction. It is essential, both for the animal's and for the human handler's sake that each person be properly trained and proficient at handling the animals under their care. New personnel should be fully trained and instructed before handling animals.

All personnel injured by animal bites or scratches should immediately report the incident to their supervisor and the Department of Environmental Health and Safety after initial first aid procedures have been completed. All animal bites are potentially serious incidents because of the high potential for disease transmission and local infection from the animals contaminating oral flora. Medical attention should be sought in all but the most trivial injuries.

Sharps

Needles, broken glass, syringes, pipettes, scalpels, scissors, etc. are all common in laboratory animal facilities and pose a hazard to personnel. Everyone in the laboratory animal facility has a responsibility to know how to handle potentially dangerous objects and how to properly store these items. Used needles, syringes, and scalpels should be disposed of in "sharps" containers that are located throughout the laboratory animal facilities. Personnel using needles and syringes should use care in the procedures and not recap any needle without consideration of the potential hazard of a needle injury. Except in rare instances where a one-handed recapping technique is used, needles should be disposed of uncapped in the appropriate biohazard sharps containers.

Chemicals

A variety of chemicals are used in the laboratory animal facility. These range from disinfectants, to alkaline and acid soaps, to grease. Proper handling of these chemicals is essential to prevent potential injury. Appropriate safety equipment including gloves, face protection, goggles, aprons, etc. should be worn whenever these chemicals are handled. Material Safety

Data Sheets for all chemicals used in the Laboratory Animal Resources are available in the office and posted within the facility.

Machinery

Tunnel washers, rack washers, autoclaves, floor polishers, etc., all pose potential risk to the operator or others if improperly used. Personnel using the equipment in the facility should be familiar with the proper procedures for use and follow standard procedures when using the equipment. The Laboratory Animal Resources supervisor should be immediately notified if any piece of equipment is not functioning normally and the equipment should not be used until a determination of potential safety problems has been made.

Noise

Exposure to intense noise can and will result in impaired hearing. Chronic noise-induced hearing loss usually involves the higher pitched sounds, is permanent, and cannot be treated medically. The Occupational Safety and Health Administration limits employee exposure to noise to 90 decibels measured on the A scale of a standard sound-level meter at slow response (dBA) averaged over an 8 hour work shift (29 CFR 1910.95). Where levels exceed 85 dBA, the exposed employees need to participate in a hearing conservation program that includes monitoring, audiometric testing, hearing protection, training, and record-keeping (29 CFR 1910.95 c-o).

In a laboratory animal facility, excessive noise can result from animals (especially pigs and dogs), cage-washing equipment, and other equipment operated in enclosed environments. The construction requirements for ease of sanitation often accentuate the level of noise since sound-deadening material is nearly absent. In areas where high noise levels occur, employees should avail themselves of noise-protection equipment and limit their time of occupancy in the area.

Ergonomic Hazards

Animal care personnel are required to handle and manipulate heavy loads and bulky materials throughout the workday. Laboratory personnel may also be involved in the handling of larger pieces of equipment for research purposes within the facility. Handling large loads improperly or performing repetitive tasks may result in chronic injuries. Proper procedures for handling all heavy loads should be adhered to and safety equipment and load assistance equipment used to reduce potential injuries. Employees with existing physical handicaps or injuries should consult with the occupation health physician and their workday procedures should be altered to prevent re-injury.

<u>Allergies</u>

Among the most common occupational hazards associated with working with laboratory animals is the development of allergies. The prevalence of allergies in animal-care workers has been estimated from 10% to 44% while it is estimated that nearly 10% of all personnel working with laboratory animals will develop occupation-related asthma.

Several studies have suggested that persons with pre-existing allergic conditions, such as hay fever, are more likely to develop allergies to laboratory animals. While nearly 90% of personnel

without any history of allergic reactions never develop allergies to laboratory animals, up to 73% of personnel with pre-existing allergic disease will develop allergies.

The usual time from onset of work with laboratory animals and the development of allergies is between 1 and 2 years. The initial symptoms are usually a running nose, nasal irritation, itchy eyes, and sometimes, rashes. Approximately 10% of those developing this allergic rhinitis will eventually progress, with repeated exposure, to occupational asthma, which can result in chronic pulmonary disease even years after the exposure ceases.

Laboratory Animal Allergens

Species	Allergen	Source of Allergen	Relative Risk
Rats	*Rat n 1A, Rat n 1B*	Urine	+++++
Mice	*Mus m1*	Urine	++++
Guinea Pigs	-	Urine, dander, fur, saliva	++
Gerbils	-	-	+
Rabbits	Glycoprotein	Fur, saliva, urine	+++
Cats	*Fel d 1*	Sebaceous glands, saliva	+++
Dogs	*Can f 1*	Saliva, hair, skin	++
Nonhuman Primates	-	Dander	+
Pigs	-	Urine	+
Sheep	-	Lanolin?	+
Birds	Protein	Feces, serum	+

The best method to minimize the potential for the development of allergies is to minimize exposure to the allergens. Animal facilities have relatively high air flow requirements, which reduce the concentration of allergens in the air by dilution. The control of the relative humidity to 40-70% also reduces the level of allergens in these rooms. Specialized caging systems include High Efficiency Particulate Air (HEPA) filtration systems to remove allergens from the exhaust air. Animals removed from the laboratory animal facility to investigator laboratories are placed in environments which permit a much greater accumulation of allergens, potentially exposing personnel, including those not involved in the project, to higher levels of allergens.

The greatest risk of exposure involves any activity that disturbs the bedding material of the animal generating airborne particles. Movement of the animals within the cage, whether normal activity or during manipulations, increases personnel exposure. Exposure can be minimized by the use of specialized bedding materials or, most effectively, by the use of containment caging such as microisolators or filter tops. The use of personal protective equipment can also minimize exposure. Standard surgical masks are not effective but N-95 commercial dust respirators can reduce the exposure up to 98%. Handling the cages and animals in laminar flow or biological safety cabinets can dramatically reduce the exposure of personnel.

Personnel with known allergies to laboratory animals should be evaluated by the occupational health physician and reevaluated on a schedule determined by the occupational health physician based upon the clinical signs and symptoms. Pulmonary function tests should be performed to assess the severity of the disease and the progression, if indicated. Medical therapy may be prescribed to reduce or prevent the development of allergic symptoms. In all cases, however, exposure reduction and avoidance measures should be instituted. At a minimum, personnel with documented laboratory animal allergies should use a dust-mist respirator certified by the National Institute for Occupation Safety and Health. The Department of Environmental Health and Safety, Wright State University will provide appropriate respirators and fit-testing when necessary. An alternative to the dust-mist respirator is the filtered airhood device (Airstream Dustmaster® hood, Racal, Middlesex, UK), which has been shown to be effective.

Personnel with established allergies to laboratory animals are always at risk of exposure and the reoccurrence of severe disease. Generally this exposure occurs through contact with contaminated equipment or clothing, or inadvertent and unexpected exposure to the animals during transport. Personnel working with animals must be aware of this potential effect and take steps to minimize exposure of personnel outside the animal facility to allergens. These actions include the wearing of protective clothing (lab coats, etc.) in the animal facility, the transportation of animals in containers/cages designed to minimize allergen exposure (barrier cages), cleaning of equipment exposed to animals prior to removal from the animal facility, etc.

Anaphylaxis is, fortunately, rare with laboratory animal allergies. Anaphylaxis, may, however, occur in allergic personnel following an animal bite or puncture wound from contaminated needles. These situations, when they occur, are life-threatening emergencies requiring prompt medical treatment. Physicians may recommend that allergic personnel continuing to work with laboratory animals carry a self-administered form of epinephrine (e.g., Epi-Pen® or Ana-Kit®) and instruct co-workers in emergency procedures.

Zoonoses

Zoonoses are diseases transmitted between animals and man under natural conditions. These diseases, many of which are often relatively innocuous in their normal host, may result in serious or fatal diseases in abnormal hosts. With the number and range of potential zoonotic diseases, it is a reaffirmation of the validity of standard containment techniques that the number of zoonotic diseases transmitted between the laboratory research animals and the research personnel is so small.

B-Virus Infection (Cercopithecine Herpesvirus 1)

Host Range - Herpes B-virus produces a mild clinical disease analogous to the human Herpes simplex virus in macaques. The disease in macaques is characterized by lingual or labial vesicles or ulcers and often keratoconjunctivitis or corneal ulcers that are apparent for 1 - 2 weeks after the disease onset. As is typical of herpesviruses, a latency period follows with reactivation and expression of the virus (shedding) in monkeys during periods of physical or psychological stress. Several aberrant species, including humans, develop a severe and fatal encephalomyelitis when inoculated with the virus.

Transmission - Transmission of B-virus to man occurs primarily through bite or scratch wounds (saliva transmission) although cases of needlestick transmission, fomite (cage) transmission, and human to human transmission have been documented.

Clinical Signs - The incubation period varies from 2 days to 30 days with wide variation. A herpetiform vesicle may develop early at the site of inoculation. Early clinical signs include myalgia, fever, headache, and fatigue followed by a progression neurological disease with numbness, hyperesthesia, paresthesia, ataxia, confusion convulsions, and ascending flaccid paralysis.

Treatment - Antiviral treatment with acyclovir or ganciclovir is effective in controlling the viral disease but management is controversial since discontinuance of acyclovir therapy is associated with increasing serologic titers to B-virus. Therapy may be life-long.

Early diagnosis and intervention is critical in managing potential B-virus exposures. Serological samples should be obtained from the macaque and the patient as soon as possible after the bite. The patient's wound site and the macaque's conjunctiva and buccal mucosa should be cultured for virus isolation. The wound should be thoroughly cleansed and disinfected with a 0.5% sodium hypochlorite solution recommended for antisepsis.

Physicians should consult the Viral Exanthems and Herpesvirus Branch, Division of Viral Diseases, Centers for Disease Control and Prevention for assistance in case management.

Prevention - Protective clothing and equipment (face shield, mask, gloves, long-sleeved garments, etc.) when handling macaques is essential. While only serologically B-virus negative monkeys should be used to minimize potential exposure, no monkey should be considered B-virus negative. Whenever possible, macaques should be anesthetized prior to any manipulations or handling where personnel may be at risk.

Lymphocytic Choriomeningitis (LCM)

Host Range - A member of the family Arenaviridae, this virus has a predilection for many rodent species and is common in wild mice throughout the world. A wide variety of laboratory animal species including mice, hamsters, guinea pigs, nonhuman primates, swine, and dogs can be infected with LCM but the laboratory mouse and hamster are the species of greatest concern with regard to transmission to man. The disease in laboratory mice and hamsters is usually clinically silent, and in the case of immunodeficient mice, may be undetectable with standard serologic techniques.

Transmission - Large quantities of virus are present in the blood, cerebrospinal fluid, urine, nasopharyngeal secretions, feces, and tissues of infected host animals. Transmission between animals may be transplacentally, by direct contact, by contact with fomites, or via injections or tumor transplantations with infected tissues. Transmission to man is usually via inhalation or contamination of mucous membranes or broken skin with infectious tissues or fluids from infected animals.

Clinical Signs - Humans develop an influenza-like illness usually characterized by fever, myalgia, headache, and malaise after an incubation period of 1-3 weeks. Severe cases in man may present with a maculopapular rash, lymphadenopathy, meningoencephalitis, orchitis, arthritis, and epicarditis. Several deaths have resulted from central nervous system involvement. Definitive diagnosis usually involves virus isolation from the blood or cerebrospinal

fluid. Antibody is detectable approximately 2 weeks after onset of the illness, limiting the usefulness of serology for diagnosis of human disease.

Treatment - Ribavirin therapy substantially reduces the mortality in patients infected with other arenavirus infections and may prove to be of value in treating LCM infections. Additional information about therapy and serological testing for LCM in available through the Special Pathogens Branch, Division of Viral and Rickettsial Diseases, CDC.

Prevention - Periodic surveillance of rodent colonies and newly acquired rodents for evidence of endemic LCM infection is essential. All tumor cell lines and other tissues should be evaluated for the presence of LCM virus prior to inoculation into animals. Animal Biosafety Level 2 is recommended for studies in adult mice infected with mouse-brain passage strains. Animal Biosafety Level 3 should be used for work with infected hamsters.

Hantavirus

Host Range - One of several genera in the family Bunyaviridae, Hantaviruses are widely distributed throughout nature among the rodent populations. Numerous genera of rodents including *Apodemus, Clethrionomys, Mus, Rattus, Pitimys,* and *Microtus* have been implicated in foreign outbreaks of typical Hantavirus hemorrhagic disease. In the United States, *Rattus norvegicus, Peromyscus* spp., *Microtus californicus, Tamias* spp., and *Neotoma* spp. have been implicated in the rural and urban outbreaks of hantaviral disease.

Transmission - Infected rodents shed the virus in their respiratory secretions, urine, saliva, and feces for an extended period following infection. Transmission between animals occurs by direct contact with infected secretions or via aerosols. Human infection usually is via aerosol exposure with only brief exposures required. Transmission may also occur via bite wound and contamination or by exposure of mucus membranes or compromised skin to infectious materials.

Clinical Signs - The clinical signs are related to the strain of hantavirus involved. The disease varies from "nephropathia endemica" consisting of fever, back pain, and nephritis with moderate renal dysfunction to "hemorrhagic fever and renal syndrome" consisting of fever, myalgia, headache, petechiae, and other hemorrhagic manifestations including anemia, gastrointestinal bleeding, oliguria, hematuria, electrolyte imbalance and shock. Recent outbreaks of natural disease in the United States have presented with fever, myalgia, headache, and cough followed by rapid respiratory failure. Serologic tests are available and additional information may be obtained through the Special Pathogens Branch, Division of Viral and Rickettsial Diseases, CDC.

Treatment - Intravenous ribavirin therapy initiated early in the disease course may be of value. Hemodynamic maintenance and respiratory support are critical.

Prevention - The isolation, identification, and elimination of infected laboratory rodents or tissues prior to the exposure of laboratory personnel or animals is essential in the prevention of hantavirus infection in either the laboratory animals or the laboratory personnel. Serologic screening of rodent colonies and incoming animals is essential in minimizing laboratory personnel exposure.

Orf Disease (Contagious Ecthyma and Contagious Pustular Dermatitis)

Host Range - This poxvirus is endemic in sheep and goat herds worldwide, including the United States. All ages of animals are affected although younger animals are more severely affected clinically. In small ruminants, Orf produces proliferative, pustular, crusty lesions around the lips, nostrils and urogenital orifices.

Transmission - Transmission is via direct contact with the virus-laden secretions from the lesions. Transmission via fomites is possible and rare person to person transmission has occurred.

Clinical Signs - The disease in humans is usually characterized by a single, or rarely multiple, lesion that is initially maculopapular or pustular and progresses to a weeping proliferative nodule. Regional lymphadenitis in uncommon and progression to a systemic disease is rare.

Treatment - Treatment is supportive. Lancing of the initial lesion is contraindicated.

Prevention - Vaccination of susceptible sheep and goats effectively prevents the disease. Protective clothing and good personal hygiene is effective in preventing exposure from infected animals.

Hepatitis A

Host Range - Humans are the definitive reservoir host for Hepatitis A virus and infection of nonhuman primates occurs due to contact with infected human populations or their waste. Most nonhuman primates are susceptible and the disease is often subclinical in these species although viral propagation and spread does occur.

Transmission - Over 200 cases of human Hepatitis A virus infection have been associated with nonhuman primates. Transmission is fecal-oral.

Clinical Signs - Incubation period is about 30 days. The clinical disease in humans varies from a mild flu-like illness of 1 - 2 weeks duration to a severely debilitating disease lasting several months. Patients experience fever, malaise, anorexia, nausea, and abdominal discomfort that is usually followed in several days by the development of jaundice.

Treatment - Treatment is essentially supportive only. No effective antiviral drug is presently available.

Prevention - An approved killed-virus vaccine is now available and protective. Protective clothing and equipment along with adequate personal hygiene and sanitation minimizes the potential of disease exposure.

Rabies

Host Range - Rabies is essentially distributed worldwide with the exception of a few countries that have eliminated the disease through import restrictions. All mammals are susceptible to infection with the rabies virus although dogs, cats, skunks, raccoons, bats, and other biting animals are the main reservoirs. Rabies in the wild animals population has been dramatically increasing over the past decade, increasing the likelihood of exposure in areas that have had little disease over the previous years.

Transmission - Usually via a bite wound although aerosol transmission has been documented in caves with bats. Personnel handling tissues of infected animals are potentially at risk. Most laboratory animal associated cases involve bite wounds from random source dogs and cats.

Clinical Signs - Patients initially experience apprehension followed by headache, malaise, fever and indefinite sensory changes referred to the site of the bite wound. Disease progression leads to paresis, paralysis, inability to swallow, delirium, convulsions, coma, and death due to respiratory paralysis.

Treatment - When exposure is documented, active immunization with rabies vaccine often prevents disease development. Treatment after the development of symptoms is futile.

Prevention - Acquisition only of animals with documented clinical health histories and vaccination to rabies virus. Animal vaccination is the most critical asset in rabies prevention. Pre-exposure vaccination for personnel at risk for exposure is strongly recommended.

Q-Fever

Host Range - Coxiella burnetti, the etiologic agent of Q-fever, has a worldwide distribution with widespread infection in a variety of domestic and wild animals including sheep, goats, cattle, cats, dogs, and domestic fowl. While sheep are the primary laboratory animal associated with human cases of Q-fever, an outbreak of Q-fever in a human cohort exposed to a post-parturient cat and her litter along with document cases of Q-fever following exposure to rabbits emphasizes the role of other laboratory animals.

Transmission - Humans usually acquire this infection following exposure to infectious aerosols although infections following ingestion have been documented. The organism is shed in the urine, feces, milk, and especially the birth products of domestic animals, which are generally asymptomatic. An infective dose of as little as one organism can produce Q-fever.

Clinical Signs - The disease in humans varies widely from asymptomatic to a variety of flu-like symptoms. Usually the disease has an abrupt onset with fever, chills, retrobulbar headache, weakness, malaise, and profuse sweating. Pneumonitis with chest pain, acute pericarditis, and hepatitis may occur. Endocarditis on native or prosthetic cardiac valves may extend relapses of the disease over years. Most cases resolve within 2 weeks of clinical signs. Serological methods are available for diagnosis of the human disease. Virus isolation poses a severe risk to the laboratory personnel and is generally not attempted.

Treatment - Tetracyclines are effective in treatment although prolonged therapy may be required.

Prevention - Exposure to post-parturient fetal membranes and fluids represents the greatest potential for infection and should be avoided. Whenever possible, only male or nonpregnant female sheep should be utilized. Physical barriers and appropriate laboratory clothing and protective equipment minimizes exposure. The organism is resistant to many disinfectants although sodium hypochlorite is effective.

For personnel at high risk, an investigational Phase 1 Q-fever vaccine is available from the Special Immunizations Program, US Army Medical Research Institute for Infectious Disease, Fort Detrick, Maryland.

Cat-Scratch Fever

Host Range - Bartonella henselae, the rickettsial agent responsible for cat-scratch fever, is associated with cats most frequently although dogs, monkeys, and porcupines have also been implicated in disease transmission. Transmission between cats, and presumably between other species, by the domestic flea has been documented. The domestic flea is actually the carrier of the bacteria.

Transmission - Transmission to humans generally occurs after a cat scratch incident.

Clinical Signs - A small erythematous papule arises at the inoculation site within several days of exposure, which is followed by a vesicle and scab formation with resolution in several days. Several weeks later regional lymphadenopathy appears in the draining lymph nodes that may persist for months. Lymph nodes may suppurate. Fever, malaise, anorexia, headache, and splenomegaly may occur. Rarely, central nervous system signs, osteolytic lesions, granulomatous hepatitis, and pneumonia may occur. Isolation of the organism from the blood, a cutaneous lesion, or biopsy material is required for definitive diagnosis. Serology is available and positive for most patients.

Prevention - Proper cat-handling techniques and protective clothing minimizes exposure. Flea control may minimize disease exposure between cats and personnel.

Tuberculosis

Host Range - Tuberculosis of animals and humans is caused by a members of the genus *Mycobacterium*, including *M. tuberculosis, M. avium-intracellulare, M. bovis, M. kansasii, M. simiae, M. marinum, and M. chelonae.* While cattle, birds, and humans serve as the main reservoirs for these organisms, numerous laboratory animals are susceptible including nonhuman primates, swine, sheep, goats, rabbits, cats, dogs, and ferrets. Nonhuman primates, however, represent the primary laboratory animal associated with transmission to humans.

Transmission - While infection can occur by direct entry into the body or ingestion, inhalation of infective aerosols is the primary means of human exposure. Infective aerosols can be generated by high-pressure hoses, tissue manipulations at necropsy, improper sample handling in a clinical laboratory, or via coughing of the infective animal.

Clinical Signs - The incubation period for the development of a primary lesion and tuberculin skin test conversion is 4 - 12 weeks. The usual clinical signs are pulmonary due to the usual site of entry and consist of cough, sputum production, and progressive pulmonary disease. The disease may become latent with recrudescence over the lifetime of the infected person. Extrapulmonary spread and systemic disease is possible with clinical signs directly related to the organ(s) infected. General symptoms include weight loss, fatigue, lassitude, fever, chills, and cachexia.

Diagnosis relies primarily on the intradermal tuberculin test in both humans and animals. Chest radiography and sputum smears and cultures are also used for definitive diagnosis.

Treatment - The appearance of multiply antibiotic resistant *Mycobacterium* has made treatment difficult or impossible in some rare cases. Isoniazid, rifampin, and streptomycin are all used in treatment regimens. Organism sensitivity should guide the treatment regimen.

Prevention - Routine surveillance of nonhuman primates for tuberculosis using the intradermal tuberculin test is critical in identifying and eliminating exposed animals. Laboratory personnel should also be screened via the intradermal tuberculin test on a routine basis. Vaccination on nonhuman primates with BCG is not recommended since it converts the tuberculin skin test to positive and does not prevent infection but only suppresses proliferation of the organism and clinical disease in the vaccinated animal.

Psittacosis (Ornithosis, Parrot Fever, Chlamydiosis)

Host Range - Only *Chlamydia psittaci* is widely distributed in animals, both avians and mammals, and recognized as a zoonotic pathogen. Many laboratory animal species including birds, mice, guinea pigs, rabbits, ruminants, swine, cats, ferrets, muskrats, and frogs have been documented to be infected with *C. psittaci*.

Transmission - Spread to humans is via direct contact or aerosol exposure to the organism in exudates, secretions, or desiccated fecal material.

Clinical Disease - Avian strains appear to be more pathogenic for humans than mammalian strains of *C. psittaci*. The clinical disease may vary from conjunctivitis to a systemic disease with fever, headache, myalgia, chills,and upper and lower respiratory tract disease. More serious manifestations include extensive pneumonia, hepatitis, myocarditis, thrombophlebitis, and encephalitis. Relapses occur is untreated infections. Serology and organism isolation are used for diagnosis

Treatment - Tetracyclines are effective in treatment.

Prevention - Limit acquisition of birds to only those from disease-free colonies. If required, wild or questionable birds may be treated with chlortetracycline to minimize disease spread potential exposure of personnel. Personal protective equipment, especially respiratory protection, and appropriate laboratory clothing can minimize transmission.

Rat-Bite Fever

Etiology and Host Range - Rat-bite fever is caused by either *Streptobacillus moniliformis* or *Spirillum minor*, two bacteria that are normally present in the oral cavities of rodents, especially rats. The organisms are distributed worldwide although most commercial laboratory animal suppliers have eliminated the organisms from their production colonies. *Streptobacillus moniliformis* is the usual cause of rat-bite fever in the United States while *Spirillum minor* predominates in Asia and the far-east.

Transmission - The vast majority of human cases result from bite wounds (usually rat) contaminated with nasopharyngeal secretions. Transmission may occur by direct inoculation with blood from infected animals and some cases have occurred without bites or direct contact.

Clinical Signs - The clinical disease produced by *Streptobacillus moniliformis* (Streptobacillary Rat-Bite Fever, Haverhill Fever) and *Spirillum minor* (Spirillar Rat-Bite Fever, Sodoku) differs.

Both, however, produce a systemic disease with bacteremia and organism localization throughout the body.

Streptobacillary Rat-Bite Fever has an incubation period that ranges from 1 to 22 days although the vast majority of cases have an incubation period of under 10 days. The onset of the disease is abrupt with fever, rigor, chills, headache, nausea, vomiting, arthralgia, and myalgia. The site of the rat bite is not involved and has generally healed by the time the patient becomes ill. Regional lymphadenopathy, characteristic of Spirillar Rat-Bite Fever, is usually not seen in Streptobacillary Rat-Bite Fever. Within several days of the disease onset, the patient develops a macular, maculopapular, or petechial rash that is most prominent on the extremities and may involve the palms and soles. Septic polyarticular arthritis develops in approximately one-half the patients. Untreated, complications include endocarditis, myocarditis, pericarditis, pneumonia, meningitis, and focal abscesses, with a mortality rate of 10-12%.

Spirillar Rat-Bite Fever has an incubation period of 1 to 3 weeks with the majority of the cases having an incubation period of over 10 days. While the rat bite may have healed during this period, the area will become swollen, indurated, and tender as the systemic phase of the disease begins. Fever, chills, headache, malaise, and regional lymphadenopathy characterize the clinical disease but the arthritis common in Streptobacillary Rat-Bite Fever does not occur. The initial clinical disease subsides after 3 to 5 days although relapses are common. Untreated Spirillar Rat-Bite Fever has a mortality rate of 5 - 10%.

Treatment - A variety of antibiotics may be used to treat both Streptobacillary and Spirillar Rat-Bite Fever. Procaine penicillin G appears to be generally effective against both organisms.

Prevention - Proper handling of laboratory rodents, especially rats is critical in reducing the potential for rodent bites and rat-bite fever. Personnel handling laboratory rodents should be familiar with the procedures or seek assistance from personnel with such experience.

Brucellosis

Host Range - Brucella melitensis, Brucella abortus, Brucella suis, and Brucella canis are all potential human pathogens associated primarily with goats, cattle, swine, and dogs respectively. Of these, only *Brucella canis* is widely distributed in laboratory animals, infecting 1 - 6% of the dog population in dog-production colonies. *Brucella abortus* is prevalent in wild populations of bison and elk and may result in the exposure of personnel working with these animals.

Transmission - Most human cases of *Brucella canis* are associated with contact with aborting bitches and the placental tissues which are typically rich in infective organisms. The organism is also shed for a prolonged period in infective dogs. Direct skin or mucous membrane contact with the organism as well as inhalation of infectious aerosol is responsible for transmission.

Clinical Signs - Brucella canis produces a milder clinical disease in humans than any of the other pathogenic *Brucella* spp., varying from subclinical or inapparent infection to a disease characterized by fever, headache, chills, myalgia, nausea, and weight loss. These flu-like symptoms are difficult to distinguish from many other diseases an the majority of human cases of brucellosis go undiagnosed. While septicemia and systemic disease may rarely occur, the disease is usually self-limiting. Chronic brucellosis, clinical disease lasting over 1 year, is relatively rare with *Brucella canis* in comparison to the other *Brucella* spp. pathogens of humans.

Diagnosis is primarily via serologic techniques, primarily serum agglutination. Isolation and cultivation of the organism is possible from the blood, bone marrow, or other tissues.

Treatment - A number of antimicrobial therapies are available for the treatment of brucellosis with the primary emphasis on the use of bacteriocidal combinations with a prolonged treatment course to minimize relapses. Combinations of tetracyclines (doxycycline or minocycline) and aminoglycosides (streptomycin or gentamicin) for 4 - 6 weeks are the primary treatment course.

Prevention - Prevention is primarily aimed at the exclusion of infected animals from the laboratory setting. All dogs should be screened for serologic reaction with *Brucella canis* prior to acquisition. Appropriate laboratory clothing and hygiene practices will reduce exposure.

Leptospirosis

Host Range - Leptospirosis has a worldwide distribution in a variety of domestic and wild animals including rats, mice, field moles, hedgehogs, squirrels, gerbils, hamsters, rabbits, dogs, domestic livestock, other mammals, amphibians, and reptiles.

Transmission - Leptospiras are shed in the urine of infected animals which often remain asymptomatic. Animals may be infected and shed the organism in their urine for life without clinical disease. Transmission occurs through direct contact of infected material with abraded skin or mucous membranes.

Clinical Signs - Early clinical disease is often quite diverse making early diagnosis nearly impossible. Disease severity may range from inapparent to a severe systemic illness with a sudden onset of fever, an intense often intractable headache, severe myalgia especially involving the calf muscles, chills, and conjunctival suffusion. Lymphocytic meningitis with a neutrophilia in the peripheral blood should arouse suspicion. Proteinuria and cylindruria usually accompany the early mild disease and blood urea nitrogen and creatinine are usually elevated. Elevated hepatic enzymes and a mild to moderate thrombocytopenia frequently occurs. Definitive diagnosis may be made by cultivation of the organism from the blood or urine (growth may take 30 or more days) or by either darkfield examination of urine or serology.

Treatment - A variety of antibiotics are useful in treatment including penicillin G, erythromycin, and doxycycline. While antibiotic therapy is effective at eliminating the organism, the lesions and tissue damage may require additional supportive treatment.

Prevention - Exclusion of infected animals from laboratory environments and vaccination of animals is the primary method of prevention. Appropriate laboratory clothing and protective equipment, especially gloves, minimizes exposure.

Campylobacteriosis

Host Range - A wide variety of animals are susceptible to infection with members of the genus *Campylobacter* and the organism has been recognized as a leading cause of diarrhea in humans. Distribution is worldwide.

Transmission - Transmission is fecal-oral. The organism is shed in the feces of infected animals and may be shed for prolonged periods following recovery from clinical disease. Younger animals are more likely to shed organisms than older animals.

Clinical Signs - The incubation period averages between 3 and 5 days with a range of 1 - 10 days. The disease in humans is usually self-limiting and brief with a gastrointestinal illness characterized by watery diarrhea often with blood, mucus, and leukocytes. Abdominal cramps, nausea, vomiting, and fever are not unusual. Systemic disease and other complications are rare. Diagnosis requires cultivation of the organism from the feces.

Treatment - Supportive fluid therapy is recommended with antibiotics only used in severe cases or those with immunosuppressive conditions. Erythromycin and ciprofloxacin are effective.

Prevention - Proper laboratory clothing and protective equipment should reduce to potential exposure to infective fecal materials. Proper personal hygiene is essential.

Salmonellosis

Host Range - Salmonellosis is distributed worldwide in a wide variety of animal species. While laboratory rodents are usually free of the disease, the potential for exposure through contaminated food and bedding sources remains. Wild rodents, amphibians, reptiles, avians, nonhuman primates, and dogs represent potential sources of zoonotic salmonellosis.

Transmission - Transmission is fecal-oral.

Clinical Signs - Salmonellosis is characterized by fever, abdominal pain and an acute enterocolitis with a watery diarrhea that often contains blood, mucus, and leukocytes. The incubation period is short, usually 8 - 48 hours, and the disease generally resolves within 5 days of onset although some patients may maintain diarrhea for as long as 2 weeks. Systemic spread of the disease is not typical but may occur with focal infections localized in nearly any body organ with resulting clinical disease. Definitive diagnosis requires isolation and culture of the organism from feces.

Treatment - The primary emphasis of treatment is on fluid and electrolyte replacement and balance. A variety of antibiotics can be used in cases where systemic spread of the bacteria occurs but the choices must be based upon culture and sensitivity tests since antibiotic resistance is common. Antibiotics are not recommended for uncomplicated enteric salmonellosis.

Prevention - Protective clothing and equipment, personal hygiene, and sanitation are the primary means of prevention in the laboratory environment.

Shigellosis

Host Range - Shigellosis is a primate pathogen and nonhuman primates are the only animals that can transmit the disease to man in any but unusual circumstances.

Transmission - Transmission is fecal-oral.

Clinical Signs - The incubation period is 24 - 72 hours and the disease begins abruptly with an acute diarrhea accompanied by fever, nausea, and occasionally vomiting. The diarrhea is initially watery containing blood, mucus, and numerous leukocytes. In contrast to salmonellosis, systemic invasion is very rare. Definitive diagnosis requires cultivation of the organism.

Treatment - Supportive care with fluid and electrolyte replacement.

Prevention - Protective clothing and equipment, personal hygiene, and sanitation are the primary means of prevention in the laboratory environment.

Toxoplasmosis

Host Range - The coccidian parasite, *Toxoplasma gondii*, is distributed worldwide in a wide variety of animals. Only domestic and wild felines, however, can serve as the definitive host and pass infective oocytes in their feces.

Transmission - The primary method of transmission is via ingestion of infectious oocysts from sources contaminated with feline feces. Ingestion of undercooked or uncooked meat from a variety of animals may also transmit the disease.

Clinical Signs - Toxoplasmosis is generally an asymptomatic or mild infection with flu-like symptoms including fever, myalgia, lymphadenopathy, and hepatitis. In pregnant women, however, the disease can have severe effects on the fetus ranging from death to delayed manifestations of infection following parturition. Primary infections in immunosuppressed humans can result in a maculopapular rash, pneumonia, skeletal myopathy, myocarditis, encephalitis, and death. Diagnosis is generally via serology.

Treatment - Pyrimethamine and sulfonamides are active against the tachyzoite forms while only the antimalarial agent atovaquone and the azalide azithromycin have activity against the tachyzoite and the tissue cysts.

Prevention - Protective clothing, protective equipment, sanitation, and personal hygiene are all important in minimizing exposure to the infective oocyst. Pregnant women without evidence of a toxoplasma titer and immunosuppressed personnel should be excluded from working with potentially infected cats whenever possible.

Dermatomycosis (Ring-Worm)

Host Range - Dermatophytes have a worldwide distribution although geographical concentrations of certain dermatophytes may occur. *Microsporum canis* is most prevalent in dogs, cats, and nonhuman primates and human infections are most likely associated with these species. *Trichophyton mentagrophytes* is more commonly associated with rodents and rabbits and human infections are generally related to these animals.

Transmission - Either via direct contact with the infected animal or via contact with contaminated equipment or materials. Dermatophyte spores are widely distributed and persistent in the environment.

Clinical Signs - Humans usually develop a solitary nodule on the hand or extremity. Ulceration and drainage of the lesions can occur. Deep visceral infections are rare.

Treatment - A number of antifungal drugs are available for treatment which may consist of topical treatment, systemic treatment (primarily peroral), or a combination of both. Griseofulvin, ketoconazole, fluconazole, and itraconazole may all be used. Amphotericin B is generally reserved for parenteral treatment of systemic mycosis.

Prevention - Protective clothing and equipment, especially gloves will minimize exposure. Personal hygiene and frequent hand-washing after handling animals minimizes exposure. Treatment of infected animals is essential for minimizing human exposure and exposure of other animals.