Diseases Transmitted by Man’s Worst Friend: the Rat

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ABSTRACT Historically, the rat has been considered a scourge to mankind, for example, rats infected with the plague bacillus that caused the Black Death, which accounted for millions of deaths in Europe during the Middle Ages. At least three pandemics (in the 5th and 6th, 8th through 14th, and 19th through 21st centuries) of plague ravaged civilizations, and the disease undoubtedly plagued humankind prior to recorded history. Also, numerous other diseases are spread to humans by rats; thus, a quote from Hans Zinsser’s text Rats, Lice, and History, “Man and rat will always be pitted against each other as implacable enemies,” conveys the general revulsion that society holds for the wild rat.

INTRODUCTION Numerous methods have been used by countless countries attempting to eradicate the rat, but it continues to successfully colonize both urban and rural settings on a global level. One novel approach first introduced in Asia and Europe and then in the United States was the use of domestic ferrets for rodent control.

Because the life cycle and transmission of Yersinia pestis are closely linked to rats and their fleas, tremendous efforts were mounted to eradicate the rat host and its flea, Xenopsylla cheopis. For example, in the Philippines, rat catcher groups of 300 men were assigned the formidable task of eliminating the omnipresent pest. When rats were encountered, they were killed immediately. Some of these work forces had fox terriers imported especially from Australia because of their agility and quickness. Others utilized trained ferrets, which responded to their masters’ calls, like dogs. The ferrets were even more effective than dogs in killing rats. A ferret would grasp a rat in its jaws, and the ferret’s teeth would then sever the rat’s spinal column. Undoubtedly, ferrets served similar roles in differing locales throughout the world to control rat infestations and hence to reduce the likelihood of further spread of the dreaded pestilence.

One author recommended that when rats are hunted in plague agent–infested areas, the rats and the sack containing the dead rats be submerged in a germicidal solution as soon as they are killed. It was strongly urged that rats in plague areas, as well as the bag containing the rats, be incinerated. Even though attention was given to treating rat bite wound infection in ferrets, discussions on ferrets hunting Y. pestis–infected rats becoming infected with the plague bacillus were not found.

The practice of using ferrets to control wild rodents also became popular in the United States during the early part of the 20th century, and tens of thousands of ferrets were raised and sold for this purpose. The Department of Agriculture distributed bulletins announcing the use of ferrets for rodent abatement. Because rodents are extremely fearful of ferrets and flee even their scent, only a few ferrets were needed to disperse literally hundreds of rodents from granaries, barns, and warehouses. A “ferretmeister” would deploy his ferrets on an infested farm or granary, and the animals would then “ferret out” the rodents from their hiding places and nests. Men and terrier dogs, strategically located, would eradicate...
the rodents as they emerged from hiding. Alternatively, small farms or granaries would maintain ferrets and allow the territorial imperative for up to about 650 ft (200 m)—considered to be the ranging domain of a ferret—with an adequate food source. The availability of commercially available rodenticides, however, has dramatically reduced the need for ferrets as rodent exterminators.

During the early 1900s, rodenticides containing live cultures of Salmonella enteritidis were distributed on a large-scale basis by commercial and public health organizations in an attempt to eliminate feral rats. These cultures were known as rat viruses and were widely used in Europe, England, and the United States as rat poisons. However, the enthusiasm for their use waned when it was discovered that the spread of the organisms could not be limited; predictably, the baiting program was implicated in several epidemics among exposed human populations. Surprisingly, as late as the 1950s in England, S. enteritidis (serovar Danzy) was isolated from adults living 4 miles apart. The source of infection was traced to contaminated cakes from a local bakery. Mice which had acquired the infection from living S. enteritidis serovar Danzy cultures in rodenticide baits had infected food in the bakery.

On a global scale, there has been a dramatic increase in the number of feral cats. During the last decade, it has been estimated that 50 million to 60 million feral cats inhabit the United States. This tremendous number raises the question of whether they are playing a role in controlling the wild rat population in both rural and urban settings. Though feral cats’ predatory habits have a profound effect on reducing the number of wild bird species and small rodents and reptiles, they supposedly do not kill rats over 200 g.

The black, or roof, rat (Rattus rattus) and the Asian black rat (Rattus tanezumi), which coexisted with humans in the small, crowded, unsanitary environs of the medieval era, have been largely displaced by the more aggressive, larger brown Norway rat (Rattus norvegicus). This species of rat lives farther from contemporary, better-constructed urban domiciles by taking up residence in backyards, sewers, industrial buildings, dumps, or granaries. In this environment, the rat often competes for food and territory with other wild rodents and therefore can share zoonotically transmitted diseases. Fortunately, human fleas, which accounted for widespread human-to-human transmission of plague, have almost been eliminated from cities in the United States, and thus the likelihood of epidemics initiated by rat zoonoses has been reduced. Nevertheless, zoonotic transmission of rat diseases still occurs, and as major cities suffer from overcrowding, structural decay, and inadequate waste removal, the rat population will increase, and the probability of transmission of these diseases to the homeless or underprivileged correspondingly will increase.

Contrary to the image of the rat depicted by Zinsser, the laboratory rat, R. norvegicus, used extensively for decades in biomedical research, has provided immeasurable benefit to humankind’s understanding of disease processes and their control and elimination. However, the use of rats in research and the current popularity of rats as “pocket pets” also afford the opportunity for this segment of the population to become infected with rat-borne diseases. The purpose of this chapter, therefore, is to highlight those zoonotic diseases of rats, and in certain cases the same diseases in other rodents, which have clinical relevance in the United States and its territories.

RAT BITES
Relapsing fevers following rat bites have been noted clinically for over 2,000 years, being first recognized in India. Early recorded descriptions of the disease are found in the Yale medical archives of the 19th century. The term Rattenbisskrankheit, or rat-bite fever, was coined.

Approximately 40,000 rat bites are reported annually, according to one carefully researched report. In another report, the authors estimated that 1% of the 2 million animal bites that occur annually are rat bites. Several studies indicate that over two-thirds of rat bites occur in children under 10 years of age. Adults bitten by rats are usually debilitated or otherwise helpless. Most bites occur on the hands and feet, but bites may also be present on the head and face of infants, sometimes with disfiguring consequences. However, rat bites also occur in personnel using these animals for research or providing for their care in pet stores and, increasingly, in household members who have pet rats. Occasionally, deaths due to rat bites have been recorded for infants or debilitated adults. One study estimated that 2% of rodent bites in humans become infected. Several bacterial pathogens have been isolated from rat bites, including Leptospira interrogans, Pasteurella multocida, and Staphylococcus spp.; however, the most commonly isolated microorganisms are Streptobacillus moniliformis and Spirillum minus.

BACTERIAL DISEASES
Rat-Bite Fever
Rat-bite fever can be caused by either of two microorganisms: S. moniliformis or S. minus. S. moniliformis
causes the diseases known as streptobacillary fever, streptobacillary rat-bite fever, and streptobacillosis. Haverhill fever and epidemic arthritic erythema are diseases associated with ingestion of water, food, or raw milk contaminated with *S. moniliformis*. Sodoku (derived from the Japanese words for rat [so] and poison [doku]), spirillosis, and spirillar rat-bite fever are caused by another bacterium, *S. minus*, which is commonly isolated from rat bites inflicted on humans residing in Asia. The bite of an infected rat is the usual source of infection. In some cases, bites of other animals, including mice, gerbils, squirrels, weasels, ferrets, dogs, and cats, or rare traumatic injuries unassociated with animal contact cause the infection. Exposure to cats and dogs that prey on wild rodents may also be the source of the organisms.

These organisms are present in the oral cavities and upper respiratory passages of asymptomatic rodents, usually rats, and exposure to rat saliva without an overt bite or scratch can transmit the organism to humans. In one study, *S. moniliformis* was isolated as the predominant microorganism from the upper tracheae of laboratory rats. Other small surveys indicate isolation of the organism in 0 of 15, 7 of 10, 2 of 20, and 7 of 14 laboratory rats and in 4 of 6 wild rats. Presumably, the incidence of *S. moniliformis* is now lower in high-quality, commercially reared, specific-pathogen-free rats used in research. Surveys of wild rats indicate 0 to 25% infection with *S. minus*. *S. minus* does not grow in *vitro* and historically has required inoculation of culture specimens into laboratory animals, with subsequent identification of the bacteria by dark-field microscopy.

*S. moniliformis* grows slowly on artificial media but only in the presence of 15% blood and sera, usually 10 to 20% rabbit or horse serum incubated at reduced partial pressures of oxygen. Sodium polyanethol sulfonate, sometimes found in blood-based media because of its properties as a bacterial growth promoter, should not be used due to its inhibitory effects on *S. moniliformis*. Growth on agar consists of 1- to 2-mm, gray, glistening colonies. The API ZYM diagnostic system can be used for rapid biochemical analysis and diagnosis. Specific PCR assays have also been used to diagnose the presence of the bacteria in both humans and rats. Fatty acid analysis can also be employed in cultured organisms.

Rat-bite fever is not a reportable disease, which makes its prevalence, geographic location, racial data, and source of infection in humans difficult to assess. The disease, though uncommon in humans, has nonetheless appeared among researchers and students working with laboratory rodents, particularly rats. Historically, wild-rat bites and subsequent illness (usually in small children) relate to poor sanitation and overcrowding.

One survey of rat bites in Baltimore, Maryland, tabulated rat-bite fever in 11 of 87 cases. The disease can also occur in individuals who have no history of rat bites but reside or work in rat-infested areas. Acute febrile diseases, especially if associated with animal bites, are routinely treated with penicillin or other antibiotics. Therefore, accurate data regarding prevalence are usually not provided.

*S. moniliformis* incubation varies from a few hours to 2 to 10 days, whereas *S. minus* incubation ranges from 1 to 6 weeks (Table 1). Fever is present in either form. Inflammation associated with the bite and lymphadenopathies are frequently accompanied by headache, general malaise, myalgia, and chills. The discrete macular rash that often appears on the extremities may generalize into pustular or petechial sequelae. Arthritis occurs in 50% of all cases of *S. moniliformis* but is less common in *S. minus*. *S. moniliformis*, which has a predilection for synovial and serosal surfaces, may be cultured from serous-to-purulent effusion recovered from affected larger joints. The organism should be considered in the list of differential diagnoses for cases of septic arthritis, particularly with synovial fluid with high inflammatory cell counts.

Rat-bite fever has a mortality rate of approximately 13% when untreated. If antibiotic treatment, usually penicillin at doses of 400,000 to 600,000 units daily for 7 days, is not instituted early, complications such as pneumonia, hepatitis, pyelonephritis, enteritis, and

<table>
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<th>Clinical feature(s)</th>
<th>Streptobacillary fever (Streptobacillus moniliformis)</th>
<th>Spirillosis (Spirillum minus)</th>
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<tr>
<td>Incubation period</td>
<td>2–10 days</td>
<td>1–6 wk</td>
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<tr>
<td>Fever</td>
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<td>Arthralgia, arthritis</td>
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<td>–</td>
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<tr>
<td>Indurated bite wound</td>
<td>–</td>
<td>+++</td>
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<tr>
<td>Recurrent fever, constitutional signs (untreated)</td>
<td>Irregular periodicity</td>
<td>Regular periodicity</td>
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Symbols: +, positive clinical sign, with increasing numbers of plus signs indicating increasing severity; –, clinical sign is not present.
endocarditis may develop. If endocarditis is present, the penicillin should be given parenterally at doses of 15 million to 20 million units daily for 4 for 6 weeks. Streptomycin and tetracyclines are also effective antibiotics for individuals with penicillin-associated allergies. Death has occurred in cases of *S. moniliformis* involving preexistent valvular disease. Recent reports of fatalities due to *S. moniliformis* in adults working in a pet store and who have rats as pets, as well as children who have pet rats, highlight the need to be vigilant in recognizing the clinical manifestations of rat-bite fever in patients with a history of rat bites or intimate exposure to rats.

**Plague**

“The houses were filled with dead bodies and the streets with funerals; neither age or sex was exempt; slaves and plebeians were suddenly taken off amidst the lamentations of their wives and children, who, while they assisted the sick and mourned the dead, were seized with disease and, perishing, were burned on the same funeral pyre. To the knights and senators, the disease was less mortal though these also suffered in the common calamity,” (Heiser V., 1936). This graphic account of the dreaded disease, the bubonic plague, was recorded in imperial Rome in the second century C.E. This pestilence occurred again and again during the ensuing centuries. By the 14th century, the disease appeared in the Far East, spread to Asia Minor, and followed the trade routes to Europe. Recent evidence supports the contention that instead of *Y. pestis* establishing reservoirs in wildlife or urban rodents in Europe, the plague organisms during the second plague pandemic were introduced by repeated climate-driven reintroductions of the bacterium into European harbors from reservoirs in Asia. Whether this perspective is true will be realized from the analysis of ancient DNA of *Y. pestis* from plague victims throughout the second plague pandemic. It did not make its arrival in the United States until 1899, when the disease appeared in California, where it still exists endemically in the ground squirrel and chipmunk.

Human infections due to *Y. pestis*, a Gram-negative coccobacillus, in the United States are sporadic and limited, usually resulting from infected-flea or rodent contact. Since 1924–1925, when a plague epidemic ravaged Los Angeles, neither urban plague nor rat-borne plague has been diagnosed in the United States. All reported cases since then have been reported in states located west of the 101st meridian. Although wild rat populations are still the primary reservoirs of the plague bacillus in many parts of the world (with transmission of *Y. pestis* to humans via fleas, particularly *X. cheopis*) and remain a continued threat in the United States, sciurid rodents (rock squirrels, California ground squirrels, chipmunks, and prairie dogs) are the primary plague bacillus reservoirs in the western part of the United States. Cricetid rodents, such as the wood rat, are occasionally cited as reservoirs. The oriental rat flea, *X. cheopis*, the common vector of the plague bacillus, is well established throughout the United States, particularly in the southern part of the country and in southern California. It is important to remember that more than 1,500 species of fleas and 230 species of rodents are infected with *Y. pestis*. Only 30 to 40 rodent species, however, are permanent reservoirs of the infection. Plague is infrequently reported in the United States, with a low incidence of 1 case in 1972 and a high incidence of 40 cases in 1983. Ninety percent of the cases have been diagnosed in New Mexico, Colorado, and California. Urban development (particularly in New Mexico) encroached into rodent habitats, where plague is enzootic, placing these populations at increased risk of contracting the disease. In addition to rodents, dogs and, increasingly, cats either have served as passive transporters of the disease or have been actively infected. The disease occurs seasonally, with the highest proportion of cases occurring between May and September (Table 2).

Transmission of *Y. pestis* via fleas to humans involves a complex interaction of the bacterium with the flea. Fleas become infected with *Y. pestis* after engorging blood from a bacteremic animal or human. Some fleas clear the bacteria even though they have ingested large numbers of yersiniae. However, *Y. pestis* usually replicates to large numbers in the midgut of the flea, which is normally sterile. Interestingly, the organisms do not invade cells or tissues of the flea, but after 72 h they aggregate into clumps in the midgut or attach to the proventriculus of the flea. The proventriculus, a valve-like chamber between the flea’s esophagus and midgut, is lined with spine-like structures, and these structures mechanically disrupt cells, allowing the blood to enter the midgut. After a week, the yersiniae grow to large numbers and block the proventriculus. Once the proventriculus is blocked, the flea cannot ingest further blood into the midgut and starves to death. In an attempt to feed more often because of the blockage, the flea ingests the host’s blood into its esophagus, where it mixes with yersiniae growing in this location and in the proventriculus. The blood now infected with *Yersinia* flows back into the wound inflicted by the flea, and the mammal becomes infected with *Y. pestis*. Experiments
have shown that only blocked fleas can transmit \( Y.\ pestis \) to susceptible hosts.

Interestingly, \( Y.\ pestis \) has evolved bacterial factors that allow it to invade the host by downregulating immune responses (e.g., the Yop and LerV effector proteins) as well as growth factors that allow \( Yersinia \) to colonize and replicate in the flea. The yersiniae require the hemin storage protein (Hms) for colonization and blockage of the proventriculus by \( Y.\ pestis \). A second virulence factor is \( Yersinia \) murine toxin (Ymt), so named because it is lethal when injected into mice. Its presence is essential to the survival of \( Y.\ pestis \) in fleas. Apparently, \textit{ymt} acts from an intracellular level in \( Y.\ pestis \) and protects the bacterium from antibacterial activity normally present in the midguts of fleas. Another gene, \textit{YfbA}, is a \( Y.\ pestis \) regulator, which is essential for both colonization and biofilm formation in the gut of cat fleas. Clearly, these examples, among many, illustrate how the organism has evolved a genetic repertoire that has allowed it to survive not only in the mammalian host but also in the flea.

Human infection is usually the result of a bite from an infected flea but can also occur via cuts or abrasions in the skin or via infected aerosols coming in contact with the oropharyngeal mucous membrane. Although today the association with plague and rats seems obvious, it was not until the bacillus \( Y.\ pestis \) was isolated and cultured that this could be definitively proven. After discovery of the infectious nature of the disease, it was soon established that epidemics among human populations closely coincided with epizootics of the disease in rats, particularly \( R.\ rattus \). It still was not apparent how the two diseases in the two hosts were linked. The hypothesis first conceived by P. L. Simond of Spain that the plague bacillus was transmitted by the rat flea, though first discounted, was proven to be correct.

Bubonic plague in humans is usually characterized by fever (2 to 7 days postexposure) and the formation of large, tender, swollen lymph nodes, or buboes. If untreated, the disease may progress to severe pneumonic or systemic plague. Inhaled infective particles, particularly from animals with plague pneumonia, may also result in the pneumonic form of the disease.

Primary pneumonic plague historically occurred by inhalation of infective droplets from a pneumonic plague patient. However, in the last several decades,
this form of the disease has occurred from exposure to infected animals (usually cats) which have developed secondary pneumonia due to septicemic spread of the organism. Owners or veterinarians attending these sick animals are then infected by inhaling aerosols containing the plague bacteria generated by the animals.

A presumptive diagnosis can be made by visualizing ovoid, Gram-negative rods exhibiting bipolar staining upon microscopic examination of fluid from buboes, blood, sputum, or spinal fluid; confirmation can be made by culture. Complement fixation, passive hemagglutination, and immunofluorescence staining of specimens can be used for serologic confirmation.

Mortality without antibiotic therapy, particularly in cases of pneumonic plague, exceeds 50% in untreated patients. Although Y. pestis is susceptible to a wide variety of antibiotics, multiple-antibiotic-resistant strains are being isolated with increasing frequency. Aminoglycosides such as streptomycin and gentamicin are the most effective antibiotics in vivo against Y. pestis. Chloramphenicol is the drug of choice for treating plague meningitis and endophthalmitis. In individuals exposed to Y. pestis, prophylactic therapy with tetracycline for a 7-day period is often prescribed.

An inactivated plague vaccine is available for laboratory personnel working with the organism and for high-risk individuals (e.g., wildlife management employees and Peace Corps volunteers) exposed to plague reservoirs in areas of endemicity. Rodent and employees and Peace Corps volunteers) exposed to plague high-risk individuals (e.g., wildlife management em-

Yersiniosis

Yersinia enterocolitica is now recognized as a cause of enteritis in humans. Cultural identification of the organism takes advantage of the fact that the bacterium replicates in culture media at refrigeration temperatures, which allows selective growth conditions to be utilized. Pigs and dogs are considered natural reservoirs for Y. enterocolitica serovar 3x biovar 4, a common cause of the disease in humans. This strain has also been isolated from R. norvegicus and R. rattus in Japan. It has been suggested that rats may play a role in the ecology of Y. enterocolitica in swine herds. Control of wild rat populations in swine herds may reduce the potential transmission of this organism via pork products. More recently, another pathogenic strain, serovar O8, was isolated from wild rodents: wood mice, geisha mice, and a vole. This strain, however, was not evident in random samples of brown or black rats taken from select locales in Japan. Both Y. enterocolitica and Yersinia pseudotuberculosis have been isolated from both Norway and black rats in the Czech Republic. Y. pseudotuberculosis has also been isolated from Norway rats in the country of Georgia, as well as Norway rats in Japan. Further epidemiological studies are needed in the United States to determine the importance of wild rats as reservoirs for Y. enterocolitica and Y. pseudotuberculosis.

Leptospirosis

Leptospirosis is a zoonotic disease of livestock, pet and stray dogs, and wildlife, including wild rats, and is considered the most common zoonoses worldwide. Rodent reservoir hosts of leptospires, besides rats, are mice, field moles, hedgehogs, gerbils, squirrels, rabbits, and hamsters. Sewer rats are noted to have a high prevalence of Leptospira spp. Human-to-human transmission is extremely rare. L. interrogans (comprising >200 serovars) has been isolated worldwide. Although particular serotypes usually have distinct host species, most serotypes can be carried by several hosts. Leptospira organisms are well adapted to a variety of mammals, particularly wild animals and rodents.

In the chronic form, the organism is carried and shed in the urine inconspicuously for long periods of time. Rodents are the only major animal species that can shed leptospires throughout their life span without clinical manifestations. Active shedding of leptospires by rodents can go unrecognized until personnel handling the animals become clinically infected or are infected by exposure to water or food contaminated by urine. L. interrogans serotype Icterohaemorrhagiae was first recovered in 1918 in the United States from wild rats sampled in New York City. This serotype, along with serotype Copenhageni, are the most common serovars infecting rats. In one recent study in Detroit, Michigan, more than 90% of adult brown Norway rats were infected with L. interrogans serotype Icterohaemorrhagiae. In an earlier study conducted in Baltimore, 45.5% of 1,643 rats were infected with Leptospira; higher prevalence rates occurred in older rats (~60%). Other studies confirm the high prevalence of this organism in wild rats inhabiting cities in the United States. Rats and mice are also common animal hosts for another serotype, L. interrogans serovar Ballum, although it has been found in other wildlife as well. Water can often be contaminated with infected-rat urine. The infection can persist unnoticed in laboratory rodents, though the carrier rates for laboratory-maintained rodents in the United States are unknown but probably low. However, there has been a report
of leptospirosis in a research colony of mice in a large research institution in the United States.

Because leptospirosis in humans is often difficult to diagnose, the low incidence of reported infection in humans may be misleading. From 1974 to 1979, only 498 cases were reported in the United States, for an incidence of 0.05 per 100,000 people per year. Outbreaks have been documented in the United States from personnel working with laboratory mice. In one study, 8 of 58 employees handling infected laboratory mice (80% of breeding females were excreting L. interrogans serovar Ballum in their urine) contracted leptospirosis. In several European laboratories, personnel have been infected with leptospires from laboratory rats. Today, however, the routine availability of specific-pathogen-free rodents mitigates the likelihood of acquiring this infection from laboratory-maintained rats and mice.

Infection with leptospires usually results from handling infected animals (contaminating the hands with urine) or from aerosol exposure during cage cleaning. Skin abrasions or exposure to mucous membranes may serve as the portal of entry. All secretions and excretions from infected animals should be considered infective. In one instance, a father apparently was infected after his daughter used his toothbrush to clean a contaminated pet mouse cage. Handling infected wild rats also increases the risk of contracting leptospirosis. A young man died of acute leptospirosis by falling into a heavily polluted river contaminated with L. interrogans serotype Icterohaemorrhagiae. Rodent bites can also transmit the disease. In Detroit, children from the inner city had a significantly higher level of L. interrogans serotype Icterohaemorrhagiae antibody than children living in the Detroit suburbs. Therefore, children living in rat-infested tenements may be at increased risk of infection.

The disease may vary from unapparent infection to severe infection and death. Infected individuals experience a biphasic disease. They become suddenly ill, with weakness, headache, myalgia, malaise, chills, and fever, and usually exhibit leukocytosis. During the second phase of the disease, conjunctival suffusion and a rash may occur. Upon examination, renal, hepatic, pulmonary, and gastrointestinal findings may be abnormal. Penicillin is the drug of choice in treating early-onset leptospirosis. Ampicillin and doxycycline also have been effective in treating people with leptospirosis. Tetracycline has been used successfully to eradicate L. interrogans serovar Ballum in a mouse colony.

Because of the variability in clinical symptoms and the lack of pathognomonic pathologic findings for humans and animals, serologic diagnosis, use of molecularly based assays, or actual isolation of leptospires is imperative. As an aid to diagnosis, leptospires can sometimes be observed by examination or direct staining of body fluids or fresh tissue suspensions. The definitive diagnosis for humans or animals is made by culturing the organisms from tissue or fluid samples or by inoculating animals (particularly 3- to 4-week-old hamsters), with subsequent culture and isolation. Culture media with long-chain fatty acids and 1% bovine serum albumin are routinely used as detoxicants. Serologic assessment is accomplished by indirect hemagglutination, agglutination analysis, complement fixation, microscopic agglutination, and fluorescent-antibody techniques. The serologic test most frequently used is the modified microtiter agglutination test. Titers of 1:100 or greater are considered significant.

**Borrelia Species**

Tick-borne relapsing fever (TBRF) is caused by at least 15 *Borrelia* spp. spirochetes and is transmitted through the painless and often unnoticed bites of *Ornithodoros* sp. ticks. Most cases are caused by *Borrelia hermsii*, which is transmitted by the tick *Ornithodoros hermsi* (Table 3). The tick usually feeds on the host at night for less than 30 min. Rodents (i.e., squirrels, deer mice, rats, chipmunks, and prairie dogs) are vertebrate reservoirs for this spirochete. Rats and other rodents are also infected with several other *Borrelia* spp., but the role for many of these *Borrelia* spp. in human disease is unknown. Rats have also been experimentally used to study the disease.

TBRF is a reportable disease in 11 western states, and approximately 25 cases are reported annually to the CDC. Symptoms occur 2 to 18 days after the bite of an infected tick and are characterized by the onset of lethargy, fever, myalgia, headache, and nausea. Typically, patients not treated with antimicrobials experience multiple episodes of similar clinical signs. Rarely, the patient presents with uveitis, myocarditis, cranial nerve palsy, or the Jarisch-Herxheimer reaction, which is attributed to decreasing bacterial numbers in the patient’s blood and a massive cytokine release and occurs during initial treatment of the spirochetal infection with an effective antibiotic. Symptoms of this reaction include hypertension, tachycardia, chills, rigors, diaphoresis, fever, and acute respiratory distress syndrome (ARDS). It is now recognized that ARDS may occur more frequently in patients with TBRF than previously recognized. In a recent review of three patients with TBRF, all three had received antibiotics prior to the onset of ARDS. It is not known whether these patients had ARDS as a result of the Jarisch-Herxheimer reaction or as a result of an underlying sepsis. As such, optimal management for
TBRF requires a prompt diagnosis and careful clinical observation during the initial treatment.

Diagnosis of the disease can presumptively be made by observations of spirochetes by dark-field microscopy or in Wright- or Giemsa-stained smears of peripheral blood collected during the febrile stage of the disease. Laboratory diagnosis is also made by culture, PCR, or serology at select reference laboratories. TBRF can be prevented by minimizing rodent infestation of homes and vacation sites (e.g., cabins), often located in coniferous forests 2,000 to 7,000 ft above sea level.

Salmonellosis
Salmonellae are Gram-negative, flagellated nonsporulating, aerobic bacilli that can readily be isolated from feces on selective media designed to suppress bacterial growth of other enteric bacteria. Salmonella serotyping requires antigenic analysis. Nontyphoidal salmonellosis is caused by any of these serotypes. Except for infection with Salmonella typhi, the causative agent of typhoid fever, salmonellosis occurs worldwide and is important for humans and animals. The genus Salmonella is comprised of motile bacteria that conform to the definition of the family Enterobacteriaceae. The nomenclature employed to describe the genus Salmonella has been confusing given the use of multiple schemes in the literature and the historical practice of considering different serotypes of Salmonella to be different species. The genus Salmonella is composed of two species, Salmonella enterica and Salmonella bongori. S. enterica has been subdivided into six subspecies. S. enterica subsp. enterica is designated subspecies I. Subspecies I strains are commonly isolated from humans and warm-blooded animals. Subspecies II, IIIa, IIIb, IV, and VI strains and

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<table>
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<tr>
<th>Species</th>
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<th>Host(s)</th>
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<td>Rodents and other vertebrates</td>
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<td>Nest-inhabiting parasites</td>
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<td>Rodents, particularly Mus musculus</td>
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<td>Dermatitis, murine typhus, rickettsialpox</td>
<td>Rodents, insectivores, straw bedding</td>
<td></td>
</tr>
<tr>
<td>Liponyssoides sanguineus</td>
<td>Dermatitis</td>
<td>Rodents, particularly Mus musculus</td>
<td></td>
</tr>
<tr>
<td>Haemogamus pontiger</td>
<td>Dermatitis</td>
<td>Birds, mammals, straw, hay</td>
<td></td>
</tr>
<tr>
<td>Haemolaelaps casalis</td>
<td>Dermatitis</td>
<td>Small mammals, straw bedding</td>
<td>F. tularensis</td>
</tr>
<tr>
<td>Eulaelaps tabularis</td>
<td>Dermatitis, tularemia</td>
<td>Wild rodents</td>
<td></td>
</tr>
<tr>
<td>Ixodids (ticks)</td>
<td>Irritation, RMSF, tularemia, tick paralysis, other diseases</td>
<td>Wild rodents, cottontail rabbits, dogs from areas of endemicity</td>
<td>Rickettsia rickettsii, F. tularensis</td>
</tr>
<tr>
<td>Dermacentor variabilis</td>
<td>Irritation, RMSF, tularemia</td>
<td>Wild rodents, dogs</td>
<td></td>
</tr>
<tr>
<td>Amblyomma americanum</td>
<td>Irritation, possible tularemia</td>
<td>Dogs, wild rodents</td>
<td></td>
</tr>
<tr>
<td>Ixodes scapularis</td>
<td>Human babesiosis, Lyme disease</td>
<td>Wild rodents, especially Peromyscus spp.</td>
<td>Borrelia burgdorferi, Babesia microti</td>
</tr>
<tr>
<td>Ixodes dammini</td>
<td>Dermatitis</td>
<td>Wild rodents</td>
<td>Borrelia spp. (frequently Borrelia hermsii)</td>
</tr>
<tr>
<td>Ornithodoros spp.</td>
<td>TBRF</td>
<td>Wild rodents</td>
<td></td>
</tr>
<tr>
<td>Fleas</td>
<td>Dermatitis, plague, murine typhus, Rodentolepis nana, Hymenolepis diminuta</td>
<td>Rat, mouse, wild rodents</td>
<td>Rodent tapeworms, Yersinia pestis, R. typhi</td>
</tr>
<tr>
<td>Xenopsylla cheopis</td>
<td>Dermatitis, plague, murine typhus</td>
<td>Rat, mouse, wild rodents</td>
<td>Rodent tapeworms, Y. pestis, R. typhi</td>
</tr>
<tr>
<td>Nasopsyllus fasciatus</td>
<td>Dermatitis, plague, R. nana, H. diminuta, murine typhus</td>
<td>Rodent tapeworms, salmonellae, R. typhi</td>
<td></td>
</tr>
<tr>
<td>Leptopsylla segnis</td>
<td>H. diminuta, R. nana, murine typhus</td>
<td>Rat</td>
<td></td>
</tr>
</tbody>
</table>

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TABLE 3 Selected ectoparasites of rodents with zoonotic potentiala

aEctoparasites found in laboratory animals that cause allergic dermatitis or from which zoonotic agents have been recovered in nature (see Yunker CE, 1964).

**Fox**
S. bongori are usually isolated from cold-blooded animals and the environment.

It is estimated that 1.4 million cases of salmonella infection occur annually in the United States, resulting in approximately 15,000 hospitalizations and 400 deaths. Although a high percentage of salmonellosis occurs via a food-borne route, it is becoming increasingly apparent that infections may be acquired through animal contact.

Rats are extremely susceptible to infection with Salmonella spp. In studies performed in the 1920s through the 1940s, the prevalence of Salmonella in wild rats surveyed in the United States varied from 1 to 18%, compared to 19% in wild rats in Europe. Rats infected with Salmonella are commonly reported in areas located around farms. In experimental studies, when rats were dosed orally with salmonellae, 10% shed the organisms in the 2 months after inoculation, and a few remained carriers when examined 5 months after experimental challenge. These rats, when placed with naïve rats, were capable of initiating new epizootics. Fortunately, the disease in laboratory rats, though common prior to 1939, has rarely been isolated in U.S. commercially reared rats since that time. However, because rats are used experimentally to study salmonella pathogenesis, personnel working with these animals must take appropriate precautions to prevent zoonotic transmission.

Salmonellae are ubiquitous in nature and are routinely found in water or food contaminated with animal or human excreta. Fecal-oral transmission is the primary mode for the spread of infection from animal to animal or to humans. Rat feces can remain infective for 148 days when maintained at room temperature. Transmission is enhanced by crowding and poor sanitation.

As with other diseases transmitted by the fecal-oral route, control depends on eliminating contact with feces, food, or water contaminated with Salmonella or animal reservoirs excreting the organism. Salmonellae survive for months in feces and are readily cultured from sediments in ponds and streams previously contaminated with sewage or animal feces. Fat and moisture in food promote the survival of Salmonella. Pasteurization of milk and proper cooking of food (56°C for 10 to 20 min) effectively destroy Salmonella spp. Municipal water supplies should be routinely monitored for coliform contamination.

An outbreak of multidrug-resistant S. enterica serotype Typhimurium associated with commercially distributed pet rodents, including rats, mice, and hamsters, was reported in 2007. Twenty-eight matching isolates identified as S. enterica serotype Typhimurium by pulsed-field gel electrophoresis were identified from humans; 13 of the patients (59%) had previous contact with rodents purchased from retail pet stores, and 2 patients (9%) had secondarily acquired the infection from a patient who had been exposed to an infected rodent. These 15 patients, whose median age was 16 years (neonate to 43 years), resided in 10 states. No single source of rodents was common among these cases, and every case household had purchased the rodents from different retail pet stores. It was ascertained that several of the rodent breeders and distributors routinely used antimicrobials (e.g., spectinomycin, leptomycin, tetracycline, and nitrofurazone) in the animals’ drinking water as a preventative measure for nonspecific rodent enteritis. Interestingly, all human, animal, and environmental samples of S. enterica serotype Typhimurium isolates tested in this outbreak were uniformly resistant to ampicillin, chloramphenicol, streptomycin, sulfisoxazole, and tetracycline (R-type ACSSuT).

Patients infected with multiple-antibiotic-resistant strains of S. enterica serotype Typhimurium have higher hospitalization rates than patients infected with susceptible strains. There are also reports of increased risk of septicemia, treatment failure, and mortality associated with multidrug-resistant S. enterica serotype Typhimurium. The spread of these multiple-antibiotic-resistant strains in rodents may have been facilitated by the widespread use of antibiotics as a prophylactic measure in the pocket pet retail industry. Indeed, treatment with oral antibiotics may eliminate normal Enterobacteriaceae enteric flora and facilitate colonization with antibiotic-resistant salmonellae, as observed with mice treated with antimicrobials. The authors of the report of this outbreak urged heightened disease surveillance in pet retail facilities, as well as increased hygiene and husbandry practices, to minimize the need for prophylactic antimicrobial therapy. Individuals purchasing rodents as pets or for food consumption by reptiles should be alerted to the possibility that these animals’ feces are potentially infectious. For example, additional outbreaks of salmonellosis were traced to households that had pet snakes. The source of human salmonella infection in these outbreaks was pet snakes, which, as part of their diet, were fed salmonella-infected frozen rats and mice that were sold commercially. The increased incidence of salmonella infections can be reduced by hand washing with soap and water after handling rodents, their cages, and their bedding.

Clinical signs of salmonellosis in humans include acute sudden gastroenteritis, abdominal pain, diarrhea, nausea, and fever. Diarrhea and anorexia may persist for several days. Although most cases are self-limiting, more severe clinical disease has been documented; 40%...
of patients were hospitalized in a recently reported outbreak. For example, a mother and infant became infected after the mother had purchased live rats and mice from a local pet store to feed her ball python. The mother was hospitalized with diarrhea, fever, and abdominal pain. She had a laparotomy and subsequently delivered a pre-term infant. Organisms invading the intestine may create septicemia without severe intestinal involvement; most clinical signs are attributed to hematogenous spread of the organisms. As with other microbial infections, the disease’s severity relates to the organism’s serotype, the number of bacteria ingested, and the host’s susceptibility. In experimental studies with volunteers, several serovars induced a spectrum of clinical disease from brief enteritis to serious debilitation. Incubation varied from 7 to 72 h. Cases of asymptomatic carriers whose infection persisted for several weeks were common.

With careful management of fluid and electrolyte balance, antimicrobial therapy is not necessary. In humans, antimicrobial therapy may prolong rather than shorten the period that Salmonella spp. are shed in the feces. In one double-blind placebo study of infants, oral antibiotics did not significantly affect the duration of salmonella carriage. Bacteriologic relapse after antibiotic treatment occurred in 53% of the patients, and 33% of these suffered a recurrence of diarrhea, whereas none of the placebo group relapsed.

**Other Possible Bacterial Infections**

Campylobacteriosis, a common diarrheal disease in humans caused by *Campylobacter jejuni* or *Campylobacter coli*, is isolated from a variety of animals, including rats. Animals can be responsible for the zoonotic spread of this organism; however, rats have not, to date, been incriminated.

Of recent interest are increasingly recognized enterohepatic *Helicobacter* spp. which cause both hepatic and intestinal disease in mice, rats, and hamsters. One of these, *Helicobacter bilis*, has been identified in Chilean patients with chronic cholecystitis and in patients with hepatocellular carcinoma and hepatobiliary carcinoma. Given that these bacteria persist in the lower bowels of rodents and are isolated in diarrheic humans, it will be interesting to note after further studies are conducted whether these new helicobacters will be linked to zoonotic transmission from wild rodents. *Helicobacter cinaedi* (previously *Campylobacter cinaedi*) was first isolated from the lower bowels of homosexuals with proctitis and colitis. It has also been isolated from the blood of homosexual patients with human immunodeficiency virus, as well as children and adult women.

In a retrospective study of 23 patients with *H. cinaedi*-associated illness, 22 of the cases had the organism isolated from blood by an automated blood culture system, with which a slightly elevated growth index was noted. This study also described a new *H. cinaedi*-associated syndrome consisting of bacteremia and fever and accompanied by leukocytosis and thrombocytopenia. Recurrent cellulitis, osteomyelitis, and/or arthritis is also noted in a high percentage of infected immunocompromised patients or hospitalized patients recovering from surgery. Although *H. cinaedi* is recovered primarily from immunocompromised individuals, the organism is also recovered from chronic alcoholics as well as immunocompetent men and women.

It should be stressed that many hospital and veterinary laboratories have difficulty isolating this organism. Because of the slow growth of *H. cinaedi*, laboratory diagnosis is unlikely if blood culture procedures that rely on visual detection of the culture media are used. Dark-field microscopy or use of acridine orange staining of blood culture media, rather than Gram staining, increases the likelihood of seeing the organism. Likewise, fecal isolation is difficult; selective antibiotic media are required, and recovery is facilitated by passing fecal homogenates through a 0.45-mm filter. Also, in a reported study, several strains of both *H. cinaedi* and *Helicobacter fennelliae* were inhibited by concentrations of cephalothin and cetzazolin, which are used frequently in selective media for isolation of enteric microaerophilic bacteria. These organisms also require an environment rich in hydrogen for optimum in vitro growth.

The fastidious microaerophile *H. cinaedi* has also been recovered from blood and fecal specimens of children and a neonate with septicemia and meningitis. The mother of the neonate had cared for pet hamsters during the first two trimesters of her pregnancy. Because *H. cinaedi* has been isolated from the normal intestinal flora of hamsters, it was suggested that the pet hamsters served as a reservoir for transmission to the mother. The mother had a diarrheal illness during the third trimester of pregnancy; the newborn was likely to have been infected during the birthing process, although this was not proven. Further studies are needed to confirm the zoonotic risk of handling *H. cinaedi*-infected hamsters. Also of interest is the isolation, based on cellular fatty acid and identification analysis, of *H. cinaedi* from the feces of dogs and a cat. It was isolated from a macaque monkey with idiopathic colitis and hepatitis as well as from asymptomatic macaques and macaques with intestinal carcinoma. Recently, *Helicobacter pullorum*, isolated from chickens and humans, was diagnosed in
mice and rats maintained in a commercial facility selling rodents to biomedical researchers. Until diagnostic laboratories embark upon routine attempts at isolating *Helicobacter* spp. from feces, the extent of the presence of these organisms in companion and pocket pets and their zoonotic potential will be unknown.

Tetracycline and various aminoglycosides appear to be effective in treating infections with *H. cinaedi*. Apparent relapses of *H. cinaedi* bacteremia in patients treated with ciprofloxacin, despite its previous use to successfully treat *H. cinaedi* infection, and the occurrence of *in vitro* resistance of *H. cinaedi* isolates to ciprofloxacin suggest that this antibiotic should be used with caution.

Beta-hemolytic group G streptococci have been isolated from rats with cervical lymphadenitis, as well as from the pharynxes of normal laboratory rats. *Streptococcus* spp. group G causes a wide variety of clinical diseases in humans, including septicemia, pharyngitis, endocarditis, pneumonia, and meningitis. Asymptomatic carriage of group G streptococci is also common in humans. At present, however, there is no documented evidence that streptococci from rats are transmitted to, or acquired by, humans. Pathogenic *Staphylococcus aureus* of the human phage type can cause clinical disease in mice and rats. This organism has been introduced into specific-pathogen-free, barrier-maintained mouse colonies and specific-pathogen-free rats and guinea pigs; the same phage type was isolated from their animal caretakers. Colonization by normal *S. aureus* strains in the nasopharyngeal area of humans presumably minimizes the zoonotic potential of animal-origin *S. aureus*.

*Clostridium difficile*, an increasingly recognized cause of enteric infections in humans, particularly antibiotic-treated hospitalized patients, forms highly resistant spores which can persist in the environment for years. Of interest, there is also an increased incidence of community-acquired *C. difficile* with no history of hospitalization or antibiotic treatment. *C. difficile* animal reservoirs have been reported, and most recently, *C. difficile* colonization was reported in wild urban Norway rats, as well as black rats trapped in Vancouver, Canada. The potential for rats to be a source of *C. difficile* infections in humans requires further study.

**VIRAL DISEASES**

**HFRS and Nephropathia Epidemica (Hantaan Virus)**

Hemorrhagic fever with renal syndrome (HFRS) and nephropathia epidemica are terms used to describe a group of rodent-borne diseases caused by several hantaviruses (family *Bunyaviridae*). Seoul virus is one of the hantaviruses that cause HFRS, and rats are the primary reservoir. This virus is shed in the urine, saliva, and feces. Unlike other hantaviruses, the Seoul hantavirus has a worldwide distribution in rats. Recently, its presence was reported in brown rats in the Netherlands. In Southeast Asia, the disease is endemic, and focal epidemics throughout the Eurasian continent and Japan have been recorded. American soldiers became infected with the disease during the Korean War. The severity of the disease depends on the particular immunotype of the virus as well as the respective natural reservoir host.

Korean hemorrhagic fever in agricultural workers occurs seasonally with bimodal peaks in the populations of the reservoir host—the striped field mouse, *Apodemus agrarius*—and its ectoparasites. HFRS is characterized by fever, headache, myalgia, and hemorrhagic manifestations that may lead to shock from massive capillary leakage of plasma protein. Although previously significant, mortality has now been reduced to 6% with hospitalization and dialysis.

Nephropathia epidemica, a less severe form, is encountered in Scandinavia, the former western Soviet Union, and several countries of Europe. The etiologic virus has been isolated and named Puuimala virus by Finnish researchers. The natural reservoir is the bank vole, *Clethrionomys glareolus*. Infected people, usually adult men with vole contact, exhibit a sudden onset of fever, abdominal or low back pain, elevated serum creatinine levels, and polyuria; fatalities are rare.

In the late 1970s, a disease resembling HFRS was reported to occur in laboratory workers in Japan, Belgium, and South Korea. Retrospective epidemiologic evaluation of the first laboratory-associated outbreak and additional urban outbreaks in Japan revealed that the reservoirs of the disease were laboratory and wild rats. Over 100 cases of HFRS in humans have been linked to exposure to laboratory rats infected with the Seoul virus. A hantavirus outbreak associated with laboratory rats was reported in China. Caesarian rederivation procedures employed for imported animals probably prevented or eliminated the spread of infection at most institutions. Pet rats can also harbor the Seoul hantavirus. People infected exhibited a range of illness, from a nonspecific influenza-like episode to acute renal insufficiency and hemorrhagic diathesis. The worldwide distribution of infected laboratory rats or their tissues has occurred. Hantavirus infection has been reported in Belgium, the United Kingdom, and France, as well as Japan. One individual had serologic evidence
of infection in the United States, and in Britain a mild clinical case was diagnosed.

Hantaan virus–related infection in wild rats, both *R. rattus* and *R. norvegicus*, raised concern regarding the potential spread of disease by international shipping. Seaports throughout the world, including many in the United States, harbor rats infected with Hantaan virus or a related virus. To date, serological evidence of disease in the United States has been noted, but no human clinical cases have been associated with this type of exposure.

The Prospect Hill virus, another hantavirus, has been isolated from meadow voles (*Microtus pennsylvanicus*) in Maryland; it has not been associated with human disease, although serologic surveys indicate inapparent infection throughout the United States, with the distribution of the virus being limited to the geographic distribution of the animal host.

**Hantavirus Pulmonary Syndrome**

In 1993, an outbreak of acute respiratory illness with significant mortality was linked to a newly recognized hantavirus. This zoonotic disease, now known as hantavirus pulmonary syndrome (HPS), was discovered in the southwestern part of the United States. This disease provided the first example of diseases now recognized as being caused by a complex of New World hantaviruses, each associated with a particular rodent species belonging to the subfamily *Sigmodontinae*, family *Muridae*. The prototype virus, *sin nombre virus*, which replicates in its natural host, the deer mouse (*Peromyscus maniculatus*), causes more than 95% of the cases of HPS in North America, which are seen primarily in the southwestern part of the United States, and most recently in Yosemite National Park.

Three other hantaviruses distinct from *sin nombre* virus are also recognized as etiological agents of HPS in North America; their rodent reservoir hosts are the white-footed mouse, *Peromyscus leucopus*, which serves as the host for New York hantavirus; the cotton rat (*Sigmodon hispidus*), the reservoir host for Black Creek Canal virus; and the rice rat, *Oryzomys palustris*, the reservoir for bayou virus. The last two viruses have been isolated in Florida, Louisiana, and eastern Texas.

Hantavirus has been isolated from the pygmy rice rat (*Oligoryzomys microtis*) in Bolivia and Argentina and has been linked to zoonotic HPS in humans residing in these countries. Serological tests to detect antibodies to hantavirus as well as confirmatory Western immunoblots are used to presumptively diagnose the disease in humans exposed to these various rodents. Reverse transcription-PCR with specific primers is used to definitively diagnose the virus in infected human or rodent biological and tissue samples.

Humans at risk are those that reside or work in areas heavily infested with reservoir hosts of hantavirus. Patients with HPS often present to emergency rooms with persistent and worsening dyspnea. Prodromal signs include fatigue and somnolence, with increasing shortness of breath and low-grade fever. Chest radiographs show interstitial and increasing bilateral interstitial alveolar infiltrates and pleural effusion. Patients often require 100% oxygen endotracheal intubation and positive and expiratory pressure support.

Elevation in creatine kinase, serum creatinine, and proteinuria can indicate renal insufficiency and myositis associated with HPS; the last two clinical manifestations are more commonly observed in cases of HPS caused by viruses of the oryzomine and sigmodon clades and much less frequently with *sin nombre* virus infection.

Hantaviruses do not cause disease in their respective rodent hosts, although virus can be detected in the salivary glands and numerous visceral organs of chronically infected animals. The virus is shed in the saliva, feces, and urine; transmission to humans is generally believed to be from aerosols generated from contaminated rodent excreta. There is also the potential that transmission can occur via ectoparasites. Detection of infected rodents or infected rodent tissue prior to entry of humans into laboratories is crucial in preventing zoonotic disease. Enzyme-linked immunosorbent assay, indirect immunofluorescence assay, and immunoblotting are available for serodiagnosis, in addition to PCR-based assays.

**Rat Hepatitis Virus**

Hepatitis E virus (HEV) has been recently recognized as a zoonotic agent, and it causes acute hepatitis in humans. The primary reservoir is the pig. A related HEV has also been isolated from rats worldwide. Antibodies to HEV have been recorded in rats, both *R. norvegicus* and *R. rattus*, throughout the United States. However, it is not known whether the rat HEV is zoonotic, given that it doesn’t infect nonhuman primates, nor does the human HEV infect rats.

**Monkeypox**

Human monkeypox caused by an orthopoxvirus was first diagnosed in the Democratic Republic of the Congo in 1970, shortly after the eradication of smallpox in the United States in 1968. It is now recognized as a zoonotic disease that occurs primarily in the rain forest located in western and central Africa.
Besides zoonotic transmission, limited person-to-person transmission can also occur, especially where monkeypox is endemic. The first documented evidence of community-acquired monkeypox occurred in the United States in 2003. The source of the two infections was identified as a common Illinois distributor where prairie dogs and Gambian rats were being housed together. The Gambian giant rats had been imported from Ghana in April 2003 by a Texas importer who subsequently sold them to the Illinois distributor. The diseased prairie dogs were then sold to pet stores in the region and were further disseminated at pet swaps. The shipment from Ghana contained approximately 800 small mammals of nine different species. The small actual source(s) could therefore have been multiple, and this highlights the serious public health hazard posed by the introduction of exotic species such as rodents from Africa. Because of this hazard and pursuant to 42 CFR 70.2 and 21 CFR 1240.30, the Communicable Disease Center and Food and Drug Administration have prohibited the transportation or importation of exotic species from Africa into the United States. Since the original outbreak in 2003 and institution of strict importation guidelines, further monkeypox cases have not been diagnosed.

Although clinically similar in some ways to smallpox, monkeypox differs from it both biologically and epidemiologically. The disease has an incubation period of 7 to 17 days. The prodrome consists of fever, backache, fatigue, and headache. In the large U.S. outbreak with 72 confirmed or suspected cases as of 30 July 2003, patients had a prodrome consisting of headaches, myalgias, chills, and drenching sweats. Over one-third of the patients had nonproductive coughs. The monkeypox rash occurring on the head, trunk, or extremities includes papules, vesicles, macules, and pustules that become encrusted over a 14- to 21-day period. The major clinical difference between monkeypox and smallpox is the pronounced lymphadenopathy noted in the majority of patients infected with monkeypox virus (Fig. 1). Mortality rates in areas of endemic monkeypox vary from 1 to 10%, with higher death rates for children. The outbreak in the United States, which occurred in Illinois, Indiana, and Wisconsin (median age of patients, 26 years [range 4 to 53 years]), affected more than 50 humans, 14 of whom required hospitalization.

Infected monkeypox patients or those suspected of having the disease should follow standard contact and airborne precautions. Appropriate diagnosis and management of exposed and ill pets should also be instituted to minimize the spread of the disease. Pet owners who suspect their animal of having a disease compatible with monkeypox should isolate the animal from humans and other animals and contact their state and local health departments. They are also advised to wear a mask and gloves when handling the animal. In most instances, it is advisable for a veterinarian to examine the suspect animal. Illnesses noted in affected rodents include fever, cough, blepharoconjunctivitis, and lymphadenopathy, followed by a nodular rash. Mortality is varied. If animals are suspected of being infected with monkeypox

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**FIGURE 1** Infected finger of a child with monkeypox (Marshfield, WI, index case). The patient was bitten by a prairie dog on 27 May 2003; the primary inoculation site was the right index finger. The photo was taken 14 days after the prairie dog bite (11 days after the onset of febrile illness [hospital day 5]). (Courtesy of Kurt Reed, Marshfield Clinic, Marshfield, WI.)

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virus, whole blood in EDTA or sera can be collected and refrigerated at 4°C before being shipped to a laboratory. If ill animals are euthanized, necropsy should be performed only in biosafety level 3 laboratories by personnel recently immunized with vaccine. Entire carcasses can be preserved for later viral isolation by freezing them at −70°C. Diagnosis of the disease in infected humans or animals is made by viral isolation from tissue culture, electron microscopy observation of the poxvirus, convalescence in infected tissues, and PCR-based assays. Sera also can be evaluated for antibodies to the virus.

Treatment of the disease is to provide supportive therapy if needed. No specific treatment has been recommended. In areas of endemicity, smallpox vaccine has been reported to reduce the risk of monkeypox among those individuals previously vaccinated. It is not known whether postexposure use of smallpox vaccine or antiviral therapy will be beneficial in treating monkeypox virus infection in humans.

**Rabies**

Rabies virus, a rhabdovirus, has been recognized as a clinical disease for centuries in both Europe and Asia. When inoculated into animals, usually via a bite, the virus produces with a high degree of probability a fatal disease in all warm-blooded species; rats should therefore be listed as a susceptible host.

Rabies occurs on all continents except Australia. Other islands, such as Hawaii, New Zealand, and Great Britain, are also fortunate in not having rabies virus in their domestic- or wild-animal population. Rabies occurs infrequently in humans, but its presence in natural reservoirs, such as wild carnivores, bats, and rarely certain rodents, such as squirrels, is endemic in certain parts of the United States as well as other parts of the world. Rabies in skunks, raccoons, and bats has increased markedly in the last several decades and historically accounts for greater than 85% of all reported cases in the United States. From 1971 through 1989, woodchucks accounted for 68% of the 200 rodent cases reported in the United States. Since 1980, wildlife has accounted for >90% of all rabid animals documented in the United States. Rodents and lagomorphs accounted for only 0.8% in 2012. From 1995 to 2010, 737 rabid rodents were reported, representing a 62.3% increase compared with the number of rabid rodents or lagomorphs reported from 1979 through 1994. The most commonly reported rodent or lagomorph continues to be groundhogs (*Marmota monax*). Infectious virus or viral RNA was detected in salivary glands or oral cavity tissues in 11 of 13 rabid rodents. Other rodents, including rats, are almost never infected with rabies virus, and no human cases of rabies of rodent origin have been reported in the last 50 years. However, in the Federal Republic of Germany, from 1961 to 1967, nine Norway rats and eight muskrats were reportedly infected with rabies virus and had supposedly bitten humans.

**Rickettsial Diseases**

**Murine Typhus (Endemic Typhus)**

Murine typhus is caused by *Rickettsia typhi*. Although this disease has been recognized for centuries, it was not until the 1920s that it was distinguished from epidemic typhus. The absence of louse infestation in humans, the seasonal occurrence of the disease, and its sporadic nature help differentiate it from louse-borne typhus (i.e., epidemic typhus). Epidemic typhus is seen only in the eastern United States in association with flying squirrels.

Murine typhus is primarily a disease of rats, with its principal vector being the oriental rat flea, *X. cheopis*, and another flea, *Nosopsyllus fasciatus*. These fleas also naturally colonize the house mouse, *Mus musculus*. The cat flea, *Ctenocephalides felis* (as well as seven other species of fleas), has also been implicated in the spread of the disease. Rickettsias are ingested in a blood meal by the flea, where they multiply in the gut and are subsequently passed out in the dejecta of the flea. Infections in rats and humans are the result of contamination of the puncture wound by flea feces. Recent experimental evidence indicates that a flea bite also can directly transmit the infection. *R. typhi* is resistant to drying and remains infectious for up to 100 days in rat feces.

Murine typhus occurs worldwide, and in the United States, it is usually diagnosed in the southeastern or Gulf states, as well as in areas along the northern portion of the Mississippi River. It also is associated with human populations subjected to areas of high-density wild-rat colonies, such as ports, granaries, farms, or rat-infested buildings in inner cities. Laboratory personnel have been infected with this agent when inoculating rodents and handling infected animals.

Since the 1970s, there has been a shift in the distribution of human cases of murine typhus to a more rural locale in southern California (Orange County) and central and southern Texas. A recent report describes the reemergence of murine typhus in patients residing in Galveston, Texas. Orange County was considered an unusual locale because it was considered a wealthy area where rat infestation was uncommon. Epidemiologic studies indicated that opossums had a high seropositivity
to murine typhus and that the cat fleas infesting the opossums were infected with either \( R. \text{typhi} \) or a newly recognized rickettsia first called the ELB agent and later named \( Rickettsia \text{felis} \). Findings extended to a survey of fleas on dogs, cats, and opossums in California, Texas, and Georgia also confirmed that fleas were infected with \( R. \text{typhi} \) or \( R. \text{felis} \), helping to explain the spread of murine typhus into rural areas in the United States. Also, human cases of typhus caused by \( R. \text{felis} \) as determined by PCR have been recorded. It has not been possible to determine the exact taxonomic specifications of \( R. \text{felis} \) because no isolates have been obtained for detailed comparative analysis.

After humans are infected with the rickettsiae, the incubation period is 7 to 14 days. Because murine typhus is difficult to diagnose either clinically or anatomically from other rickettsial diseases, specific serologic tests are extremely important in making the correct diagnosis. The acute febrile disease is usually characterized by general malaise, headache, rash, and chills, with signs ranging from mild to severe. An encephalitic syndrome can also occur. In one report, 25% of 180 patients with the disease had delirium, stupor, or coma. Fortunately, these findings resolve with lowering of the febrile response. The fatality rate for all ages is about 2% but increases with age. In a recent study of 22 patients residing in the Canary Islands, murine typhus was diagnosed based on a titer of immunoglobulin M antibody to \( R. \text{typhi} \) of 1:40 or at least a 4-fold increase in titers of immunoglobulin G against \( R. \text{typhi} \) as determined by direct immunofluorescence within 8 weeks after symptoms. These patients, in addition to having fevers of intermediate duration, had a distinct clinical presentation characterized by a higher incidence of complications, especially renal damage (including acute kidney failure and abnormal urinalysis). Interestingly, all had had contact with animals, most frequently dogs.

Recovery of rickettsial organisms or antigens from biological specimens is inconsistent and is not routinely done except in labs equipped to process and identify these samples. It must be remembered that rickettsiae are hazardous and have accounted for numerous infections of laboratory personnel. Currently, serological diagnosis is accomplished by enzyme-linked immunosorbent assay and radioimmunoprecipitation assay; however, the indirect immunofluorescence technique remains the most commonly used. Unfortunately, this test cannot distinguish epidemic from endemic typhus. The CDC considers a 4-fold rise in titer detected by any technique (except the Weil-Felix technique) as evidence of rickettsial infection. A complement fixation titer of 1:16 or greater in a single serum sample from a patient with clinically compatible signs is also considered diagnostic.

Proper antibiotic therapy is the most effective measure to prevent morbidity or mortality due to rickettsial infections. Tetracycline and chloramphenicol have proven to be effective in hastening recovery and preventing neurologic sequelae, such as deafness due to involvement of cranial nerve VIII. Doxycycline and minocycline are also effective antibiotics in treating the disease.

Fleas can be controlled by applying insecticides (organochlorines, as well as others) as residual powders or sprays in areas where rats nest or traverse. It is imperative that insecticides be applied prior to the use of rodenticides; this will prevent fleas from leaving the dead rodents and feeding on human hosts.

**Rickettsialpox**

A variety of rodents are infected with other rickettsial diseases. \( M. \text{musculus} \) is the natural host for the causative agent of rickettsialpox, \( Rickettsia \text{akari} \), a member of the spotted fever group of rickettsiae. This organism is also isolated from \( R. \text{rattus} \) and \( R. \text{norvegicus} \), and rats under certain circumstances may transmit the disease to humans. The disease is transmitted by the mite \( Liponyssoides \) (\( Allodermanyssus \) \( sanguineus \)). The disease has been diagnosed in New York City and other eastern cities, as well as Russia, Egypt, and South Africa. The incubation period is approximately 10 to 24 days, and the clinical disease is similar to murine typhus. The rash of rickettsialpox commences as a discrete maculopapular rash, which then becomes vesicular. The palms and soles are usually not involved. About 90% of affected persons develop an eschar, with a shallow ulcer covered by a brown scab (Fig. 2). Although headaches are common and may be accompanied by stiff necks, lumbar cerebrospinal fluid (CSF) samples are normal. Pulmonary and gastrointestinal involvement is almost never encountered. Diagnosis, treatment, and control are similar to those described for murine typhus and \( Y. \text{pestis} \).

**MYCOSES**

**Dermatophytes**

In almost all rat- and mouse-associated ringworm infections in humans, \( Trichophyton \text{mentagrophytes} \) has been isolated as the etiological agent. Classical murine ringworm, reportedly caused by \( Trichophyton \text{quinceanum} \), is usually restricted to feral rodents, but successful crossing of cultures of this strain with tester...
strains of perfect-state *T. mentagrophytes* (*Arthroderma benhamiae*) proves that *T. quinckeanum* is not a distinct species and is indistinguishable from *T. mentagrophytes*.

Dermatophytes are distributed worldwide, with some species reportedly being more common in certain geographic locations. From a study of 1,288 animals from 15 species of small mammals in their natural habitats, 57 *T. mentagrophytes* strains were isolated, most commonly from the bank vole (*C. glareolus*), followed by the common shrew (*Sorex araneus*) and house mouse (*M. musculus*). Agricultural workers exposed to these mammals in granaries and barns risked contracting *T. mentagrophytes* infections; indeed, 77% of 137 agricultural workers were infected with ringworm. Only 23% of the workers showed signs of infection.

In laboratory mice and rats, ringworm infection is often asymptomatic, going unrecognized until personnel become infected. In one study, for the 8-month period before dermatophyte-infected mice were treated, almost half the people handling the mice developed ringworm, although less than 1% of the mice showed any signs of disease.

Transmission occurs via direct or indirect contact with asymptomatic carrier animals, skin lesions of infected rodents, contaminated grain, or animal bedding. Causal fungi present in air, in dust, or on surfaces of animal holding rooms are also transmittal sources.

Ringworm is in many cases nonfatal, usually self-limiting, and, because it is sometimes asymptomatic, often ignored by the affected person. The dermatophytes cause scaling, erythema, and occasionally vesicles and fissures; the fungi cause thickening and discoloration of the nails. On the skin of the trunk and extremities, lesions may be circular with a central clearing. The locations of the fungus signify the clinical categories, for example, tinea capitis or tinea unguium. When humans are infected by one of the dermatophytes recovered from mice, the fungus appears on the body and/or extremities, most commonly on the arms and hands.

Zoophilic *T. mentagrophytes* produces an acute inflammatory response which often undergoes rapid resolution; the infection may produce furunculosis, widespread tinea corporis, and deep involvement of the hair follicles.

Topical fungicides or oral griseofulvin is effective in eradicating dermatophytes from animals and humans. Strict environmental and personal hygiene helps lower the incidence of ringworm. Personnel should wear rubber gloves when touching infected rodents.

**HELMINTH DISEASES**

**Roundworms**

*Angiostrongylus (parastrongylus) cantonensis*: the rat lungworm

A clinical syndrome known as eosinophilic meningitis is caused in humans who accidentally ingest raw aquatic animals, e.g., prawns (transport hosts) and snails or slugs (intermediate hosts), harboring infective larvae of the lungworm or eat larvae which have contaminated vegetables. In humans, the infective larvae migrate to the central nervous system (CNS) and may undergo 1 to 2 molts but do not develop into adult worms; thus, the human is a dead-end host. The rat serves as the reservoir host, where the adult worm develops, and passes infective eggs in its feces, which are then ingested by the intermediate host. Spread of the organism to rats has been linked to dispersal of the African land snail (*Achatina fulica*).

Historically, this disease was restricted to the Far East and the Pacific Rim, including Hawaii and Tahiti. Recently, the disease has been reported in Cuba, and the lungworm has been recovered from rats in Puerto Rico and New Orleans, Louisiana. The presence of the parasite was recently recognized in gastropods in southern Florida. It is therefore likely that the disease will be more commonly diagnosed in the Americas in the future.

Eosinophilic meningitis may often be subclinical or have an indistinct 2- to 4-month prepatent period. The distinguishing clinical feature of the disease is the presence of elevated eosinophils (>10%) of the leukocytes.

found in abnormal CSF. Other CNS signs can also be present, such as severe headache, meningeal irritation (nuchal rigidity), and increased intracranial pressure. Visual impairment may occur if there is ocular involvement. A febrile response is usually mild or absent. Only the most severe infections result in permanent impairment or in some cases death.

Occasionally (in <10% of the cases), larval or young-adult worms can be recovered from the CSF. The infection must be distinguished from other helminth CNS infections, such as paragonimiasis, fascioliasis, trichinosis, strongyloidiasis, cysticercosis, echinococcosis, and ascariasis. A microenzyme-linked immunosorbent assay for antibodies directed against the antigens of the parasite in either serum or CSF has been developed and is helpful in confirming the diagnosis.

Effective anthelmintic regimens have not been developed (although ivermectin shows promise in animal trials), and potential therapeutic intervention designed to kill the parasite may exacerbate the inflammatory response and clinical signs. Clinical treatment is usually supportive to relieve headache and nausea. In some cases, corticosteroids have been used. Thiabendazole has been used with some success during the first week of infection. Prevention of the infection is obviously preferred. This is accomplished by avoiding eating raw vegetables and underwashed or unfrozen snails and aquatic crustaceans and frogs in areas of endemicity.

Tapeworms

*Rodentolepis (hymenolepis) nana*: the dwarf tapeworm of humans

The dwarf tapeworm is a common parasite for both rats and mice. The infection in humans occurs most frequently in children who live in warm climates. Its presence in humans is noted worldwide, and it is the most frequently detected tapeworm in the United States. *R. nana* is unique among tapeworms, because it does not require an intermediate host to complete its life cycle. The adult tapeworm develops after the egg is ingested; the hooked oncosphere invades the intestinal mucosa and develops into a cysticercoid larva, and 2 weeks later, the larva matures into an adult worm. The *R. nana* eggs can contaminate hands, eating utensils, food, or aerosolized dust and then be accidentally ingested. Internal autoinfection may also occur. The tapeworm can also use fleas and beetles for the development of its life cycle; these in turn can then be ingested by humans. Personal hygiene, sanitation, and rodent control are important in preventing transmission. Humans with mild infection and in a good nutritional state usually have no symptoms, or the infection may cause diarrhea, anorexia, vomiting, pruritus of the nose and anus, or urticaria. In severe infections, signs are consistently present and include diarrhea, abdominal pain, anorexia, and CNS signs. Niclosamide for 5 to 7 days is the treatment of choice after demonstration of the characteristic eggs in the feces.

*Hymenolepis diminuta*: the rat tapeworm

This tapeworm, often described as the tapeworm of rats, is especially common in the Norway rat and the black rat; however, it is rarely diagnosed in humans, though it has been seen in patients from several parts of the United States and Europe.

The rat tapeworm requires an intermediate host for larval development. This is usually the larval stage of rat fleas, but other arthropods, such as many beetle species, earwigs, and meal moths, can serve as intermediate hosts.

Symptoms of the infection are usually not noted, and diagnosis is made by recovery of the eggs in feces. The eggs are distinguished from *R. nana* by the lack of polar filaments.

Treatment with niclosamide, similar to the regimen used to treat *R. nana*, is recommended. Control is dependent on elimination of rodents from the premises.

**ARTHROPOD INFESTATIONS**

Several arthropods found on rats, mice, and other wild rodents are vectors of human disease, and some cause allergic dermatitis as well (Table 3). Fleas are seldom found in laboratory rodents but are common parasites of feral rodents. The oriental rat flea, *X. cheopis*, and another flea, *N. fasciatus*, naturally infest both mice and rats; they are vectors for murine typhus and *Y. pestis*. That *X. cheopis* easily establishes itself in animal facilities can be demonstrated by the flea bites that two students received while working in animal rooms housing mice.

*Mites*

*Ornithonyssus bacoti*: the tropical rat mite

*O. bacoti* can be found on many rodents; the brown Norway rat and the black roof rat are probably the primary host species. Since the time of the first report of human *O. bacoti*-associated dermatitis in Australia in 1913 and a 1923 report on a human in the United States, many other cases have been described throughout the world (Table 4).

*O. bacoti* is an obligate bloodsucking parasite, usually tan but red when engorged with blood. Both the
male and female feed on a rodent as their preferred host. The female is 700 μm to 1 mm in length; the male is smaller. Eggs are laid in bedding or wall crevices by the female, which survives for about 70 days and feeds about every 2 days during this period. The mite has five developmental stages: adult, egg, nonfeeding larva, bloodsucking protonymph, and nonfeeding deutonymph. After feeding, the adults and protonymphs leave their host and seek refuge in cracks and crevices or in the bedding of pet or laboratory rodents housed in solid-bottom cages. The life cycle from adult to egg requires 7 to 16 days at room temperature. Unfed protonymphs have survived for 43 days.

The mite often gains access to the premises on wild rodents and lives in crevices. If wild rodents are not readily available or are captured, the mite will seek blood elsewhere, either from a laboratory rodent (if in an animal research facility) or from a human. In some infestations, the rodent shows no clinical signs. However, in more chronic cases, dermatitis and anemia may develop. In the past, this mite has been a troublesome parasite in certain laboratory animals, especially rats, mice, and hamsters.

Tropical rat mites produce painful, pruritic lesions on humans. Examination of patients often discloses papular lesions on the wrists, arms, abdomen, and chest.

<table>
<thead>
<tr>
<th>Host</th>
<th>Person(s) affected</th>
<th>Environment(s)</th>
<th>Lesions</th>
<th>Anatomical locations</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>200 adults and children</td>
<td>Residence, theater</td>
<td>Urticarial wheals and papules in adults; papules, urticarial wheals, and vesicles in children</td>
<td>Ankles, trunk, back, and neck in adults; beltline, upper part of shoulders in children</td>
<td>Dove and Shelmire 1931</td>
</tr>
<tr>
<td>Rat</td>
<td>4 women, 1 man</td>
<td>Department store</td>
<td>Wheals, papules, a few wheals with central puncture</td>
<td>Arms and forearms in women; hands, ankles, legs, beltline, shoulders, and neck in man</td>
<td>Weber 1940</td>
</tr>
<tr>
<td>Rat</td>
<td>Employees</td>
<td>Department store</td>
<td>Macular skin eruptions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat</td>
<td>Infants, adult occupants</td>
<td>Foundling home</td>
<td>Papular urticaria, grouping of bites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat</td>
<td>8-yr-old boy, with 5 siblings and both parents affected with milder symptoms</td>
<td>Residence</td>
<td>Excoriated urticarial papules</td>
<td>Trunk, upper parts of arms, buttocks</td>
<td>Dowlati and Maguire 1970</td>
</tr>
<tr>
<td>Norway rat</td>
<td>60-yr-old</td>
<td>Residence</td>
<td>1- to 4-mm papules, excoriated macules</td>
<td>Neck, shoulders, back, scalp, forearms, arms, abdomen</td>
<td>Hetherington et al. 1971</td>
</tr>
<tr>
<td>Rat</td>
<td>56-yr-old father and 2 sons; 73-yr-old woman</td>
<td>Residence (apartment over food store)</td>
<td>&quot;Insect bites,&quot; papular excoriated dermatitis</td>
<td>Thorax, extremities, buttocks, genitalia, entire body</td>
<td>Wainschel 1971</td>
</tr>
<tr>
<td>Rat</td>
<td>69-yr-old woman</td>
<td>Residence</td>
<td>Papules with erythema</td>
<td>Breast, shoulders, arm</td>
<td>Charlesworth and Clegern 1977</td>
</tr>
<tr>
<td>Rat</td>
<td>3 female adults, 3 children</td>
<td>Residence</td>
<td>Papular urticaria (erythematous)</td>
<td>Neck, shoulders, arms, legs, abdomen, back</td>
<td>Theis et al. 1981</td>
</tr>
<tr>
<td>Mice</td>
<td>5 research personnel, 2 animal care technicians</td>
<td>Animal research laboratory</td>
<td>Raised erythematous papules and nodules (several mm to &gt;1 cm)</td>
<td>Wrist, arm, abdomen, chest</td>
<td>Fox and Brayton 1982</td>
</tr>
<tr>
<td>Gerbils; rodents (species not specified)</td>
<td>3 children, 23-yr-old medical student</td>
<td>Residence (apartment above restaurant)</td>
<td>Erythematous rash</td>
<td>Torso, arms</td>
<td>Beck 2008</td>
</tr>
<tr>
<td>Rat</td>
<td>40 residents, 5 caretakers</td>
<td>Institution for disabled people</td>
<td>Pruritic red papules</td>
<td>Upper extremities, namely, neck, upper back, face</td>
<td>Baumstark et al. 2007</td>
</tr>
<tr>
<td>Rat</td>
<td>Male</td>
<td>Residence</td>
<td>Reddish papules, dermatitis</td>
<td>Arms, torso, back</td>
<td>Rosen et al. 2002</td>
</tr>
<tr>
<td>Rodents</td>
<td>10 medical students (9 males, 1 female)</td>
<td>Library</td>
<td>Erythematous papules</td>
<td>Neck, axilla, abdomen, both extremities</td>
<td>Chung et al. 1998</td>
</tr>
<tr>
<td>Rodents</td>
<td>6 medical students</td>
<td>Residence in centuries-old house</td>
<td>Red papules and seropapules</td>
<td>Legs, arms, waist, laterally on the trunk</td>
<td>Engle et al. 1998</td>
</tr>
<tr>
<td>Rats/mice</td>
<td>15 technicians</td>
<td>Animal facility</td>
<td>Red papules and seropapules</td>
<td>Legs, arms, waist, laterally on the trunk</td>
<td>Kelafer et al. 2005</td>
</tr>
</tbody>
</table>

TABLE 4 Reports of *Ornithonyssus bacoti*–induced dermatitis in humans in the United States from 1931 through 2008
Raised erythematous papules and nodules several millimeters to more than 1 cm in size occur singly or in a linear configuration (Fig. 3). Epidemiologically, cases usually occur in clusters that involve a common source of exposure to the mite. Experimentally, cases have been shown to be a vector of pathogens. In the laboratory, mite transmission of various rickettsial species, *Francisella tularensis*, and coxsackievirus between laboratory animals has been shown.

Treatment consists of symptomatic relief and eradication of the infestation. Treatment includes topical or systemic steroids, antihistamines, and camphor/menthol lotions. Historically, other approaches have included the use of potent acaricides such as lidane; however, this treatment is infrequently used because of potential serious adverse effects such as seizures.

**PRACTICAL TIPS**

- Owners of pet snakes who feed their animals live or frozen rodents should be aware of the risk of acquiring infections of multiple-antibiotic-resistant *Salmonella*.
- Fatalities due to infections with *S. moniliformis*, the causative agent of rat-bite fever, occur in previously healthy adults or children who acquire the infection from a bite or close contact with rats.

**FIGURE 3** Tropical rat mite dermatitis. Note the three bites, referred to as “breakfast, lunch, and dinner.” doi:10.1128/microbiolspec.IOL5-0015-2015.f3

**Diseases Transmitted by Man’s Worst Friend: the Rat**

- Acute respiratory distress syndrome is now a recognized clinical sequela to infections with *B. hermsii*, the causative agent of TBRF.
- The tropical rat mite *O. bacoti* causes dermatitis in people living in residences infested with wild rats or mice, as well as in individuals with pet rodents or laboratory personnel handling rodents infested by the parasite.
- *R. (Hymenolepis) nana* is a tapeworm with a direct life cycle; it can cause persistent diarrhea in patients with a heavy parasite burden. It is recognized as the most common tapeworm in humans residing in the United States.
- Rat lung worm, and its intermediate host, the land snail, is present in Florida, Hawaii, Louisiana, and Puerto Rico and poses a zoonotic risk from ingested contaminated vegetables.

**RECOMMENDED READINGS**


