

Table. Seroconversion and respiratory symptoms due to influenza infection and vaccination status among U.K. pilgrims

Influenza vaccination in autumn 2002	Seroconversion		Respiratory symptoms	
	Yes	No	Yes	No
Vaccinated	9	21	23	7
Nonvaccinated	35	50	70	15
Total	44	71	93	22

inhibition against the following influenza antigens: A/NewCalidonia/20/99, A/Wuhan/371/91, A/Sydney/5/97, A/Panama/2007/99, B/Sichuan/379/99, and B/Harbin/7/94. A diagnosis of influenza was made based on seroconversion with at least a fourfold rise in antibody titer. Based on seroconversion, the influenza attack rate among all pilgrims was 38% (44/115). The attack rate was 30% among the vaccinated and 41% among the nonvaccinated participants (Table) (odds ratio for influenza in vaccinees = 0.61, $p = 0.28$). Of the 44 patients, 42 (37%) were infected with influenza A H3N2; 1 had influenza A H1N1, and 1 had influenza B infection. Six influenza A H3N2 patients were dually infected; two patients seroconverted to A H1N1, and four patients seroconverted to influenza B. Nearly half (21/44) of the patients with influenza received a course of antimicrobial drugs while on the hajj compared with 38% (27/71) of those who did not seroconvert. The attack rate in the vaccinated patients was lower than the rate in nonvaccinated patients, which is consistent with some protective effect of the influenza vaccine.

Even though blood was collected from five convalescing patients within 3 weeks of their return from the hajj, some of the patients may have acquired influenza B infection immediately after their return to the United Kingdom, as it was the main strain circulating in the United Kingdom in late February to March 2003. Many pilgrims from throughout the world, some of whom may carry H3N2 drift variants, mingle closely during the hajj. This type of exposure increases the risk for worldwide spread of new drift variants and other contagious

respiratory diseases (3). Given the potential for the high influenza attack rate documented in this study, all pilgrims, regardless of age, should be offered influenza vaccination before they travel on the hajj during winter months. On-site testing for influenza should be available to medical services in Makkah (and countries of origin), and treatment with a neuraminidase inhibitor should be offered to persons who test positive and have been symptomatic for <48 hours (4). This treatment should lessen the transmission risk to pilgrims during the crowded events during travel and on their return home (5). When pilgrims return from the hajj, physicians should be informed that pilgrims may bring back new drift variants of influenza; physicians should consider the diagnosis and treat persons at risk and their close contacts (4).

**Haitham El Bashir,*
Elizabeth Haworth,†
Maria Zambon,‡ Shuja Shafi,†
Jane Zuckerman,‡
and Robert Booy***

*Queen Mary's School of Medicine and Dentistry at Barts and The London, London, United Kingdom; †Health Protection Agency, London, United Kingdom; and ‡Royal Free and University College Medical School, London, United Kingdom

References

1. El Sheikh SM, El Assouli SM, Mohammed KA, Albar M. Bacteria and viruses that cause respiratory tract infections during the pilgrimage (hajj) season in Makkah, Saudi Arabia. *Trop Med Int Health*. 1998;3:205-9.
2. Qureshi H, Gessner BD, Lebouilleux D, Hasan H, Alam SE, Moulton LH. The incidence of vaccine preventable influenza-like illness and medication use among

Pakistani pilgrims to the Haj in Saudi Arabia. *Vaccine*. 2000;18:2956-62.

3. Pickles H. Screening international travelers in China for SARS. *Commun Dis Public Health*. 2003;6:216-20.
4. National Institute for Clinical Excellence. Technology Appraisal No. 58. Guidance on the use of zanamivir, oseltamivir, and amantadine for the treatment of influenza [monograph on the Internet]. London: The Institute; 2004 [cited 2004 Jan 5]. Available from http://www.nice.org.uk/pdf/58_Flu_fullguidance.pdf
5. Welliver R, Monto AS, Carewicz O, Schatteman E, Hassman M, Hedrick J, et al. The Oseltamivir Post Exposure Prophylaxis Investigator Group. Effectiveness of oseltamivir in preventing influenza in household contacts: a randomized controlled trial. *JAMA*. 2001;285:748-54.

Address for correspondence: Haitham Elbashir, Research Centre for Child Health, Luckes House, Royal London Hospital, Stepney Way, London, E1 1BB, United Kingdom; fax: 44-207-377-7709; email: h.elbashir@qmul.ac.uk

Streptomyces thermovulgaris Bacteremia in Crohn's Disease Patient

To the Editor: Invasive infections with *Streptomyces* spp. are rare; in reference to two cases reported in *Emerging Infectious Diseases* (1,2), we describe here the first documented case of bacteremia with *Streptomyces thermovulgaris*. An 81-year-old woman was admitted to the emergency room of Diakonessenhuis, Utrecht, the Netherlands, with severe abdominal pain in the right lower quadrant and feculent vomitus. The patient had a history of Crohn's disease, for which she had undergone resection of the ileum and cecum, and was receiving high-dose corticosteroid therapy (prednisone 25 mg

daily). The patient also had steroid-induced osteoporosis and an internal pacemaker. On admission, the patient had a temperature of 35.6°C, a leukocyte count of $8.4 \times 10^9/L$ with 30% bandforms, and a C-reactive protein level of 18 mg/L. Moreover, the patient had severe metabolic acidosis and was hemodynamically unstable, suggesting septic shock subsequent to a presumed bowel perforation.

Blood samples were drawn and cultured, and empiric treatment was initiated with ceftriaxone and metronidazole. Exploratory laparotomy showed colonic inflammation. The patient was transferred to the intensive care unit postoperatively. On day 9 of hospitalization, the blood culture taken on day 1 before antimicrobial drug was started, turned positive in the automatic blood culture system. Gram staining showed gram-positive nocardioform rods, and subculture on tryptic soy agar with 7% sheep blood yielded polymorphous colonies that sunk into the agar and showed filamentous growth.

Despite intensive antimicrobial and supportive therapy, sepsis progressed into multiple organ failure with severe neuropathy. On day 25 of hospitalization, the patient died. Autopsy demonstrated no possible infective focus except severe inflammation of the colon and distal ileum. Permission for cerebral section was not granted. The blood isolate showed strictly aerobic growth at 37°C and 50°C with β -hemolysis and was positive for catalase, caseinase, gelatinase, and nitrate reduction; the isolate was negative for oxidase, urease, and esculin hydrolysis and was nonmotile at 37°C. The isolate was sent to the National Institute of Public Health, Bilthoven, the Netherlands, for identification. Biochemical analysis, fatty acid analysis, and 16S rRNA typing identified the strain as *S. thermovulgaris*. The strain was susceptible to ceftriaxone (MIC 0.32 $\mu\text{g/mL}$) by

Etest (BA Biodisk, Solna, Sweden). Further susceptibility testing performed by agar diffusion showed that the organism was also susceptible to amoxicillin, vancomycin, a combination of trimethoprim and sulfamethoxazole, and erythromycin.

Bacteremia produced by a strain of *S. thermovulgaris*, as we report here, is the first documented case of isolation of this microorganism from human material. The streptomycetes are classified as a separate genus within the aerobic actinomycetes and are most well known for the many antimicrobial substances isolated from the approximately 600 different species (3). Streptomycetes, aerobic, spore-forming, gram-positive bacteria with filamentous growth, are ubiquitous in soil and can cause mycetomas (4). Streptomycetes are widely distributed in terrestrial and aquatic habitats with soil, fodder, and compost as their primary reservoirs. The amount of actinomycetes (the taxonomic group to which the streptomycetes belong) in soil is estimated to be 10^7 – 10^8 microorganisms per gram (5), and in total biomass equal to that of all other bacteria together and slightly less than that of fungi. *S. thermovulgaris* belongs to the thermophilic streptomycetes, which do not grow at temperatures $<37^\circ\text{C}$ and are believed to affect biodegradation of organic waste products at higher temperatures (6). The *S. thermovulgaris* strains in the American Type Culture Collection have been isolated from manure, manured soil, and compost.

S. anulatus, *S. somaliensis*, and *S. paraguayensis* are the species that have been implicated most frequently as causing human disease, but streptomycetes such as *S. albus* (7), *S. coelicolor*, *S. lavendulae*, *S. rimosus*, *S. bikiniensis*, and *S. violaceoruber* have also been implicated (2). Invasive infections caused by streptomycetes are very rare, and few cases of bacteremia have been reported (1,2,8).

Reported clinical isolates are often associated with decreased immunity, as in the case of *S. bikiniensis* from a patient with osteosarcoma (2), and in the case of *Streptomyces* spp. from patients with HIV (9). Our patient had severe immunosuppression as a result of intensive steroid treatment for therapy-resistant Crohn's disease. Autopsy identified no possible focus of infection other than the patient's intestines, which were severely inflamed with massive ulceration. Cultures taken at autopsy were negative.

Because of the large numbers of streptomycetes in the agricultural environment, eating contaminated food probably occurs frequently; however, in healthy people it will not lead to invasive infection. In our patient, the heavily inflamed, ulcerated gut likely enhanced the opportunity for infection from the intestines.

Because it is a soil bacterium, *Streptomyces* spp. would not likely contaminate a hospital environment. Moreover, studies have never shown *Streptomyces* spp. as contaminants (10); therefore, any clinical isolate should be considered potentially relevant. After antibiotic therapy was initiated, repeated blood cultures showed no persisting *Streptomyces* bacteremia, which can be explained by the strain's susceptibility to the antimicrobial agents that were given.

In conclusion, we have described the first documented case of *S. thermovulgaris* bacteremia. Immunocompromised patients are susceptible to colonization and infection with a broad range of both common and uncommon pathogens. Although the clinical value of positive blood cultures with less common pathogens such as streptomycetes must always be carefully weighed, they may not simply be discarded as contaminants.

The work described in this article was conducted at the Diakonessenhuis Utrecht, Utrecht, the Netherlands.

Miquel Bart Ekkelenkamp,*
Wilma de Jong,† Willem Hustinx,†
and Steven Thijsen†

*Utrecht University, Utrecht, the Netherlands; and †Diakonessenhuis, Utrecht, the Netherlands

References

- Carey J, Motyl M, Perlman DC. Catheter-related bacteremia due to *Streptomyces* in a patient receiving holistic infusions. *Emerg Infect Dis*. 2001;7:1043–5.
- Moss WJ, Sager JA, Dick JD, Ruff A. *Streptomyces bikiniensis* bacteremia. *Emerg Infect Dis*. 2003;9:273–4.
- McNeil MM, Brown JM. The medically important aerobic actinomycetes: epidemiology and microbiology. *Clin Microbiol Rev*. 1994;7:357–417.
- Dieng MT, Sy MH, Diop BM, Niang SO, Ndiaye B. Mycetoma: 130 cases. *Ann Dermatol Venerol*. 2003;130:16–9.
- Collier L, Balows A, Sussman M, editors. Topley and Wilson's microbiology and microbial infections. London: Arnold; 1998.
- Holt JG, editor. Bergey's manual of systematic bacteriology. Baltimore: Williams and Wilkins; 1989.
- Avram A. *Streptomyces albus*, the causative agent of black-grain mycetoma. *Sabouraudia*. 1970;7:241–6.
- Dunne EF, Burman WJ, Wilson ML. *Streptomyces* pneumonia in a patient with human immunodeficiency virus infection: case report and review of the literature on invasive streptomyces infections. *Clin Infect Dis*. 1998;27:93–6.
- Holtz HA, Lavery DP, Kapila R. Actinomycetales infection in the acquired immunodeficiency syndrome. *Ann Intern Med*. 1985;102:203–5.
- Weinstein MP, Murphy JR, Reller LB, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. II. Clinical observations, with special reference to factors influencing prognosis. *Rev Infect Dis*. 1983;5:54–70.

Address for correspondence: Steven F.T. Thijsen, Arts-microbioloog, Diakonessenhuis, Bosboomstraat 1, 3582 KE Utrecht, the Netherlands; fax: 31-30-2566695; email: SThijsen@diakhuis.nl

Human West Nile Virus, France

To the Editor: West Nile virus (WNV) is a mosquito-transmitted flavivirus, widely distributed in Africa, the Middle East, Asia, and southern Europe. Since the 1990s, its geographic distribution has expanded and caused epidemics of meningoencephalitis (1). Recently introduced into the United States, it expanded rapidly from New York throughout the country and caused illness in 9,862 human patients in 2003 (2). In France, the first reported WNV outbreak that affected horses and humans occurred during the summer of 1962 in the Camargue region (1). After 1965, no human or equine WNV infections were reported until September 2000, when a large outbreak of equine encephalitis occurred in France (3). No human cases were reported at that time. In September 2003, a human living in Fréjus (Département du Var, southeastern France) was diagnosed with acute WNV infection in Nice University Hospital. At the same time, an equine case was diagnosed 20 km from the patient's home; consequently, public health authorities initiated a retrospective study of patients hospitalized in the French Mediterranean region in which viral meningoencephalitis was suspected. We report four human cases from Fréjus Hospital.

Twenty patients who had been hospitalized at some time from August 1 to October 15, 2003, for febrile meningitis, encephalitis, or polyradiculoneuritis were screened. Four patients in whom cerebrospinal fluid (CSF) analysis indicated a viral cause were included. In addition, serum samples from two patients who had experienced flulike symptoms with exanthema during the same period were tested further. Serologic diagnosis of acute WNV infection was based on immunoglobulin (Ig) M-capture and direct IgG enzyme-linked

immunosorbent assay followed by 80% plaque reduction neutralization titer (PRNT₈₀) by using the France 2000 WNV strain (3).

Patient 1, 46 years old, and patient 2, 25 years old, had a flulike syndrome with maculopapular exanthema; WNV seroconversion was seen on a pair of sera collected on days 3 and 16 for patient 1, and days 3 and 12 for patient 2, after onset of fever. Patients 3 and 4 had meningoencephalitis with maculopapular exanthema. In patient 3, a fourfold increase in WNV neutralizing antibodies was seen in serum samples on 2 consecutive days (days 3 and 15 after onset of fever). In patient 4, WNV IgM antibodies were detected in CSF (day 4 after onset of fever), and neutralizing antibodies (titer = 160) were reported in a serum specimen on day 75. Attempts to detect WNV RNA by reverse transcription–polymerase chain reaction, or to isolate the virus from serum specimens in patients 1 and 2 and CSF in patient 4, were negative because of the low level and short duration of WNV viremia (4). All patients recovered.

On the basis of serologic results, we describe the first human clinical WNV infections in France since 1964 (5). The four patients lived in the same city, had not traveled, and had an onset of their illness during the last week of August 2003. Of note, four clinical infections were identified, but many more WNV subclinical and asymptomatic infections likely occurred simultaneously.

After the reemergence of WNV in horses in the Camargue region in 2000, surveillance on sentinel birds (ducks and chickens) showed a low circulation of WNV in 2001 and 2002 in this area. Meanwhile, no clinical human or equine cases were detected. During the summer of 2003, WNV reemerged in humans 200 km east of Camargue, in the Département du Var, along the Mediterranean coast. A