agnosed in Uberlândia in the state of Minas Gerais in southeastern Brazil. The diagnoses were confirmed serologically by ELISA for IgM and IgG antibodies to Sin Nombre virus antigen. Because of previous reports of hantavirus interhuman transmission in Argentina and Chile [3, 4], there was some concern about this possibility among health professionals involved in the care of these patients. A serological survey was carried out in September 1998 that included workers at the 2 hospitals where the patients were admitted. Blood samples were obtained from 37 HCWs who had close contact with the patients and from 21 clerical workers; all the study participants gave informed consent.

These individuals were asked whether they had had fever, malaise, and/or respiratory symptoms since admission of the patients to the hospitals. Blood samples from the HCWs were obtained 15–24 days after the first close contact with one of the patients. The serological tests were done at the Section of Arthropod-Borne Viruses, Adolfo Lutz Institute, São Paulo State Health Secretary, São Paulo, São Paulo, Brazil. Serum samples were tested by ELISA for IgG antibody to Sin Nombre virus antigen, according to the protocol of the Centers for Disease Control and Prevention [6].

Only 2 health professionals reported having had fever and flu-like symptoms during the period between contact with 1 of the patients and collection of the blood specimen. No antibodies to Sin Nombre virus were detected in serum samples from any of the study participants. These results suggest that no interhuman transmission occurred in the hospitals where the patients with HPS were admitted for medical care. They agree with previously reported findings regarding infection with Sin Nombre virus [5]. Thus far, considering the viruses known to be associated with HPS, interhuman transmission seems to be a feature restricted to Andes virus [3, 4].

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Chronic Prosthetic Device Infection with Francisella tularensis

Infection of mechanical joints and prosthetic devices occurs at a rate of ~2% [1]. Zoonotic organisms are rarely implicated in prosthetic device infections. Brucella melitensis osteomyelitis involving an extra-articular bone implant [2] and chronic Brucella prosthetic valve endocarditis [3] have been described. Francisella tularensis is not a recognized cause of prosthetic device infection, although a single case of ventriculoperitoneal shunt infection with F. tularensis following exposure to a rabbit carcass has been reported [4]. We report a case of chronic prosthetic joint device infection caused by F. tularensis, which we believe to be the first reported case.

A 68-year-old man with degenerative joint disease secondary to rheumatoid arthritis underwent elective right-sided total knee arthroplasty (TKA) on 6 March 1997. The patient’s only medication was methotrexate (5 mg weekly). Postoperative infection with Enterococcus faecalis occurred but resolved after a prolonged course of amoxicillin.

After an asymptomatic period of 6 months, the patient presented in March 1998 with a swollen, painful, warm right knee, and there was copious serous draining from the anterior surgical scar. Subsequently, spontaneous drainage of thick yellow material was noted. No fever, systemic symptoms, lymphangitis, or lymphadenopathy was noted. The peripheral WBC count was 11,400 cells/mL with no left shift, and the erythrocyte sedimentation rate (ESR) was 47 mm/h.

The patient was receiving oral cloxacillin for infection following a right shoulder arthroplasty when the knee infection became active. The orthopedic diagnosis was an infected right infrapatellar bursa. A gallium scan showed hyperemia and gallium accumulation surrounding the right knee, consistent with soft-tissue and bursal infection, but no evidence of osteomyelitis. Repeated aspirates and wound specimens contained variable numbers of polymorphonuclear leukocytes, but cultures of these specimens were negative. Parenteral cloxacillin (2 g

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every 6 h for 10 days) was given, followed by oral cloxacillin (500 mg 4 times daily). Serous discharge continued during the antibiotic therapy.

On 22 May 1998 the patient underwent removal of the right knee prosthesis for persistent infection. During surgery, granulation tissue within the joint was noted. A joint spacer with erythromycin-containing cement was inserted. Stains and cultures of specimens obtained from the joint and surgical site during the operation were negative for bacteria, mycobacteria, and fungi.

After surgery, the patient was treated with parenteral cefazolin (2 g every 8 h for 6 weeks) and then with oral trimethoprim-sulfamethoxazole. Wound drainage and increased erythema were again noted on 15 July, and the patient was not tolerating the trimethoprim-sulfamethoxazole. Therapy with ciprofloxacin (500 mg twice a day) was initiated; 1 week later there was no improvement, and rifampin (300 mg twice a day) was added to the treatment regimen. There was a prompt, marked response to this change: the local symptoms and discharge resolved, the wound healed, and the ESR decreased from 84 mm/h to 47 mm/h.

On 20 August the spacer was removed, and a new TKA device was inserted. At surgery the patient was asymptomatic, and there was no evidence of infection in the joint. A swab of the femoral head revealed light pus and light amount of growth of *Staphylococcus epidermidis*, which was susceptible to cloxacillin and cefazolin.

After surgery, the patient received a 6-week course of parenteral cefazolin (2 g every 8 h) and oral rifampin. After 6 weeks the cefazolin was replaced with oral ciprofloxacin (500 mg twice a day); administration of rifampin was continued.

An aspirate of the knee obtained on 27 March 1998, when the infection initially recurred, contained a few polymorphonuclear leukocytes. No growth was present on MacConkey agar, but small colonies grew on a chocolate agar plate 72 h after inoculation, and gram staining revealed small gram-negative organisms. *F. tularensis* was suspected on the basis of growth, morphology, and a weak catalase test. It was susceptible to ciprofloxacin and aminoglycosides. The isolate was sent to a reference laboratory for confirmation of its identification.

Unfortunately, preliminary results were not available on the chart, and this information was not available throughout the patient’s course. On 3 November 1998, the reference laboratory reported that the small gram-negative bacillus was *F. tularensis* biovar type B (*F. tularensis* biovar *paleaeurctica*). Serology performed subsequently showed a tularemia antibody titer of 1:320. Ciprofloxacin and rifampin were administered until March 1999, at which point the patient was asymptomatic and the ESR was 23 mm/h. There has been no evidence of recurrent infection after discontinuation of antibiotic therapy.

On further review of the patient’s history after the report of isolation of *F. tularensis*, the patient recalled removing a wood tick embedded in his left shin ~6 months before the initial TKA. He did not seek medical attention. Local erythema with a central ulcer occurred at the tick site, but systemic signs or symptoms were not present. The patient recalled incurring another tick bite 13 years before the initial TKA. An erythematous mass with purulent discharge in the left popliteal fossa developed after removal of the tick. No systemic symptoms were recalled, but incision and drainage were required. The patient denied having had tick or animal exposure after the initial surgery.

It was presumed that the asymptomatic lymphohematogenous spread of *F. tularensis* was associated with 1 of the 2 previous exposures, probably the more recent, resulting in distant lymph node infection. Organisms probably remained viable within the lymph nodes. Cell-mediated immunity is important in the host immune response to tularemia, and the methotrexate treatment for rheumatoid arthritis may have promoted persistent infection.

After surgery, the right knee prosthetic device was probably seeded with *F. tularensis*, resulting in a persistent, low-grade infection, resolving only when antibiotics with bacteriocidal activity against tularemia were used. Clinically mild disease with *F. tularensis* biovar type B, which often causes subclinical disease, has been described elsewhere [5, 6]. We are uncertain whether the joint was seeded immediately after the initial surgery or whether it became infected later. The infection attributed to *E. faecalis* immediately after the surgery fully resolved with therapy with antibiotics lacking efficacy against *F. tularensis*, so it seems unlikely that *F. tularensis* contributed to this immediately postoperative infection.

There was no apparent clinical response after 7 days of ciprofloxacin, but a dramatic resolution of symptoms occurred with the addition of rifampin. Response to treatment was further demonstrated upon surgical exploration, during which no evidence of infection was observed. Although clinical experience with fluoroquinolones has been limited, they have been found to be effective against *F. tularensis* in vitro and in vivo [7]. Rifampin is noted to have a relatively low MIC against *F. tularensis*, but clinical experience is lacking.

This case, which to our knowledge is the first documented occurrence of *F. tularensis* prosthetic joint infection, reminds us that history of domestic and wild animal exposure, travel, outdoor activity, and insect exposure should be elicited in an effort to diagnose prosthetic device infection that fails to resolve after seemingly appropriate antibiotic therapy.

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References

Austrian Syndrome Caused by Highly Penicillin-Resistant *Streptococcus pneumoniae*

The finding of pneumococcal meningitis and pneumonia in an alcoholic patient requires that the diagnosis of endocarditis be excluded. This tetrad was first described by Osler but is also known as the Austrian syndrome. Nowadays, this entity is uncommon, since the incidence of *Streptococcus pneumoniae* endocarditis has significantly decreased (from 10%–15% of endocarditis cases in the preantibiotic era to 1%–3% now). Penicillin-resistant strains of *S. pneumoniae* account for 44%–58% of cases in some European countries and for 24% in the United States [1], and are a matter of concern worldwide. Herein we report what we believe is the first case of an alcoholic patient with infective endocarditis, meningitis, and pneumonia caused by *S. pneumoniae* resistant to penicillin and cefotaxime.

A 53-year-old alcoholic man with fever, headache, and impaired consciousness level was admitted to the hospital. Physical examination revealed a temperature of 39°C, confusion (Glasgow score of 9), and meningeal signs. A lumbar puncture showed the following values: glucose, 9–103 g/dL in blood; protein, 259 mg/dL; and WBCs, 1300/μL (90% neutrophils). A chest radiograph showed an upper-left-lobe infiltrate.

He was admitted to the intensive care unit, intubated, and treated with cefotaxime (3 g every 4 h), ampicillin (3.5 g every 6 h), dexamethasone (0.4 mg/kg iv every 12 h for 2 days), phenytoin, and mannitol. Cranial CT findings were within normal limits. Blood and CSF cultures were positive for *S. pneumoniae* (MICs: penicillin, 2 μg/mL; cefotaxime, 1 μg/mL; and vancomycin, <0.5 μg/mL). Intrathecal (3 doses) and iv vancomycin was added to the therapeutic regimen, and ampicillin was withdrawn. The CSF became culture-negative after 72 h of therapy.

On day 5 a systolic mitral murmur became evident. An echocardiogram disclosed a mitral vegetation and moderate valve insufficiency. The patient was still intubated in the intensive care unit and in poor condition. On day 17, his hemodynamic status deteriorated and the rupture of a tendinous cord was diagnosed. Emergency valve substitution was performed, revealing a destroyed valve and purulent pericarditis.

After surgery, multiple complications arose (multifactorial renal failure, *Pseudomonas aeruginosa* pneumonia, and *Clostridium difficile* diarrhea). He was discharged 4 months after admission in good condition. He received therapy with cefotaxime for 10 days and with vancomycin for 5 weeks.

Only 3 cases of pneumococcal endocarditis caused by a penicillin-resistant pneumococcus have been described previously [1–3] (table 1). Pneumococcal endocarditis classically affects middle-aged men with chronic underlying diseases (alcoholism in 28% of cases). Its course is usually acute and very aggressive, with a high rate of local and systemic complications. Endocarditis may become evident after apparent recovery from pneumonia or meningitis. The mortality rate ranges from 59% to 63%, and combined medical-surgical treatment seems the best option.

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<tr>
<th>Table 1. Characteristics of patients with endocarditis caused by <em>Streptococcus pneumoniae</em> that was highly resistant to penicillin.</th>
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<td>Age in y, sex [reference]</td>
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<td>2, M [3]</td>
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<td>63, F [1]</td>
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<td>53, M [PR]</td>
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NOTE. F, female; M, male; PR, present report.

* Imipenem, cefuzonam, and ampicillin were administered one after the other.