endemic. The ongoing MoH investigation will attempt to determine whether these factors have contributed to the recent increased transmission. MoH surveillance data indicate that, on average, approximately 1,500–2,500 malaria cases are reported annually in the Dominican Republic; in 2004, a total of 2,012 cases had been reported through November.

Effective surveillance systems and rapid communication among surveillance networks are crucial to detecting cases of malaria and intervening in areas that are usually nonmalarious. During this outbreak, rapid communication among surveillance networks in North America, Europe, and the Caribbean led to prompt diagnoses and timely public health interventions to prevent additional cases among residents of and travelers to the Dominican Republic.

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Fatal Rat-Bite Fever — Florida and Washington, 2003

Rat-bite fever (RBF) is a rare, systemic illness caused by infection with *Streptobacillus moniliformis*. RBF has a case-fatality rate of 7%–10% among untreated patients (*1*). *S. moniliformis* is commonly found in the nasal and oropharyngeal flora of rats. Human infection can result from a bite or scratch from an infected or colonized rat, handling of an infected rat, or ingestion of food or water contaminated with infected rat excreta (*1*). An abrupt onset of fever, myalgias, arthralgias, vomiting, and headache typically occurs within 2–10 days of exposure and is usually followed by a maculopapular rash on the extremities (*1*). This report summarizes the clinical course and exposure history of two rapidly fatal cases of RBF identified by the CDC Unexplained Deaths and Critical Illnesses (UNEX) Project in 2003. These cases underscore the importance of 1) including RBF in the differential diagnoses of acutely ill patients with reported rat exposures and 2) preventing zoonotic infections among persons with occupational or recreational exposure to rats.

Case Reports

Florida. In early September 2003, a previously healthy woman aged 52 years visited an emergency department (ED) with a 2-day history of headache, abdominal pain, diarrhea, lethargy, right axillary lymphadenopathy, progressive myalgias, and pain in her distal extremities. On physical examination, she was afebrile and hypotensive (blood pressure: 82/40 mmHg) with left-sided abdominal tenderness and scleral icterus; no rash was noted. Laboratory tests indicated a mildly elevated white blood cell count of 13,800 cells/μL (normal: 5,000–10,000 cells/μL), thrombocytopenia (71,000 platelets/μL [normal: 130,000–500,000 platelets/μL]), elevated alanine aminotransferase of 112 U/L (normal: 20–52 U/L), elevated aspartate aminotransferase of 154 U/L (normal: <40 U/L), elevated total bilirubin of 5.8 mg/dL (normal: 0.2–1.2 mg/dL), elevated blood urea nitrogen of 55 mg/dL (normal: 7–23 mg/dL), and elevated creatinine of 2.9 mg/dL (normal: 0.7–1.5 mg/dL).

The patient was admitted to the intensive care unit, where she became increasingly hypoxic with marked anemia (hemoglobin: 8.6 g/dL [normal: 12–16 g/dL]) and increasingly severe thrombocytopenia (32,000 platelets/μL). She was treated with ciprofloxacin, metronidazole, and vancomycin for possible gram-negative sepsis and received two blood transfusions; however, she died approximately 12 hours after admission. A maculopapular rash was noted postmortem. No autopsy was performed.

Peripheral blood smears obtained before death revealed abundant neutrophils and intracellular collections of filamentous bacteria (Figure). Premortem blood from a tube containing no additives or separators was inoculated onto a blood agar plate and incubated in CO_2 at 95°F (35°C). After 72 hours, the culture demonstrated slight growth of gram-negative filamentous bacteria. UNEX was contacted for assistance, and diagnostic specimens were submitted to CDC for further laboratory evaluation. At CDC, the isolate was subcultured onto media enriched with 20% solution of sterile normal rabbit serum and incubated in a candle jar for 48 hours. Biochemical analyses identified the bacterial isolate as *S. moniliformis*. The 16S rRNA gene sequences amplified from DNA extracted from the patient's blood and the bacterial isolate were consistent with *S. moniliformis*.

The patient had been employed at a pet store. She was bitten on her right index finger by a rat in the store 2 days before symptom onset and 4 days before arriving at the ED. She self-treated the wound by using antiseptic ointment immediately after being bitten. In addition, she had regular contact with several pet rats, cats, a dog, and an iguana at her home; however, no bites from these animals were reported. None of the animals were tested for *S. moniliformis*.

trust•wor•thy: *adj*

('trəst-"wər-thē) 1 : worthy of belief

2 : capable of being depended upon;

see also *MMWR*.

know what matters.

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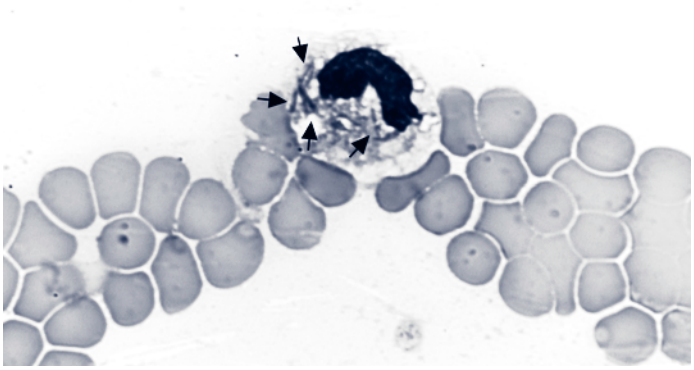
FIGURE. *Streptobacillus moniliformis* bacilli in a neutrophil (peripheral blood smear, Wright stain, original magnification: 100X)



Photo/CDC

Washington. In late November 2003, a previously healthy woman aged 19 years was pronounced dead on arrival at a hospital ED. No laboratory studies were performed in the ED. An acquaintance reported that the patient had experienced a 3-day history of fever, headache, myalgias, nausea, and profound weakness without cough, vomiting, diarrhea, or rash. Before her transport to the ED, she exhibited anxiety, confusion, and labored breathing. ED staff noted that she appeared jaundiced. The body was transported to the coroner's office, where an autopsy was performed.

Cultures of blood and tissue from autopsy were negative for pathogenic organisms. A toxicology screen was negative. Serologic assays for leptospirosis, Epstein-Barr virus, cytomegalovirus, and viral hepatitis were negative for recent infection. Histopathology revealed findings suggestive of a systemic infectious process that included disseminated intravascular coagulopathy and inflammatory cell infiltrates in the liver, heart, and lungs. UNEX was contacted for assistance, and project staff facilitated the submission of diagnostic specimens to CDC for further laboratory evaluation. Immunohistochemical assays performed at CDC for *Leptospira* spp., *Bartonella quintana*, spotted fever and typhus group rickettsiae, flaviviruses, hantaviruses, and influenza viruses were negative. Clusters of filamentous bacteria were identified in sections of the liver and kidney by using a silver stain. The 16S rRNA gene sequence amplified from DNA extracted from paraffin-embedded, formalin-fixed samples of liver and kidney was consistent with *S. moniliformis*.

The patient worked as a dog groomer and lived in an apartment with nine pet rats. One pet rat with respiratory symptoms had recently been prescribed oral doxycycline after having been evaluated at a veterinary clinic. Doxycycline was subsequently used to treat a second ill rat. None of the rats were tested for *S. moniliformis*. The patient had no known animal bites during the 2 weeks preceding her death.

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Editorial Note: Although rapidly fatal pediatric cases of RBF have been described previously (*2,3*), similar mortality among adults has not been reported. Mortality attributed to severe systemic complications (e.g., endocarditis, myocarditis, meningitis, pneumonia, or multiple organ failure) has been documented in certain adult patients (*1,4*). Both patients described in this report died within 12 hours of presentation, allowing little opportunity for assessment and treatment. These case reports demonstrate that infection with *S. moniliformis* can cause fulminant sepsis and death in previously healthy adults. As a result, prevention of severe disease might depend on increasing the awareness of appropriate risk-reduction activities and possible symptoms of RBF among persons who have exposure to rats. Intravenous penicillin is the treatment of choice, and prompt therapy can prevent severe complications (*1*). Because rapid laboratory confirmation of infection with *S. moniliformis* might not be possible, clinicians should consider initiating empiric therapy for patients with a compatible clinical presentation and exposure history.

Clinicians should consider RBF in the differential diagnosis for unexplained febrile illness or sepsis in patients reporting rat exposure. Initial symptoms might be nonspecific (Box), but a maculopapular rash and septic arthritis commonly develop (*1,5*). However, as demonstrated by the cases in this report, patients can have severe disease before the onset of typical symptoms. Despite its name, approximately 30% of patients with RBF do not report having been bitten or scratched by a rat (*1,5*). Risk factors for RBF include handling rats at home and in the workplace (e.g., laboratories or pet stores). RBF is rare in the United States, with only a few cases documented each year (*1,6,7*). However, because RBF is not a nationally notifiable disease, its actual incidence has not been well described.

In the cases described here, diagnosis of RBF was delayed in part because of the inability to rapidly isolate or identify *S. moniliformis*. If infection with *S. moniliformis* is suspected,

BOX. Epidemiology, clinical findings, diagnosis, treatment, and prevention and reporting of rat-bite fever (RBF) caused by *Streptobacillus moniliformis*

Epidemiology/Ecology
- Zoonotic disease caused by infection with *S. moniliformis*, a fastidious gram-negative bacillus.
- *Spirillum minus* also causes RBF outside the United States.
- *S. moniliformis* is part of the normal respiratory flora of rats. Other rodents might also be reservoirs.
- Transmitted to humans by contact with infected rats or by ingestion of rat excreta. Person-to-person transmission has not been reported.
- Incubation period: 2–10 days.
- Cases are rare, but disease incidence is not well characterized.
- Case-fatality rate as high as 10% in untreated patients.

Clinical Findings
- Initial symptoms are nonspecific and include fever, chills, myalgias, arthralgias, headache, and vomiting.
- Patients can have a maculopapular rash on the extremities or septic arthritis 2–4 days after fever onset.
- Severe manifestations can include endocarditis, myocarditis, meningitis, pneumonia, sepsis, and death.

Diagnosis
- Blood or synovial fluid culture, collected in tubes without sodium polyanethol sulfonate (SPS). Inoculate into media supplemented with 20% solution of sterile normal rabbit serum and incubate in humid environment with 5%–10% CO_2 at 98.6°F (37°C). Hold cultures ≥5 days.
- Pleomorphic bacilli in Gram-, Wright-, or silver-stained blood smears or tissues supports diagnosis.
- For assistance, contact a state public health laboratory or CDC Meningitis and Special Pathogens Branch, telephone 404-639-3158.

Treatment
- Intravenous penicillin, 1.2 million units/day for 5–7 days, followed by oral penicillin or ampicillin 500 mg four times a day for 7 days if improvement is observed.
- Oral tetracycline 500 mg four times a day or intramuscular streptomycin 7.5 mg/kg twice daily are alternatives.

Prevention and Reporting
- Wear protective gloves, practice regular hand washing, and avoid hand-to-mouth contact when handling rats or cleaning rat cages.
- Adults should closely supervise children aged <5 years to prevent bites and hand-to-mouth contact.
- If bitten by a rat, promptly clean and disinfect the wound.
- Efficacy of antimicrobial prophylaxis is unknown.
- Not a notifiable disease; however, unexplained deaths and critical illnesses or rare diseases of public health importance might be reportable in certain states.

specific media and incubation conditions should be used (*8*) (Box). In the absence of a positive culture, identification of pleomorphic gram-negative bacilli in appropriate specimens might support a preliminary diagnosis (*1*). In the event of an unexplained death in a person with rat exposure, performing an autopsy might also be critical to identifying an etiology.

Because of the high prevalence of colonization and asymptomatic infection with *S. moniliformis* among rodents (Box), testing and treatment of rats is not practical. Disease prevention should center on risk reduction among persons with frequent rat exposure. Adherence to simple precautions while handling rats can reduce the risk for RBF and other potential rodent-borne zoonotic infections, wound infections, and injuries. Persons should wear gloves, practice regular hand washing, and avoid hand-to-mouth contact when handling rats or cleaning rat cages (*1,9*). If bitten by a rat, persons should promptly clean and disinfect the wound, seek medical attention, and report their exposure history. A tetanus toxoid booster should be administered if ≥10 years have lapsed since the last dose (*9,10*).

Clinicians should contact their state health departments for assistance with diagnosis of unexplained deaths or critical illnesses and cases or clusters of suspected RBF or other zoonotic infections. UNEX coordinates surveillance for unexplained deaths possibly attributed to infection throughout the United States. Cases are reported by a network of health departments, medical examiners/coroners, pathologists, and clinicians. Epidemiologic and clinical data are collected, and available clinical and pathologic specimens are obtained for reference and diagnostic testing at state, CDC, and other laboratories. State and local health departments may contact UNEX for assistance with the evaluation of unexplained deaths that occur in their jurisdictions.

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Brief Report

Tularemia Associated with a Hamster Bite — Colorado, 2004

In April 2004, the Colorado Department of Public Health and Environment (CDPHE) was notified about a boy aged 3 years with diagnosed tularemia associated with a hamster bite. Tularemia has not been associated previously with pet hamsters. CDPHE conducted an investigation to determine whether other owners of hamsters were at risk. Clinicians and public health officials should be aware that pet hamsters are a potential source of tularemia.

During January 2–February 8, the boy was exposed to six hamsters that his family had purchased from a pet store in the Denver metropolitan area. Each hamster reportedly died from "wet tail disease" (i.e., diarrhea) within 1 week of purchase. One hamster bit the child on the left ring finger shortly before it died. Seven days later, the child had fever, malaise, painful left axillary lymphadenopathy, and skin sloughing at the bite site. After treatment with amoxicillin clavulanate failed, the patient underwent excisional biopsy of a left axillary lymph node 49 days after symptom onset for persistent painful lymphadenopathy and intermittent fever. Tissue culture yielded a suspected *Francisella tularensis* isolate, which was confirmed by real-time polymerase chain reaction and timed-release fluorescence at the CDPHE laboratory. Convalescent serology was positive at a titer of 4,096, and the isolate was identified by CDC as type B. No other risk factors for tularemia exposure were identified, including no other animal contact, no exposure to game meat, and no known mosquito, tick, or fly bites. The patient improved after treatment with ciprofloxacin.

Workers at the pet store reported an unusual number of deaths among hamsters but not other animals during January–February; no carcasses were available for testing. One of two cats kept as store pets had a positive serologic test for *F. tularensis* at a titer of 256. Neither cat had appeared ill to store employees.

Lists of employees, pet suppliers, and customers who purchased hamsters during December 2003–February 2004 were obtained from the store owner. Fifteen of 18 customers were located and interviewed. Eight of these had hamsters that died within 2 weeks of purchase, but all carcasses had been disposed of and were unavailable for testing. One customer and one employee who had febrile illness after being bitten by hamsters from the store were negative for *F. tularensis* by serologic testing. The same customer's hamster was available, and it was also negative for *F. tularensis* by serology and culture.

Approximately 80% of the 50 hamsters at the pet store came from customers who had pets with unanticipated litters. The other 20% were purchased from two small-pet breeders. These breeders were contacted, and neither reported an unusually high number of deaths of hamsters or other animals. One breeder also supplied animals to two pet stores in Wyoming. The Wyoming Department of Health had not been notified of any tularemia cases linked to these stores.

Confirmation of a hamster as the infectious source was limited by the delay between the patient's illness onset and diagnosis and subsequent lack of availability of implicated hamsters for testing. Nonetheless, the hamster that bit the patient was the most likely cause of infection because no other exposures or risk factors were identified. The positive serologic test for *F. tularensis* in a pet cat at the store suggested that other animals in the store might have been exposed to *F. tularensis*. In addition, the proximity of the onset of the patient's illness to the timing of the hamster bite, reports of illness among hamsters, and the deaths of hamsters at the pet store indicated an infected hamster as the likely source of illness. A possible scenario, similar to an outbreak of tularemia that involved zoo primates (*1*), is that infected wild rodents infested the store and spread the infection to hamsters by urinating and defecating through metal screens covering hamster cages. The infected cat might have had a subclinical or unrecognized illness after catching or eating an infected wild rodent.

The storeowner was advised to set traps for wild rodents and to inform the state health department of any recurrent animal deaths or reports of ill customers or staff. No other cases have been identified.

Although tularemia has been associated with hamster hunting in Russia (*2*), it has not been associated previously with pet hamsters in the United States. However, clinicians and public health officials should be aware that pet hamsters might be a potential source of tularemia. Moreover, because *F. tularensis* is a potential agent of biologic terrorism (*3*), clinicians should have a heightened awareness of tularemia.

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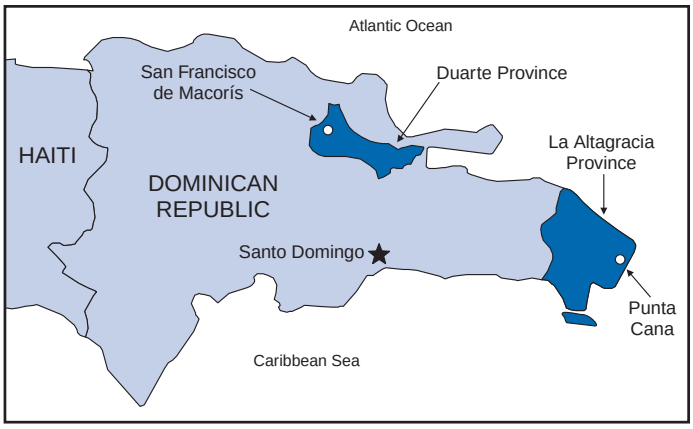
Transmission of Malaria in Resort Areas — Dominican Republic, 2004

Malaria is caused by any of four *Plasmodium* parasites carried by *Anopheles* mosquitoes and usually is transmitted by the bite of an infective female *Anopheles*. In rural areas of the Dominican Republic, *P. falciparum* malaria is endemic, with the highest risk in the far western region of the country, and prophylactic medication with chloroquine is recommended for incoming travelers. Conversely, urban and resort areas in the Dominican Republic have been considered nonmalarious, and prophylactic medication has not been recommended for persons traveling to these areas (*1*). However, since November 2004, CDC has received reports of three malaria cases in U.S. travelers returning from areas in La Altagracia and Duarte provinces (Figure) previously considered nonmalarious. An additional 14 cases of malaria in La Altagracia Province, in the far eastern region of the country, have been reported in European and Canadian travelers. This report describes three of these 17 malaria cases and summarizes the overall investigation, which led to expansion of CDC recommendations for chloroquine prophylaxis to include all of La Altagracia and Duarte provinces.

FIGURE. Provinces with resort and urban areas where malaria is not endemic but where 17 cases were reported — Dominican Republic, 2004



Case Reports

Case 1. During the third week of November 2004, a woman aged 47 years was admitted to an intensive care unit (ICU) in the United States with multisystem organ failure, including acute respiratory distress syndrome and renal failure. She had a 6-day history of fever, chills, abdominal pain, headache, nausea, and vomiting that began 24–36 hours after returning from a 1-week vacation to a resort in Punta Cana in La Altagracia Province. The patient had been examined twice by a health-care provider in an outpatient setting and sent home. Two days before hospital admission, she had jaundice. On admission, the patient had *P. falciparum* malaria on blood smear (35% parasitemia), anemia (hemoglobin: 10.4 g/dL [normal: 12–18 g/dL]), leukocytosis (white blood cell count: 35,000/μL [normal: 5,000–10,000/μL]), severe thrombocytopenia (platelet count: 5,000/μL [normal: 130,000–400,000/μL]), and was obtunded. The patient was started on intravenous

INSIDE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION