Rat Bite Fever

Streptobacillus moniliformis Infection:
Streptobacillary Fever, Streptobacillosis
Epidemic Arthritic Erythema, Haverhill Fever, Streptobacilliosis

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.

Early experiments suggested that guinea pig and rat strains of *S. moniliformis* might differ in their culture characteristics and clinical signs in rodents. There is no conclusive evidence yet to confirm these observations.

Species Affected

Streptobacillus moniliformis

Rats are thought to be the reservoir hosts for *Streptobacillus moniliformis*, and usually carry this organism asymptomatically. 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.

Mice can be infected either subclinically or symptomatically with *S. moniliformis*. The length of time this organism persists in mice is uncertain, with estimates varying from no persistence to 6 months. Gerbils and African squirrels are potential hosts, based on their (rare) association with human cases of rat bite fever. In addition, *S. moniliformis* has been linked to diseases in guinea pigs and turkeys, and clinical cases in two non-human primates, two dogs, an owl and a koala (*Phascolarctos cinereus*). Bacteria similar to *S. moniliformis* (described as ‘‘*S. actinoides*”) were also found in the lungs of calves and sheep with pneumonia, although it is not certain they were the same organism.

Animals that eat rodents, including dogs, ferrets, a weasel and a pig, might be infected or colonized, as they have been implicated in a few human cases. However, there was usually no concrete evidence that the organism came from the animal, in these case reports. Nucleic acids of *S. moniliformis* were recently detected in the mouths of dogs, but other carnivores have not yet been tested for this organism. Many species of animals have never been systematically examined for *S. moniliformis*.

Spirillum minus

Rats are also thought to be the reservoir hosts for *Spirillum minus*, and carry it asymptomatically. It is difficult to assess the host range of this organism, as it has

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been identified only by its morphology, and it could be confused with similar bacteria. In addition to rats, *Sp. minus* is reported to infect mice, and illness was reported in experimentally infected guinea pigs and rhesus macaques. In older reports, rabbits could be infected in some experiments, but not others; not all authors agree that this species is susceptible. One clinical case in a person occurred after a cat bite.

Zoonotic potential

Humans can be affected by both *Streptobacillus moniliformis* and *Spirillum minus*.

Geographic Distribution

Streptobacillus 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 *Spirillum minus* have been reported mainly from Asia, but occasional cases of rat bite fever have been attributed to this organism in North America, Europe and Africa, and organisms with a similar appearance can be found in the blood of rodents.

The limitations of diagnostic testing for *S. moniliformis* and *Sp. minus* may make it difficult to identify the causative organism with certainty, especially in older reports. This could affect geographic distribution, as documented cases of spirillary rat bite fever are rare in some areas. For example, one early case of "spirillary rat bite fever" in Edinburgh occurred in a patient who also had organisms consistent with *S. moniliformis* in the blood. The case was attributed to *Sp. minus* because a few spirilla were recovered from the patient's enlarged lymph nodes, and because only this organism was thought to cause rat bite fever at the time. The bacteria in the blood were dismissed as a secondary contaminant. Neither organism was found in another early case from the U.S., but the disease was attributed to *Sp. minus* because spirilla were seen in the blood of wild mice on the property where the patient was bitten.

Transmission

In rats, *Streptobacillus 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, or between guinea pigs in bites before they develop conjunctivitis.

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.

Carnivores 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 to 1,000 ppm free chlorine), accelerated hydrogen peroxide and quaternary ammonium compounds. It can also be inactivated by heating at 121°C (moist heat) for 15 minutes or 160-170°C (dry heat) for at least one hour.

Sp. minus has not been cultured in artificial media and its disinfectant susceptibility is unknown.

Infections in Animals

Incubation Period

In one experiment, mice developed visible abscesses of the neck approximately 7 days after oral inoculation of *S. moniliformis*, and death from septicemia usually occurred 3-5 days later. In other experiment, mice developed arthritis within 5 days of intravenous inoculation. Guinea pigs inoculated subcutaneously with *S. moniliformis* developed abscesses at the inoculation site in about 5-6 days.

In guinea pigs inoculated with clinical specimens containing *Sp. minus*, the signs appeared in approximately 1-2 weeks in one experiment, and 14-18 days in another. The organism was found in the blood of guinea pigs in 5-37 days, and in the blood of mice in 5-30 days.

Clinical Signs

Streptobacillus moniliformis

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

Different strains of mice seem to vary in their susceptibility; some experimentally infected inbred mice

become bacteremic but remain asymptomatic. Clinical signs and syndromes reported in infected mice include septic lymphadenitis (especially affecting the ventral cervical lymph nodes), arthritis, various other purulent lesions, and acute or subacute septicemia. In outbreaks of septicemia, some mice may be found dead. 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 with *S. moniliformis*. Deformation, ankylosis, or spontaneous amputation of the limbs or tail has been reported in some mice. If the spinal column is involved, there may be posterior paralysis, kyphosis and priapism. Abortions and stillbirths have been reported in pregnant mice. Although most outbreaks have been reported in laboratory mice, an outbreak in spinifex hopping mice (*Notomys alexis*) at a zoo was characterized by sudden death. Intraperitoneal injection of these isolates into laboratory mice caused arthritis.

S. moniliformis has been associated with cases of granulomatous pneumonia or cervical lymphangitis in guinea pigs. Cervical lymphangitis is characterized by swelling and large abscesses in the cervical lymph nodes. Some cases are fatal. This syndrome has been difficult to reproduce experimentally. It was seen in a few guinea pigs that were either fed guinea pig isolates of *S. moniliformis,* or inoculated subcutaneously; however, most injected guinea pigs only developed inoculation site abscesses. In a recent study, guinea pigs inoculated with a rat origin strain remained asymptomatic.

Rare clinical cases have been attributed to *S. moniliformis* in other species, although the evidence is not definitive in all cases. This organism was isolated from an abscess in one dog. It was also found in another dog with a fatal illness characterized by 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 with infected feet was reported in the U.K.

Spirillum minus

Rats usually carry *Sp. minus* asymptomatically. A few older studies described experimental infections in rodents; however, 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 certain 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.

Communicability

Rats and other animals can transmit *S. moniliformis* and *Sp. minus* in bites and scratches. *S. moniliformis* can also be spread by other means, such as contamination of food with excrement from rats. Carnivores might usually be colonized only temporarily, but may be able to transmit the organism in bites.

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 sulphonate (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, it 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. *S. moniliformis* does not always stain well with Gram stains. Alternatives include carbolfuchsin or Giemsa. Staining with acridine orange and examination under a fluorescent microscope have also been reported to aid visualization of the organism.

Serological tests are used to monitor SPF laboratory animal colonies for *S. moniliformis*. Agglutination and complement fixation tests were used in the past, but they have generally been replaced by enzyme-linked immunosorbent assays (ELISAs) and indirect immunofluorescence. 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 to 0.5 µm by 3 to 5 µm) reported to have 2-3 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

By analogy with rat bite fever in humans, penicillins might be the drugs of choice (in species that do not have adverse reactions to these drugs), but other antibiotics may also be effective. Cervical abscesses in guinea pigs, as well as other abscesses, may require surgical removal or incision and drainage.

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 asymptomatically by rats. Up to 25% of the wild rats in some countries are thought to carry *Sp. minus.* An estimated 50% to 100% of wild rats are infected with *S. moniliformis.* In Japan, a recent PCR survey detected the latter organism in 92% of wild *R. norvegicus* and 58% of wild *R. rattus.* 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%. Susceptibility to illness varies between strains of mice, and some inbred strains are infected subclinically. 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 reported *S. moniliformis* DNA in the mouth of 15% of dogs that had contact with rats.

Post Mortem Lesions

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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.

The lesions in a dog infected with *S. moniliformis* were purulent polyarthritis, endocarditis and pneumonia.

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 7-10 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 1-3 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 on the extremities. Many cases of rat bite fever resolve spontaneously within two weeks. However, 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 and focal organ abscesses. One patient developed ammonitis (infection of the amniotic fluid). Most deaths occur in infants and in patients who develop endocarditis, especially when it is untreated. Endocarditis is often, but not always, seen in patients with damaged heart valves. Fulminant, fatal sepsis has been reported 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 with septic arthritis after treatment.

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 in spirillary rat bite fever, 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 rate bite fever, but pharyngitis and vomiting are reported to be more pronounced. Severe arthralgia and frequent relapses have also been reported.

Communicability

Person-to-person transmission has not been reported.

Diagnostic Tests

Streptobacillary rat bite fever

In humans, streptobacillary rat bite fever is usually diagnosed by culture of 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. Culture of the organism is described under diagnostic tests for animals. 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.

Several PCR assays have been described. In some case reports, these tests were used to identify *S. moniliformis* in clinical specimens. *Leptotrichia* spp. can cause false positive reactions in PCR tests, and sequencing of the amplicons may be necessary to distinguish these organisms.

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

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; specific information on rodent control is available from the CDC (see Internet Resources, below). 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 decreases 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.

Bites from rodents should be avoided as much as possible. Proper handling techniques can help prevent bites. 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 commonly used antibiotics. 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, as laboratories now mainly use SPF rats and mice. Nevertheless, outbreaks have occasionally been reported even in SPF animals. Human infections have also been linked to bites from other animals (e.g., African squirrels, a gerbil, a cat, dogs, non-human primates, ferrets, a weasel and a pig), but such cases seem to be rare, and definitive evidence for the animal's involvement is not available for most cases.

Although rat bite fever cases tend to be sporadic, outbreaks can occur, especially when people are exposed to 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 and 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/index.html

CDC. Information on wild rodent control
http://www.cdc.gov/rodents/prevent_infestations/index.html

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.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/

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