2. Raoult D, Berbis P, Roux V, Xu W, Maurin M. A new tick-transmitted disease due to *Rickettsia slovaca*. Lancet. 1997;350: 112–3.
3. Parola P, Paddock CD, Raoult D. Tick-borne rickettsioses around the world: emerging diseases challenging old concepts. Clin Microbiol Rev. 2005;18: 719–56.
4. Oteo JA, Ibarra V, Blanco JR, Martinez dA, V, Marquez FJ, Portillo A, et al. *Dermacentor*-borne necrosis erythema and lymphadenopathy: clinical and epidemiological features of a new tick-borne disease. Clin Microbiol Infect. 2004;10:327–31.
5. Fournier PE, Roux V, Caumes E, Donzel M, Raoult D. Outbreak of *Rickettsia africae* infections in participants of an adventure race from South Africa. Clin Infect Dis. 1998; 27:316–23.
6. La Scola B, Rydkina L, Ndihokubwayo JB, Vene S, Raoult D. Serological differentiation of murine typhus and epidemic typhus using cross-adsorption and western blotting. Clin Diag Lab Immunol. 2000;7:612–6.
7. La Scola B, Raoult D. Laboratory diagnosis of rickettsioses: current approaches to the diagnosis of old and new rickettsial diseases. J Clin Microbiol. 1997;35:2715–27.
8. Brouqui P, Bacellar F, Baranton G, Birtles RJ, Bjoersdorff A, Blanco JR, et al. Guidelines for the diagnosis of tick-borne bacterial diseases in Europe. Clin Microbiol Infect, 2004;10:1108–32.
9. Raoult D, Lakos A, Fenollar F, Beytout J, Brouqui P, Fournier PE. Spotless rickettsiosis caused by *Rickettsia slovaca* and associated with *Dermacentor* ticks. Clin Infect Dis. 2002;34:1331–6.
10. Lakos A. Tick-borne lymphadenopathy—a new rickettsial disease? Lancet. 1997;350:1006.

Address for correspondence: Didier Raoult, Unité des Rickettsies, Faculté de Médecine, 27, Boulevard Jean Moulin, 13385 Marseille Cedex 5, France; fax: 33-4-91-38-77-72; email: Didier.Raoult@medecine.univ-mrs.fr

Cutaneous Anthrax, Belgian Traveler

To the Editor: Anthrax is a rare zoonotic disease among travelers. The clinical spectrum includes cutaneous lesions, respiratory anthrax, pharyngeal inflammation, gastrointestinal infection, septicemia, and meningitis. Interest in anthrax increased after the bioterrorist attacks in the United States in 2001. The following case history describes a cutaneous infection suspected to be anthrax in a tourist who had indirect contact with dead mammals in a disease-endemic area.

After indirect contact with dead antelopes and a hippopotamus in Botswana, an acute necrotic lesion developed on a finger of a 31-year-old, healthy, female Belgian woman. The lesion became covered with a black crust, followed by massive swelling of the hand and arm. The clinical aspect and history strongly suggested cutaneous anthrax. This diagnosis was supported by seroconversion to protective antigen of *Bacillus anthracis* and the presence of antibodies against lethal factor. The bacterium itself could not be cultured or identified by polymerase chain reaction (PCR). Other members of the group with which she traveled were contacted, but no other cases were reported.

The Belgian woman traveled with friends to Namibia, Botswana, and South Africa from December 12, 2004, until January 22, 2005. She visited Chobe National Park in Botswana early January 2005. On January 8, a small, painless, vesicular lesion developed on the dorsal side of her fourth left finger. This lesion increased in size quickly and developed a black aspect with a red elevated border. Small vesicles appeared in the immediate vicinity of the primary lesion. No pus was noted. Her general condition was good. She treated herself with amoxicillin-clavulanic acid 2 gm/day for 3 days. The next day, massive edema of the finger, hand, and left arm developed. When admitted to a hospital in Johannesburg, her left arm and hand were massively swollen with painful left axillary lymphadenopathy. Her temperature never exceeded 37.8°C. Wound cultures showed only the presence of viridans streptococci, bacteria that are not implicated in wound infections. The patient was treated with intravenous ciprofloxacin, gentamicin, tetracycline, flucloxacillin, and topical mupirocin. She was discharged after 6 days with oral flucloxacillin and returned to Belgium on January 22. On February 4, her general condition was excellent; the edema had diminished. A painless necrotic lesion on the left fourth finger measured 3 cm^2 (Figure). She mentioned minor discomfort of her left underarm and loss of sensation at the distal radial side of the left underarm. She could not extend the terminal phalanx of the fourth left finger because the underlying tendon had been destroyed. The left axillary lymph nodes were still slightly swollen. No evidence indicated parapox viral infection or necrotic arachnidism. Upon questioning, she mentioned that in Chobe National Park, some fellow travelers had manipulated the legs of dead antelopes. One person had climbed on a dead hippo for a picture and sank into the putrefying carcass. He soon afterwards cleaned a small abrasion on the patient's finger. Some hours later, all group members washed their hands in a common small plastic basin containing water and chloroxylenol.

Full blood count, erythrocyte sedimentation rate, and biochemistry were normal. Antistreptolysin O levels were within normal limits. Serologic test results for rickettsiae, orthopoxviruses, and *Bartonella henselae* were negative. The patient was not

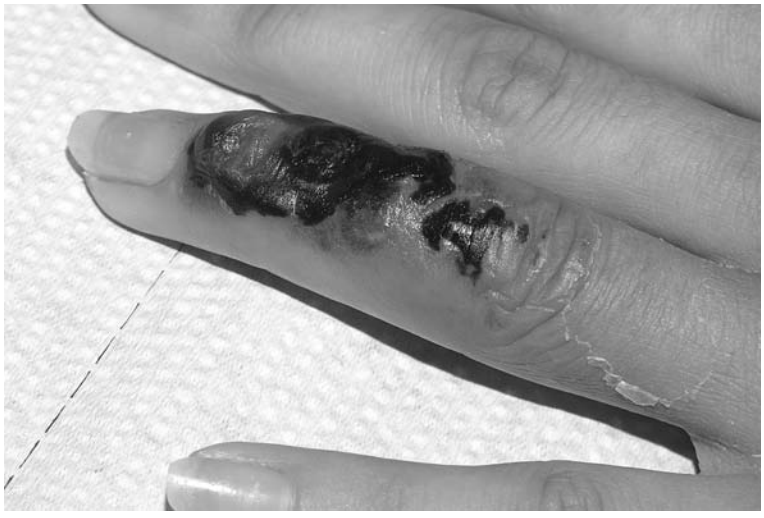

Figure. Initial skin lesion, suggestive of cutaneous anthrax. By the time the picture was taken, the massive edema of hand and arm had subsided.

immunocompromised. Because cutaneous anthrax was suspected, wound crusts, swabs for bacterial cultures, and Dacron swabs used for PCR were mailed as quickly as possible to the Belgian national reference laboratory. All cultures remained sterile. PCR was negative for *B. anthracis.* Because of the positive clinical outcome with antimicrobial drugs for 16 days, no additional antimicrobial drugs or steroids were prescribed. Further recovery was uneventful and only a small scar remains. While waiting for serologic test results, a ProMed alert was issued (*1*). Members of the travel group were contacted and warned but no other cases were identified. Consecutive serum samples were analyzed for *B. anthracis* protective antigen antibodies (anti-PA) (Centers for Disease Control and Prevention, Atlanta, GA, USA). The serum collected on February 4 was negative. On February 16, anti-PA immunoglobulin G (IgG) was detected with a titer of 9.5 (weakly positive). On April 18, no anti-PA IgG could be detected. Paired serum samples (February 4 and 16) were also mailed to the Institut für Microbiologie der Bundeswehr in Munich, Germany. In the German laboratory, the anti-PA enzyme-linked immunosorbent assay result was negative, but specific antibodies against lethal factor of *B. anthracis* were detected.

Anthrax is essentially a disease of grazing animals and is relatively common in persons who have contact with these animals (*2–4*). It is occasionally reported in travelers (*5*). In this case, many arguments existed for cutaneous anthrax, but the diagnosis could not be proven. Clinical symptoms (malignant edema) and history of indirect contact with carcasses of wildlife in a disease-endemic area suggested anthrax. Bacterial cultures remained negative, presumably because of previous administration of antimicrobial drugs. The clinical diagnosis was supported by seroconversion to protective antigen and the presence of antibodies against lethal factor. In cutaneous anthrax, antibodies to protective antigen develop in 68%–92% of cases (*6,7*). Previous cases of cutaneous anthrax in Belgium date from the 1980s, when a man became infected while unloading Indian bone meal in Antwerp Harbor. In 1986, cutaneous anthrax developed in a Turkish woman after being injured while cooking a sheep (*8*). In 2002, a suspected case in a Belgian farmer was reported (*9*). Many cases of cutaneous anthrax heal spontaneously, but a 5%–10% chance of systemic complications exists. This case illustrates 1 of the dangers of touching dead animals in nature. Travelers should be warned that even indirect contact can lead to problems.

Acknowledgments

We thank Wolf Splettstösser (anthrax serology), Arno Buckendahl (anthrax serology), Hermann Meyer (Orthopoxvirus serology), Pamela Riley (anthrax serology), Mark Van Ranst (PCR anthrax), Els Keyaerts (PCR anthrax), and Patrick Butaye (biosafety level 3 laboratory, culture, and PCR anthrax) for their assistance in preparing this article.

Erwin Van den Enden,*
Alphons Van Gompel,*
and Marjan Van Esbroeck*

*Institute of Tropical Medicine, Antwerp, Belgium

References

1. Van den Enden E, Van Gompel A. Suspected cutaneous anthrax, Belgium ex Botswana. ProMed 7 March 2005 (available from http://www.promedmail.org/pls/promed/f?p=2400:1202:2622289434529024647)
2. Irmak H, Buzgan T, Karahocagil MK, Sakarya N, Akdeniz H, Caksen H, et al. Cutaneous manifestations of anthrax in Eastern Anatolia: a review of 39 cases. Acta Med Okayama. 2003;57:235–40.
3. Maguina C, Flores Del Pozo J, Terashima A, Gotuzzo E, Guerra H, Vidal JE, et al. Cutaneous anthrax in Lima, Peru: retrospective analysis of 71 cases, including four with a meningoencephalic complication. Rev Inst Med Trop Sao Paulo. 2005;47:25–30.
4. Tutrone WD, Scheinfeld NS, Weinberg JM. Cutaneous anthrax: a concise review. Cutis. 2002;69:27–33.
5. Paulet R, Caussin C, Coudray JM, Selcer D, de Rohan Chabot P. Forme viscerale de charbon humain importée d'Afrique. Presse Med. 1994;23:477–8.
6. Swartz MN. Recognition and management of anthrax—an update. N Engl J Med. 2001;345:1621–6.
7. Quinn CP, Dull PM, Semenova V, Li H, Crotty S, Taylor TH, et al. Immune responses to *Bacillus anthracis* protective antigen in patients with bioterrorism-related cutaneous or inhalational anthrax. J Infect Dis. 2004;190:1228–36.

8. Gyssens IC, Weyns D, Kullberg BJ, Ursi JO. Een patiënte met cutane anthrax in België. Ned Tijdschr Geneesk. 2001;145:2386–8.
9. Braam RL, Braam JI. Een patiënte met cutane anthrax in België. Ned Tijdschr Geneesk. 2002;16;146:538–9.

Address for correspondence: Erwin Van den Enden, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium; fax: 32-3-247-6452; email: evdenden@itg.be

Japanese Encephalitis, Singapore

To the Editor: Japanese encephalitis (JE) is an endemic flavivirus disease in Asia. The JE virus (JEV) is one of the leading causes of viral encephalitis: 35,000–50,000 cases occur every year (*1*). While most infections are subclinical, the disease has a high case-fatality rate (≈25%) and considerable incidence of serious neurologic sequelae with the development of overt meningoencephalitis (*1*).

JEV is transmitted principally by *Culex tritaeniorhynchus* and less frequently by *Cx. vishnui* and *Cx. gelidus*, which breed in flooded rice fields. The virus circulates in waterfowl such as herons and egrets, and pigs serve as amplifying hosts. Hence, the distribution of JEV is significantly linked to irrigated rice production and pig rearing (*2*).

JEV was previously endemic in Singapore, but since the phasing out of pig farming (completed in 1992), the incidence of reported disease has become very low. Routine serologic testing for JEV has correspondingly been dropped from local hospital microbiology laboratories. We describe an indigenous case of JEV meningoencephalitis in Singapore.

In May 2005, a 53-year-old previously healthy man of Chinese ethnicity was seen at Singapore General Hospital with a 1-week history of fever and abdominal pain. Altered mental status had developed shortly after the onset of fever. He had worked in the western part of Singapore as a lifeguard at a community swimming pool and had not traveled, even to offshore islands, for the past year.

On examination, he was febrile with a temperature of 39.3°C and disoriented to time and place. Nuchal rigidity was present, and hyperreflexia was demonstrated in both upper limbs, although lower limb reflexes were normal. The rest of the initial physical examination was unremarkable.

Laboratory studies showed a leukocyte count of 4.91×10^9/L, hemoglobin concentration of 14.3 g/dL, and platelet count of 171×10^9/L. Serum and liver biochemistry results were normal. Magnetic resonance imaging of the brain showed mild leptomeningeal enhancement. An electroencephalogram showed generalized slow waves, consistent with severe diffuse encephalopathy. A lumbar puncture was performed. The opening pressure was elevated at 24 cm/H_2O; cerebrospinal fluid (CSF) leukocyte count was 192/mm^3, consisting mostly of lymphocytes; CSF glucose was 2.4 mmol/L (44% of serum glucose concentration); and CSF total protein was elevated at 1.5 g/L. CSF and blood cultures for bacteria, fungi, and mycobacteria were negative, as were CSF isolates for enteroviruses and herpes simplex virus.

Results of paired acute- and convalescent-phase serologic testing for dengue immunoglobulin M (IgM) and IgG were negative, as were the microscopic agglutination test for leptospirosis and the Widal test for typhoid. Subsequent polymerase chain reaction (PCR) testing of serum and CSF on day 10 of illness yielded negative results for Nipah/Hendra virus, West Nile virus, enterovirus, herpesviruses, measles virus, and alphaviruses.

However, the patient's serum but not CSF tested positive for flavivirus RNA when a universal flavivirus reverse transcription (RT)–PCR assay that targets the conserved sequence of the NS5 region was used (*3*). JEV was definitively identified as the etiologic agent when the serum sample tested positive with a second RT-PCR specific to the conserved sequences in the NS3 region of the JEV genome, modified to a real-time platform (*4*). Comparison of the 197-nt sequence of this JEV-specific RT-PCR product with the library of human, mouse, and viral genome databases managed by the National Center for Biotechnology Information site using the BLASTN program (available from http://www.abcc.ncifcrf.gov/app/htdocs/appdb/appinfo.php?appname) showed 93% homology with reported JEV sequences.

The patient had a prolonged and complicated hospital stay. He became comatose and went into type 2 respiratory failure within 72 hours of hospitalization; pinpoint pupils, bradycardia, and hypothermia developed. These developments necessitated mechanical ventilation at the medical intensive care unit, where the patient subsequently improved after 6 days of supportive care and was extubated. Flaccid paraparesis with urinary retention developed at this point, and magnetic resonance imaging of the spine demonstrated signal enhancement at the level of the conus medullaris. Motor power gradually improved with intensive rehabilitation and was normal by the time of the patient's discharge 2 months after admission. However, intermittent self-catheterization was still required for detrusor hyperreflexia.

This is the sixth case of JE reported in Singapore from 1991 to July 2005. Three imported cases were reported from 1991 to 2000. Two