

Rat Bite Fever

Streptobacillus moniliformis

Infection:

Streptobacillary Fever,
Streptobacillosis
Epidemic Arthritic Erythema,
Haverhill Fever,
Streptobacillosis

Spirillum minus Infection:

Sodoku,
Spirillary Fever

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Importance

Rat bite fever is a human illness that can be caused by two different bacteria, *Streptobacillus moniliformis* and *Spirillum minus*. Although this disease is readily cured with antibiotics, untreated infections are sometimes fatal. Both *S. moniliformis* and *Sp. minus* are acquired primarily from rodents, especially rats. At one time, rat bite fever was mainly a hazard of exposure to wild rats or laboratory rodents; however, pet owners, pet shop employees and veterinary staff may be at increased risk with the growing popularity of rodent pets. Clinical cases can be a diagnostic challenge, as the initial symptoms are nonspecific and there are few good, widely available, diagnostic tests. *S. moniliformis* is fastidious and can be difficult to isolate, while *Sp. minus* is uncultivable and can be identified only by its morphology.

In animals, *S. moniliformis* is known mainly as a pathogen of rodents. This organism can cause septicemia, abscesses and arthritis in mice, and cervical lymphangitis or pneumonia in guinea pigs. Outbreaks in laboratory colonies can result in major economic losses, in addition to the zoonotic risks to personnel. Rare clinical cases or outbreaks have also been reported in other species of mammals and birds; however, the host range of *S. moniliformis*, and its effects on most animals, are still incompletely understood. Very little is known about *Sp. minus* infections in animals.

Etiology

Rat-bite fever is caused by two unrelated bacterial species, *Streptobacillus moniliformis* and *Spirillum minus*. *S. moniliformis* is a Gram negative, pleomorphic bacillus in the family Leptotrichiaceae. *Sp. minus* is a short, thick, Gram negative spiral. The latter organism has never been cultivated in artificial media, and much about it, including its taxonomic relationships, is poorly understood. The two forms of the disease in people are known, respectively, as streptobacillary rat bite fever and spirillary rat bite fever. In animals, infections caused by *S. moniliformis* may be called streptobacillosis. Haverhill fever is a *S. moniliformis* infection acquired by ingesting contaminated food or water.

Species Affected

Streptobacillus moniliformis

Rats are thought to be the reservoir hosts for *S. moniliformis*, and usually carry this organism asymptotically. It can be found in both *Rattus rattus*, the black rat, and *R. norvegicus*, the Norwegian rat, which is the ancestor of most laboratory and pet rats. *S. moniliformis* can also infect or colonize other species, although its full host range is still uncertain. It can cause illness in laboratory mice (*Mus musculus*) or infect them asymptotically, and spinifex hopping mice (*Notomys alexis*) were affected at a zoo. How long the organism can persist in laboratory mice is uncertain; estimates vary from no persistence to 6 months. Gerbils and African squirrels might also be hosts, based on their (rare) association with human cases of rat bite fever. In addition, *S. moniliformis* has been linked to illnesses in guinea pigs, turkeys and nonhuman primates, as well as clinical cases in two dogs, an owl and a koala (*Phascogaleos cinereus*). Bacteria similar to *S. moniliformis* (described as “*S. actinoides*”) were found in the lungs of calves and sheep with pneumonia, but it is not certain they were the same organism.

Animals that eat rodents might be infected or colonized, as a few human cases occurred after bites from dogs, ferrets, a weasel and a pig. The ability of these animals to act as hosts remains to be confirmed, because there could have been other sources of the organism, and there was usually no concrete evidence that it came directly from the biting animal. Nucleic acids of *S. moniliformis* were recently detected in the mouths of dogs, although the organism has not yet been isolated. Other carnivores have not been tested. Many species of animals have never been systematically examined for *S. moniliformis*.

Spirillum minus

Rats are thought to be the reservoir hosts for *Spirillum minus*, and carry it asymptotically. This organism is also reported to infect mice. However, it is very

difficult to assess its full host range, as *Sp. minus* has been identified only by its morphology and could be confused with bacteria that have a similar appearance. Guinea pigs and rhesus macaques became ill after inoculation with blood or tissue extracts thought to contain this organism. Similar experiments in rabbits were equivocal. One clinical case in a person occurred after a cat bite.

Zoonotic potential

Humans can be affected by both *S. moniliformis* and *Sp. minus*.

Geographic Distribution

S. moniliformis seems to be cosmopolitan, and streptobacillary rat bite fever has been documented on most continents. Although there are only a few published human cases from Asia (Taiwan and Thailand), the illness may be underdiagnosed. A recent study found that *S. moniliformis* was common among wild rats in Japan.

Human infections with *Sp. minus* have been reported mainly from Asia, but a few cases of rat bite fever were attributed to this organism in North America, Europe and Africa, and organisms with a similar appearance can be found in the blood of rodents. However, the attribution of some or all of these human cases may be uncertain. One early case from the U.S. was linked to *Sp. minus* not because the organism was found in the sick individual, but because spirilla were seen in the blood of wild mice on the property where the patient had been bitten. In another early case from Edinburgh, there was some evidence for both organisms in the patient.

Transmission

In rats, *S. moniliformis* is thought to be a commensal and part of the normal nasopharyngeal flora. It has also been found in the middle ear, salivary gland, larynx and upper trachea of rats. Proposed methods of transmission from rats to other animals include bites, aerosols or fomites, and contaminated food or water. Experimental infections have been established in rats and guinea pigs by oronasal or parenteral inoculation, and in guinea pigs by feeding. Mice have been infected by intranasal or parenteral inoculation, by feeding (the organism is thought to enter the body via the mouth and pharynx) and by contact with rats.

Sp. minus is also carried in asymptomatic rats, but there is little or no definitive information on its transmission. Rodents can be infected by inoculating them with contaminated blood or tissues. *Sp. minus* occurs in the blood of animals, and possibly in conjunctival exudates. Whether it is shed in the saliva, and under what conditions, is still unclear. Some early experiments suggested that *Sp. minus* was not transmitted readily between mice by casual contact. Limited evidence suggests that guinea pigs might transmit this organism in bites after they develop conjunctivitis (possibly

implicating conjunctival secretions in the contamination of saliva), but not before.

People usually become infected with *S. moniliformis* and *Sp. minus* after bites or scratches from rats, occasionally other rodents, and possibly carnivores. Human infections with *S. moniliformis* have also been documented after handling a rat, being exposed to its urine, kissing it or sharing food. Haverhill fever, caused by *S. moniliformis*, results from eating or drinking food or water that has been contaminated with rat excrement. Person-to-person transmission of rat bite fever or Haverhill fever has not been reported.

If carnivores are hosts, they probably acquire the organism when they bite or eat rodents, and colonization might be temporary.

Disinfection

S. moniliformis is susceptible to various disinfectants including 70% ethanol, sodium hypochlorite (500–1,000 ppm free chlorine), accelerated hydrogen peroxide and quaternary ammonium compounds. It can also be inactivated by moist heat of 121°C (250°F) for 15 minutes or dry heat of 160–170°C (320–338°F) for at least one hour.

Sp. minus has never been cultured in artificial media and its disinfectant susceptibility is unknown.

Infections in Animals

Incubation Period

Incubation periods for *S. moniliformis* in experimentally infected mice were a) approximately 7 days from oral inoculation to the development of visible neck abscesses, with deaths from septicemia usually occurring 3 to 5 days later, and b) 5 days or less for the development of arthritis after intravenous inoculation. Guinea pigs inoculated subcutaneously with *S. moniliformis* developed abscesses at the inoculation site in about 5 to 6 days.

Guinea pigs inoculated with *Sp. minus* in tissues or blood developed clinical signs after approximately 1 to 2 weeks in one experiment, and 14 to 18 days in another. This organism has also been found in the blood of guinea pigs after 5 to 37 days, and in the blood of mice after 5 to 30 days.

Clinical Signs

Streptobacillus moniliformis

Rats usually carry *S. moniliformis* asymptotically. Occasionally, this organism has been reported as a secondary invader in subcutaneous abscesses, bronchopneumonia, chronic pneumonia or otitis media.

Mouse strains differ in their susceptibility to *S. moniliformis*; some strains of inbred mice become bacteremic but remain asymptomatic after experimental infection, while other laboratory and wild mice become ill. Clinical signs and syndromes reported in mice include

septic lymphadenitis (especially affecting the ventral cervical lymph nodes), arthritis, various other purulent lesions, and acute or subacute septicemia. In outbreaks of streptobacillary septicemia, some mice may be found dead, while others may be depressed and hunched for 1 to 2 days before death. Conjunctivitis, photophobia, cyanosis, diarrhea, anemia, hemoglobinuria and emaciation may also be seen. Dermatitis, characterized by brown crusts over the mammae of nursing females, was reported in one outbreak. Chronic arthritis, with swelling of the limbs or tail, may be a sequela of infection, and deformation, ankylosis, and spontaneous amputation of the limbs or tail have also been reported. If the spinal column is involved, there may be posterior paralysis, kyphosis and priapism. Abortions and stillbirths can also occur. An outbreak in spinifex hopping mice at a zoo was characterized by sudden death, but intraperitoneal injection of these isolates into laboratory mice caused arthritis.

In guinea pigs, *S. moniliformis* has been linked with cases of granulomatous pneumonia or cervical lymphangitis. Cervical lymphangitis in guinea pigs is characterized by swelling and large abscesses in the cervical lymph nodes, and can sometimes be fatal. This syndrome has been difficult to reproduce experimentally, and its causes are still being investigated. It was seen in a few guinea pigs that were either fed guinea pig isolates of *S. moniliformis*, or inoculated subcutaneously; however, most animals only developed inoculation site abscesses. In a recent study, guinea pigs inoculated with a rat origin strain remained asymptomatic; however, it is possible that there are separate rat- and guinea pig-associated strains of *S. moniliformis*, and only guinea pig isolates cause cervical abscesses.

Rare clinical cases have been attributed to *S. moniliformis* in other species, although the evidence for its involvement was not always definitive. This organism was isolated from an abscess in one dog. It was also found in another dog with a fatal illness characterized by purulent polyarthritis, endocarditis and pneumonia, and clinical signs of anorexia, diarrhea, vomiting and arthritis in the hind legs. Septic arthritis and endocarditis were described in two naturally infected nonhuman primates, and experimentally infected rhesus macaques can develop a febrile illness. Pleuritis caused by *S. moniliformis* was reported in a koala. Several outbreaks were reported in turkeys. The clinical signs in these birds included polyarthritis, synovitis, tendon sheath swelling and joint lesions, and some infections were fatal. Turkeys, but not chickens, were susceptible to experimental infection with this isolate. A tawny owl (*Strix aluco*) with infected feet was reported in the U.K.

Spirillum minus

Rats usually carry *Sp. minus* asymptotically. A few older studies described experimental infections in rodents, but they used very crude preparations (e.g., tissue isolates from a rat bite fever patient, or blood containing spirilla

from rats or sick guinea pigs), and it is impossible to be sure that *Sp. minus* was the causative organism. Guinea pigs became ill after inoculation with organisms from rats, or tissues from a person with rat bite fever. The clinical signs included fever, conjunctivitis, keratitis, lymphadenopathy, weight loss and hair loss. Some of these infections were fatal. The same inocula did not cause illness in rats or mice, although spirilla were found in the blood. A febrile illness was reported in experimentally infected rhesus macaques. One study found that rabbits developed edematous, indurated, inflammatory lesions at the inoculation site, followed by regional lymphadenopathy and edema of the face (eyelids, lips, nose, base of the ears) and genitals. In other studies, rabbits did not become infected.

Post Mortem Lesions [Click to view images](#)

In laboratory mice, septic lymphadenitis usually affects the ventral cervical lymph nodes. Other subcutaneous lymph nodes may also be involved later in the illness. There may be few lesions in mice with acute septicemia. In subacute cases, mice may have multifocal, suppurative, embolic, interstitial nephritis, as well as focal necrosis of the spleen and liver, splenomegaly and lymphadenopathy. Brown crusts, caused by severe, acute, diffuse neutrophilic dermatitis, were reported over the mammae of nursing mice in one outbreak. In mice that survive longer, the predominant finding is septic polyarthritis characterized by numerous subcutaneous and periarticular abscesses. Fibrosis of the joints, joint deformation and spontaneous amputation of the limbs and tails may be seen in some animals.

Cervical lymphangitis in guinea pigs is characterized by swelling, inflammation and large abscesses in the cervical regional lymph nodes. Lesions can occur in other organs if the infection becomes disseminated.

Diagnostic Tests

Streptobacillus moniliformis

S. moniliformis infections in animals can be diagnosed by isolation of the organism, serology or molecular techniques. In most cases, diagnostic tests are used to monitor colonies of SPF laboratory animals for this organism; however, some tests can also be used in clinical cases.

S. moniliformis can be difficult to culture from laboratory animals. It is fastidious and must be grown in media enriched with serum, blood or ascitic fluid. The laboratory should be informed that this organism is suspected, as it does not grow well on non-enriched media. Although *S. moniliformis* is microaerophilic, some isolates from guinea pigs were reported to require anaerobic conditions for growth. *S. moniliformis* is inhibited by sodium polyanethol sulphionate (SPS), an anticoagulant that is often used in automatic blood culture systems. In liquid media, cultures usually have a “puff-ball” or “bread crumb-like” appearance. Colonies on blood agar have been described as circular, convex, grayish, smooth and glistening. Cell wall deficient L-forms of *S. moniliformis*

are readily formed *in vitro*, and have a “fried egg” appearance similar to *Mycoplasma* colonies. The identity of the organism can be confirmed by conventional biochemical and carbohydrate fermentation analysis, PCR, sequencing of the 16S rRNA gene or gas-liquid chromatographic analysis of the fatty acid profile. High-resolution polyacrylamide gel electrophoresis can be used to distinguish *S. moniliformis* strains.

On microscopic examination, *S. moniliformis* is Gram negative and pleomorphic. Depending on the medium and the age of the culture, organisms from colonies can occur as single rods or coccobacilli, or in long, unbranched filamentous chains, which may form loops or curls. Filaments may have spherical, oval, fusiform or club-shaped swellings. Occasionally, single rods also have lateral bulbar swellings. Clumps of *S. moniliformis* may look like proteinaceous debris in some specimens. This organism does not always stain well with Gram stains. Alternatives include carbolfuchsin or Giemsa. Staining with acridine orange and examination under a fluorescent microscope are also reported to aid visualization.

Serological tests such as enzyme-linked immunosorbent assays (ELISAs) and indirect immunofluorescence are used to monitor SPF laboratory animal colonies for *S. moniliformis*. False positive reactions in the ELISA test can be recognized by immunoblotting (Western blotting) and PCR tests. Some laboratory animals may not develop antibodies after infection.

PCR assays can also be used to monitor laboratory animals for this organism. The presence of *Leptotrichia* spp. can cause false positives. Amplicon sequencing has been recommended to confirm PCR results in laboratory animal colonies.

Spirillum minus

Spirillum minus cannot be cultured in artificial media. Detection of this organism has relied on finding organisms with the typical morphology in darkfield or phase contrast preparations, or after Giemsa, Wright or silver staining. *Sp. minus* is a short, spiral-shaped, Gram-negative (or Gram variable) rod (0.2–0.5 µm by 3–5 µm) reported to have 2 to 3 coils (although some sources report more) and bipolar tufts of flagella. If microscopy is unsuccessful, inoculation into mice, guinea pigs or *Sp. minus*-free rats has been used for diagnosis in human cases. Spirochetes may be found after 5–15 days in the blood of these animals, by dark-field microscopy.

Because *Sp. minus* cannot be cultured, no serological or molecular (PCR) tests are available.

Treatment

Penicillins are the drugs of choice in humans, and might also be a good choice in animals (in species that do not have adverse reactions to these drugs), but other antibiotics may also be effective. Abscesses, including

cervical abscesses in guinea pigs, may require incision and drainage or surgical removal.

There are few published reports of treatment in animals. During one outbreak in mice, breeding animals were treated with ampicillin in the drinking water, together with tetracycline to prevent the survival of penicillin-resistant L-forms. Although most of the mice recovered, some later relapsed and died of septicemia. Another group reported that streptomycin was more effective than penicillin in experimentally infected mice with arthritis, although penicillin was also used successfully. A dog with an abscess attributed to *S. moniliformis* recovered after treatment with 'strepto-penicillin' antibiotics, although the organism was described as having resistance to many antibiotics during *in vitro* testing.

Prevention

Laboratory rodents, or breeding colonies for rodent pets, can be cleared of infection by establishing cesarean derived, barrier maintained SPF stocks. These animals are monitored regularly for *S. moniliformis* infections. Such colonies have been established for laboratory rats, mice and guinea pigs. Although research animals usually come from SPF colonies, rodents sold as pets may be conventionally bred. Pets and SPF animals should be protected from contact with animals that may carry *S. moniliformis* or *Sp. minus*, such as wild rats.

To reduce the incidence of cervical abscesses in guinea pigs, abrasive materials should not be used in feed or litter, and malocclusions and overgrown teeth should be corrected.

Morbidity and Mortality

S. moniliformis and *Sp. minus* are usually carried asymptotically by rats. An estimated 50–100% of wild rats are infected with *S. moniliformis*, and up to 25% of the wild rats in some countries are thought to carry *Sp. minus*. At one time, *S. moniliformis* was also found in 10% to 100% of laboratory rats. With the advent of cesarean derived, barrier maintained SPF colonies, this organism has become rare in laboratory stocks. However, it is still found in conventionally bred rats (e.g., pets), and a few outbreaks have been reported even in SPF animals.

Outbreaks of streptobacillosis have been reported in both wild mice and laboratory mice, as well as in exotic mice at a zoo. Most, but not all, of the infections in laboratory mice occurred before SPF animals were introduced. In some outbreaks, the morbidity and mortality rates approached 100%. Some inbred strains of mice do not seem to be susceptible to illness. Sporadic infections with *S. moniliformis* have also been reported in guinea pigs. Cervical abscesses in these animals are sometimes fatal.

Little is known about infection or colonization in carnivores or other species. One study found *S. moniliformis* DNA in the mouth of 15% of dogs that had contact with rats.

Infections in Humans

Incubation Period

The stated incubation period for streptobacillary rat bite fever varies widely between sources. Combined, the estimates range from 2 days to more than 3 weeks, but most cases are reported to develop in less than 7 to 10 days. The incubation period in a case series of streptobacillary septic arthritis was 4 days to 7 weeks.

The reported incubation period for spirillary rat bite fever encompasses the range from one day to a month, with some sources estimating that it might be as long as 4 months. The U.S. Centers for Disease Control and Prevention (CDC) estimates an incubation period of 1 to 3 weeks. Most sources suggest that the spirillary form is slower to develop than the streptobacillary form, and typically occurs more than 10 days after a bite.

Clinical Signs

Streptobacillary rat bite fever

Wounds infected by *S. moniliformis* usually heal without inflammation, often before the first symptoms of rat bite fever appear. The illness usually begins abruptly with a fever and chills. Other common symptoms include severe myalgia and joint pain, headache, nausea and vomiting. Infants and young children can develop severe diarrhea, which may lead to weight loss. Most patients also have a maculopapular, purpuric or petechial rash. This rash occurs most often on the extremities, particularly the hands and feet, but it can sometimes involve the entire body. Hemorrhagic vesicles, pustules and papules, which are very tender, may also be seen. Many cases of rat bite fever resolve spontaneously within two weeks, but complications and deaths can occur in untreated cases.

At least half and perhaps as many as 75% of all patients with streptobacillary rat bite fever develop polyarthritis or polyarthralgia, often within a week of the onset of symptoms. The arthritis may affect the knees, ankles, shoulders, elbows, wrists and hands, and it may be migratory, affecting multiple joints. It can persist for months or even several years, with periods of remission and exacerbation. In most cases, the arthritis is thought to be nonsuppurative (sterile), and might be caused by an immunological mechanism. Septic arthritis (which often involves multiple joints) is reported infrequently. Some authors suggest that joint abnormalities, such as osteoarthritis, might predispose patients to the septic form. The septic and nonsuppurative forms of streptobacillary arthritis are generally similar in appearance, and can be difficult to distinguish. Some patients with septic arthritis had relatively few of the systemic signs, such as rashes, which would be expected with rat bite fever.

Other rare but serious complications reported in the literature include tenosynovitis, anemia, endocarditis, pericarditis, myocarditis, hepatitis, kidney dysfunction,

systemic vasculitis, prostatitis, pancreatitis, meningitis, pneumonia, sepsis, focal organ abscesses, and amnionitis (infection of the amniotic fluid). Most deaths occur in infants and in patients who have endocarditis, especially when it is untreated. Endocarditis is often, but not always, seen in patients with damaged heart valves. Sepsis can also be fatal, and fulminant, fatal sepsis has been reported even in previously healthy adults.

Most treated patients respond well, but prolonged migratory polyarthralgias, fatigue and slow resolution of the rash are possible. Long-term complications were not reported in patients that were treated for septic arthritis.

Spirillary rat bite fever

Spirillary rat bite fever is similar to streptobacillary rat bite fever. However, in this form of the disease, an indurated, painful and often ulcerated lesion occurs at the site of the bite. This skin lesion may appear when the fever develops, if the wound initially healed without complications. The regional lymph nodes are often swollen and tender. Febrile relapses separated by afebrile periods are often seen in spirillary rat bite fever; these relapses can recur several times over 1 to 3 months. They rarely continue for more than a year. Although rash is less common than in the streptobacillary form, some patients develop a distinctive rash consisting of large violaceous or reddish macules. Erythematous plaques or urticaria may also be seen, especially near the site of the bite. Arthritis is uncommon, but other complications resemble those seen in streptobacillary rat bite fever (e.g., endocarditis, myocarditis, hepatitis and meningitis). Untreated infections can be fatal.

Haverhill fever

Haverhill fever is very similar to streptobacillary rat bite fever, but pharyngitis and vomiting are reported to be more pronounced. Severe arthralgia and frequent relapses have also been reported.

Diagnostic Tests

Streptobacillary rat bite fever

Streptobacillary rat bite fever is usually diagnosed by culture, similarly to the methods used in animals. Clinical samples may be taken from the blood, other body fluids, affected tissues (e.g. abscesses) or the wound. *S. moniliformis* may be found in the synovial fluid in cases of septic arthritis, but in most patients, the joint fluid is sterile. As with samples from animals, the laboratory should be informed that this organism is suspected, as it does not grow well on non-enriched media, and it is inhibited by SPS in automatic blood culture systems.

Inoculation into rodents was also used for diagnosis in the past, but other techniques (e.g., PCR) are now preferred if culture is unsuccessful. Several PCR assays have been described, and were used in some case reports. Serological assays, such as slide agglutination tests, were employed in

the past, but they were not considered to be reliable. There are currently no validated serological tests for diagnosis in humans.

Spirillary rat bite fever

Spirillary rat bite fever is usually diagnosed by identifying spirilla that have a morphology consistent with *Sp. minus* in blood, exudates or tissues, including lymph node aspirates, the bite wound or erythematous plaques. If microscopy is unsuccessful, blood or wound aspirates can be inoculated into mice, guinea pigs or *Sp. minus*-free rats for diagnosis. Spirilla may be found after 5 to 15 days in the blood of these animals, by dark-field microscopy. Because *Sp. minus* cannot be cultured, no serological or molecular (PCR) tests are available.

Treatment

Rat bite fever can be treated successfully with antibiotics. Penicillin is considered to be the treatment of choice for both forms, but streptomycin, tetracycline, doxycycline, cephalosporin and other antibiotics have also been used. Penicillin-resistant strains of *S. moniliformis* seem to be rare, although they have been reported. The choice of drug also depends on penetration into the affected site (e.g., in cases of suppurative arthritis). Treatment of uncomplicated cases results in a shorter clinical course and may prevent severe complications.

Combinations of antibiotics have been recommended for patients with *S. moniliformis* endocarditis. Surgery may also be required in some cases. Antibiotics must be combined with adjunct treatments, such as arthroscopy, arthrotomy or joint lavage, in some patients with septic arthritis.

Prevention

The risk of infection can be reduced by avoiding exposure to rats, particularly wild rats. Wild rat populations around homes should be controlled; (see Internet Resources for information on rodent control from the CDC). Food and water storage should be designed to prevent contamination by rodents, and potentially contaminated water and food sources should be avoided. Pasteurization of milk and sterilization of drinking water decrease the risk of Haverhill fever. SPF rodents rather than conventional animals should be used, whenever possible, in laboratories or when breeding pets. These animals, as well as pets, should be housed in areas free of wild rodents.

Proper handling techniques can help prevent bites from laboratory or pet rodents. Protective clothing, including gloves, can also be helpful. Hand-to-mouth contact should be avoided when handling a rodent or cleaning its cage, and the hands should be washed after contact. Bite wounds or scratches should be cleaned promptly and thoroughly. In addition, the CDC suggests that people who become ill after being bitten by a rat seek medical attention, and report their

exposure history to ensure that rat bite fever is considered in the differential diagnosis.

Morbidity and Mortality

There are relatively few confirmed cases of rat bite fever reported in the literature. For example, only 200 cases had been documented in the U.S, as of 2004. However, this disease may be underdiagnosed, as it is not notifiable, obtaining a definitive diagnosis can be challenging, and the illness responds to the antibiotics commonly used for empirical treatment of infections. Rat bite fever cases may be increasing with the growing popularity of rats as pets.

As with many diseases, the risk of illness varies with occupational and recreational exposure, as well as living conditions. Higher risk groups include laboratory workers, the owners of pet rats, pet shop personnel and veterinarians, as well as people who are exposed to wild rats. The greatest risk of illness is from exposure to wild rats or conventionally bred rats, but SPF rats or mice have occasionally been involved, and other animals (e.g., African squirrels, a gerbil, carnivores and other species) have been implicated in rare cases. Although rat bite fever cases tend to be sporadic, outbreaks can occur, especially when people are exposed to a common source of contaminated food or water. Large outbreaks of Haverhill fever were reported in Haverhill, MA in 1926; in Chester, USA in 1925; and at a boarding school in Essex, U.K. in 1983. The first two of these outbreaks were associated with contaminated, unpasteurized milk products, and the third was linked to contaminated water from a spring.

Rat bite fever can be treated readily with antibiotics, but untreated *S. moniliformis* infections are estimated to be fatal in approximately 7–13% of patients, and untreated *Sp. minus* infections in approximately 7–10%. Most deaths occur in infants or in patients who develop endocarditis. Although endocarditis and pericarditis are rare, the case fatality rate can be as high as 53% in these patients, especially if the condition is not treated.

Internet Resources

Centers for Disease Control and Prevention (CDC).

Rat bite fever information

<http://www.cdc.gov/rat-bite-fever/>

CDC. Information on wild rodent control

<http://www.cdc.gov/rodents/>

Public Health Agency of Canada.

Pathogen Safety Data Sheets

<http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php>

The Merck Manual

<http://www.merckmanuals.com/professional/index.html>

The Merck Veterinary Manual

<http://www.merckmanuals.com/vet/index.html>

References

- Acha PN, Szyfres B (Pan American Health Organization [PAHO]). Zoonoses and communicable diseases common to man and animals. Volume 1. Bacterioses and mycoses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Rat bite fever; p. 226-229.
- Aldred P, Hill HC, Young C. The isolation of *Streptobacillus moniliformis* from cervical abscesses of guinea pigs. *Lab Anim.* 1974;8:275-7.
- Banerjee P, Ali Z, Fowler DR. Rat bite fever, a fatal case of *Streptobacillus moniliformis* infection in a 14-month-old boy. *J Forensic Sci.* 2011;56(2):531-3.
- Berger C, Altwegg M, Meyer A, Nadal D. Broad range polymerase chain reaction for diagnosis of rat-bite fever caused by *Streptobacillus moniliformis*. *Pediatr Infect Dis J.* 2001;20(12):1181-2.
- Boot R, Bakker RH, Thuis H, Veenema JL, De Hoog H. An enzyme-linked immunosorbent assay (ELISA) for monitoring rodent colonies for *Streptobacillus moniliformis* antibodies. *Lab Anim.* 1993;27(4):350-7.
- Boot R, Oosterhuis A, Thuis HC. PCR for the detection of *Streptobacillus moniliformis*. *Lab Anim.* 2002;36(2):200-8.
- Boot R, van de Berg L, van Lith HA. Rat strains differ in antibody response to *Streptobacillus moniliformis*. *Scand J Lab Anim Sci.* 2010;37(4): 275-83.
- Boot R, van de Berg L, Koedam MA, Veenema JL, Vlemminx MJ. Resistance to infection of guinea pigs with a rat *Streptobacillus moniliformis*. *Scand J Lab Anim Sci.* 2007;34:1-5.
- Boot R, Van de Berg L, Reubsaet FA, Vlemminx MJ. Positive *Streptobacillus moniliformis* PCR in guinea pigs likely due to *Leptotrichia* spp. *Vet Microbiol.* 2008;128:395-9.
- Bottone EJ. *Spirillum minus*. An atlas of the clinical microbiology of infectious diseases. New York: Parthenon Pub. Group; 2004. p 136.
- Buranakitjaroen P, Nilganuwong S, Gherunpong V. Rat-bite fever caused by *Streptobacillus moniliformis*. *Southeast Asian J Trop Med Public Health.* 1994;25(4):778-81.
- Centers for Disease Control and Prevention [CDC]. Fatal rat-bite fever--Florida and Washington, 2003. *Morb Mortal Wkly Rep.* 2005;53(51):1198-202.
- Centers for Disease Control and Prevention [CDC]. Rat bite fever [online]. CDC; 2012 Jan. Available at: <http://www.cdc.gov/rat-bite-fever/index.html>. Accessed 26 Dec 2012.
- Centers for Disease Control and Prevention [CDC]. Rat-bite fever--New Mexico, 1996. *Morb Mortal Wkly Rep.* 1998;47(5):89-91
- Centers for Disease Control and Prevention [CDC]. Rat bite fever. Technical information [online]. CDC; 2005 Oct. Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/ratbitefever_t.htm. * Accessed 9 March 2006.
- Chen PL, Lee NY, Yan JJ, Yang YJ, Chen HM, Chang CM, Lee HC, Ko NY, Lai CH, Ko WC. Prosthetic valve endocarditis caused by *Streptobacillus moniliformis*: a case of rat bite fever. *J Clin Microbiol.* 2007;45(9):3125-6.
- Dendle C, Woolley IJ, Korman TM. Rat-bite fever septic arthritis: illustrative case and literature review. *Eur J Clin Microbiol Infect Dis.* 2006;25(12):791-7.
- Dworkin J, Bankowski MJ, Wenceslao SM, Young R. A case of septic arthritis from rat-bite fever in Hawai'i. *Hawaii Med J.* 2010;69(3):65-7.
- Elliott SP. Rat bite fever and *Streptobacillus moniliformis*. *Clin Microbiol Rev.* 2007;20(1):13-22.
- Euzéby JP: List of prokaryotic names with standing in nomenclature [online] - Genus *Streptobacillus*. *Int J Syst Bacteriol.* 1997;47:590-2. [updated Dec 2012]. Available at: <http://www.bacterio.cict.fr/s/streptobacillus.html>. Accessed 26 Dec 2012.
- Freels LK, Elliott SP. Rat bite fever: three case reports and a literature review. *Clin Pediatr (Phila).* 2004;43(3):291-5.
- Futaki K, Takaki I, Taniguchi T, Osumi S. M.D. *Spirochaeta morsus muris*, N.Sp., the cause of rat bite fever. *J Exp Med.* 1917;25:33-44.
- Gaastra W, Boot R, Ho HT, Lipman LJ. Rat bite fever. *Vet Microbiol.* 2009;133(3):211-28.
- Garrity GM, Bell JA, Lilburn T. *Spirillum minus*. In: Garrity GM, Brenner DJ, Krieg NR, Staley JT, editors. *Bergey's Manual of Systematic Bacteriology*. Volume 2, Part C, The alpha, beta,, delta and epsilon proteobacteria. 2nd. ed. New York, NY: Springer; 2005. p. 875.
- Glasman PJ, Thuraisingam A. Rat bite fever: a misnomer? *BMJ Case Rep.* 2009;2009: bcr04.2009.1795.
- Glastonbury JR, Morton JG, Matthews LM. *Streptobacillus moniliformis* infection in Swiss white mice. *J Vet Diagn Invest.* 1996;8(2):202-9.
- Graves MH, Janda JM. Rat-bite fever (*Streptobacillus moniliformis*): a potential emerging disease. *Int J Infect Dis.* 2001;5(3):151-5.
- Hayashimoto N, Yoshida H, Goto K, Takakura A. Isolation of *Streptobacillus moniliformis* from a pet rat. *J Vet Med Sci.* 2008;70(5):493-5.
- Hof H. Miscellaneous pathogenic bacteria. In: Baron S, editor. *Medical microbiology*. 4th ed. New York: Churchill Livingstone; 1996. Available at: <http://www.gsbs.utmb.edu/microbook/ch016.htm>. * Accessed 7 March 2006.
- Holden FA, MacKay JC. Rat-bite fever - an occupational hazard. *Can Med Assoc J.* 1964;91:78-81.
- Hudsmith L, Weston V, Szram J, Allison S. Clinical picture, rat bite fever. *Lancet Infect Dis.* 2001;1(2):91.
- Institute for Laboratory Animal Research (ILAR), National Research Council. *Infectious diseases of mice and rats*. Washington DC: National Academy Press; 1991. *Streptobacillus moniliformis*; p. 176-9.
- Ishiwara K, Ohtawara T, Tamura K. Experimental rat bite fever: first report. *J Exp Med.* 1917;25: 45-64.
- Johnson RC. *Leptospira*, *Borrelia* (including Lyme disease) and *Spirillum*. In: Baron S, editor. *Medical microbiology*. 4th ed. New York: Churchill Livingstone; 1996. Available at: <http://www.gsbs.utmb.edu/microbook/ch035.htm>. * Accessed 7 March 2006.
- Johnson-Delaney CA. Safety issues in the exotic pet practice. *Vet Clin North Am Exot Anim Pract.* 2005;8(3):515-24, vii.
- Kahn CM, Line S, editors. *The Merck veterinary manual*. Whitehouse Station, NJ: Merck and Co; 2010. Poultry. Infectious skeletal disorders; p. 2480.

- Kahn CM, Line S, editors. The Merck veterinary manual [online]. Streptococcal lymphadenitis (Cervical lymphadenitis, Lumps). Whitehouse Station, NJ: Merck and Co; 2003. Accessed 23 Dec 2012.
- Kayser FH. *Spirillum minus*. In: Medical microbiology. Kayser FH, Bienz KA, Eckert J, Zinkernagel RM, editors. Stuttgart/New York; Georg Thieme Verlag; 2005. p. 306.
- Kimura M, Tanikawa T, Suzuki M, Koizumi N, Kamiyama T, Imaoka K, Yamada A. Detection of *Streptobacillus* spp. in feral rats by specific polymerase chain reaction. Microbiol Immunol. 2008;52(1):9-15.
- Kirchner BK, Lake SG, Wightman SR. Isolation of *Streptobacillus moniliformis* from a guinea pig with granulomatous pneumonia. Lab Anim Sci. 1992;42(5):519-21.
- Koopman JP, Van den Brink ME, Vennix PP, Kuypers W, Boot R, Bakker RH. Isolation of *Streptobacillus moniliformis* from the middle ear of rats. Lab Anim. 1991;25(1):35-9.
- Levey JS, Levey S. Chemotherapy of joint involvement in mice produced by *Streptobacillus moniliformis*. Exp Biol Med. 1948;68(2):314-7.
- MacCluskie JAW. *Spirillum minus* derived from a spontaneous infection in a mouse – with special reference to pathogenicity as a means of differentiating it from strains in the rat. J Pathol. 1930;33:863-9.
- Mackie TJ, McDermott EN. Bacteriological and experimental observations on a case of rat bite fever: *Spirillum minus*. J Pathol. 1926;29:493-5.
- Mooser H. Experimental studies with a spiral organism found in a wild rat. J Exp Med. 1924;39(4):589-602.
- Mooser H. Experimental studies with a spiral organism found in a wild rat and identical with the organism causing rat bite fever. J Exp Med. 1925;42(4):539-59.
- Nolan M, Gronow S, Lapidus A, et al. Complete genome sequence of *Streptobacillus moniliformis* type strain (9901). Stand Genomic Sci. 2009;1(3):300-7.
- Porter RS, Kaplan JL, editors. The Merck manual [monograph online]. 19th ed. Whitehouse Station, NJ: Merck and Co.; 2009. Rat bite fever. Available at: http://www.merckmanuals.com/professional/infectious_diseases/spirochetes/rat-bite_fever.html. Accessed 26 Dec 2012.
- Public Health Agency of Canada. Pathogen Safety Data Sheet: *Streptobacillus moniliformis* [online]. Pathogen Regulation Directorate, Public Health Agency of Canada; 2011 Feb. Available at: <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/streptobacillus-eng.php>. Accessed 23 Dec 2012.
- Savage NL, Joiner GN, Florey DW. Clinical, microbiological, and histological manifestations of *Streptobacillus moniliformis*-induced arthritis in mice. Infect Immun. 1981;34(2):605-9.
- Smith W. Cervical abscesses of guinea pigs. J Pathol: 1941;53:29-37.
- Stehle P, Dubuis O, So A, Dudler J. Rat bite fever without fever. Ann Rheum Dis. 2003;62(9):894-6.
- Taylor JD, Stephens CP, Duncan RG, Singleton GR. Polyarthritis in wild mice (*Mus musculus*) caused by *Streptobacillus moniliformis*. Aust Vet J. 1994;71(5):143-5.
- Valverde CR, Lowenstine LJ, Young CE, Tarara RP, Roberts JA. Spontaneous rat bite fever in non-human primates: a review of two cases. J Med Primatol. 2002;31(6):345-9.
- van Nood E, Peters SH. Rat-bite fever. Neth J Med. 2005 Sep;63(8):319-21.
- van Rooyen CE. The biology, pathogenesis and classification of *Streptobacillus moniliformis*. J Pathol. 1936;43:455-72.
- Wang TK, Wong SS. *Streptobacillus moniliformis* septic arthritis: a clinical entity distinct from rat-bite fever? BMC Infect Dis. 2007;7:56.
- Wildlife diseases in the U.K.[online]. Cases reported in the year 2002. Report to the Department of Environment, Food and Rural Affairs (DEFRA) and the Office International des Epizooties (OIE). SVS Project ED1600-Diseases of Wildlife 32 p. Available at: <http://www.defra.gov.uk/corporate/vla/science/documents/science-end-oie02.pdf>. * Accessed 2 March 2006.
- Wilkins EG, Millar JG, Cockcroft PM, Okubadejo OA. Rat-bite fever in a gerbil breeder. J Infect. 1988;16(2):177-80.
- Wouters EG, Ho HT, Lipman LJ, Gaastra W. Dogs as vectors of *Streptobacillus moniliformis* infection? Vet Microbiol. 2008;128(3-4):419-22.
- Wullenweber M. *Streptobacillus moniliformis*-a zoonotic pathogen. Taxonomic considerations, host species, diagnosis, therapy, geographical distribution. Lab Anim. 1995;29:1-15.
- Wullenweber M, Jonas C, Kunstyr I. *Streptobacillus moniliformis* isolated from otitis media of conventionally kept laboratory rats. J Exp Anim Sci. 1992;35(1):49-57.
- Wullenweber M, Kaspereit-Rittinghausen J, Farouq M. *Streptobacillus moniliformis* epizootic in barrier-maintained C57BL/6J mice and susceptibility to infection of different strains of mice. Lab Anim Sci. 1990;40(6):608-12.
- Wullenweber M, Kaspereit-Rittinghausen J, Farouq M. *Streptobacillus moniliformis* epizootic in barrier-maintained C57BL/6J mice and susceptibility to infection of different strains of mice. Lab Anim Sci. 1990;40(6):608-12.

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