

these were not taken into account in the search conducted by Vonberg and Gastmeier. Third and finally, an editorial written by Trépanier and Lessard<sup>5</sup> in 2003 interestingly affirmed that 5 deaths caused by contaminated propofol were reported during this time period (>4, as asserted by Vonberg and Gastmeier<sup>1</sup> and by Mattner and Gastmeier<sup>4</sup>).<sup>6</sup> Table 1 of this letter presents the appropriate distribution of the outbreaks caused by contaminated propofol reported between 1990 and 2005.

In summary, limitations of the inclusion criteria were likely caused by natural methodological issues concerning the bibliographic source used by Vonberg by Gastmeier. Given the restrictions and gaps in the results of their review, we suggest a traditional systematic search of major bibliographic databases (eg, PubMed/Medline, EMBASE, Lilacs, and others).<sup>6</sup> With a more robust data search, a more complete review could be conducted. Actually, the contamination of propofol is a worldwide problem that has been a focus of manufacturers, who have made pharmacological reforms such as addition of preservatives and/or modification of physical properties (ie, lipophilic solubility). The issue of determining the overall mortality related to the contamination of medical drugs is important, but the results of this particular review need to be discussed in depth to avoid the reporting of false rates.

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## Potential Risk of Aerosol-Borne *Francisella tularensis* Transmission in the Operating Room

*To the Editor*—Tularemia, a potentially life-threatening zoonosis, is caused by the Gram-negative bacterium *Francisella tularensis* that occurs naturally in the Northern Hemisphere.<sup>1</sup> At least 6 distinct clinical syndromes have been described, and ulceroglandular tularemia is the most frequent disease manifestation in North America and Central Europe.<sup>2</sup> Recently, outbreaks in the United States, Turkey, and some European countries have led to the recognition of tularemia as an emerging infectious disease.<sup>3</sup> *F. tularensis* is a highly infectious agent; a quantity of just 10–25 bacteria can infect a human and cause severe clinical disease. Hence, *F. tularensis* is considered a ‘category A’ bioterrorism agent. Transmission may occur through inhalation of infectious aerosols, direct contact with infected animals (eg, rodents), arthropod bites, or oral ingestion of contaminated tissues or water.<sup>1</sup> Similar to other bacterial zoonotic pathogens like *Bacillus anthracis* and *Brucella melitensis*, the causative agents of anthrax and brucellosis, respectively, person-to-person transmission of tularemia does generally not occur and infected patients do not need to be isolated. However, biological specimens from patients with tularemia may constitute a significant threat to healthcare workers. Indeed, *F. tularensis* ranks among the 5 most frequently reported laboratory-acquired infections, and inhalation of infectious aerosols is considered a major transmission route in these cases.<sup>4</sup> After a recent case of ulceroglandular tularemia at our hospital, we investigated the possibility of tularemia as an airborne healthcare-associated infection in the operating room.

A 48-year-old male patient presented with painless cervical swelling on the right side accompanied by occasional fever and night sweats during the preceding 2 months. The patient worked as a falconer and reported having frequent contact with raptors and other wild animals. On clinical examination, cervical lymphadenopathy was noted. Ultrasound examination and subsequent magnetic resonance imaging (MRI) showed multiple enlarged, partially necrotic lymph nodes. Infectious and neoplastic etiologies were considered, and 1 enlarged lymph node was surgically removed. Histopathology showed a

phlegmonous and abscess-forming inflammation with no signs of malignancy. Culture and polymerase chain reaction (PCR) assays for bacteria, mycobacteria, and fungi were negative. The patient's symptoms worsened despite antibiotic treatment with cefuroxime. A second surgical lymph node excision was performed 4 weeks later, showing a necrotizing granulomatous inflammation with epithelioid cell granulomas. Bacterial cultures were negative, but PCR revealed *F. tularensis* as the causative agent. The serology report revealed a markedly increased titer of *F. tularensis*-specific IgM, thus confirming the diagnosis. Antibiotic treatment with doxycycline (200 mg/day for 3 weeks) was started and led to a rapid decrease of lymphadenitis and resolution of all clinical symptoms. After the diagnosis had been established, one of the surgeons reported to the infection prevention team that he had had painful, unilateral tonsillitis some days after the first surgery. Concerns arose regarding whether the anesthesiologist, the surgeons, and the nurses involved in the 2 surgical procedures might have been at risk of acquiring tularemia through infectious aerosols. Overall, 5 healthcare workers who had close contact with the infected tissue specimens were serologically screened for tularemia 21 days after exposure, but all tested negative.

The tularemia guidelines issued by the World Health Organization (WHO) recommend monitoring the body temperature of an incidentally exposed individual for 14 days after the event and initiating post-exposure prophylaxis with ciprofloxacin or doxycycline in case of fever or any arising clinical symptoms.<sup>5</sup> In the case presented here, however, none of the exposed individuals reported an acute feverish illness, and all tested negative on serology 3 weeks after exposure, thus excluding tularemia.<sup>6</sup> To minimize the risk of healthcare-associated infections, WHO recommends that clinicians report any suspicion of tularemia to the diagnostic laboratory. However, even in endemic areas, tularemia is rarely taken into account by clinicians, resulting in a low notification rate to the laboratory. Human infections with *F. tularensis* had never before been reported from the federal state of Germany where the patient lives (Saarland); thus, tularemia was not initially considered in the differential diagnosis.

Human-to-human transmission of tularemia has never been unambiguously documented, but a literature review concluded that aerosolized *F. tularensis* bacteria remain viable for prolonged time periods and may be inhaled by others.<sup>7</sup> Various factors need to be taken into consideration to predict the risk of infection via aerosols, ie, the actual number of viable bacterial cells within a handled specimen, the size of droplets arising from the aerosol, and the intensity of an individual's exposure.<sup>8</sup> While tularemia is commonly acquired via inhalation by hunters when handling infected animals, it remains to be elucidated whether this transmission route may also occur during exposure to infected human specimens. The pathogen load in human lymph nodes is probably much lower than in organs from infected rodents, and *F. tularensis* is mainly located inside macrophages, which might decrease the

potential infectivity of human specimens. Yet, given the very low infectious dose of *F. tularensis*, it may be speculated that aerosols generated during surgical procedures on bacteria-containing specimens in the operating room constitute a significant risk of infection for the medical staff who are directly involved. For brucellosis, this exceptional route of transmission has recently been confirmed.<sup>9</sup>

We conclude that there is a need for an increased awareness of the various transmission routes of *F. tularensis* and the potentially arising implications for infection control and prevention in hospital settings. Further research is warranted to accurately assess the significance of aerosols as vectors of infectious diseases in the operating room.

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## Port-Related Nontyphoidal *Salmonella* Bacteremia

To the Editor—*Salmonella* species, a genus of the family Enterobacteriaceae, includes *Salmonella enterica* serovar Typhi and nontyphoidal *Salmonella* (NTS) spp.<sup>1,2</sup> Human infections caused by NTS are often associated with contaminated food products and always develop in an immunocompromised host.<sup>3</sup> The clinical presentations of NTS infection include gastroenteritis, primary bacteremia, mycotic aneurysm, infective endocarditis, urinary tract infection, meningitis, empyema thoracis, and osteomyelitis.<sup>3–7</sup> We performed a study to identify cases of unusual presentation of NTS infection related to subcutaneously implanted port reservoir and to further investigate their associated clinical and microbiological characteristics.

This study was conducted at 1 institution, a 900-bed hospital in southern Taiwan. From the computerized database of the bacteriology laboratory, we identified patients whose cultures

yielded NTS. The medical records of all patients with port-related infection caused by NTS included in this study were retrospectively reviewed.

The diagnosis of port-related NTS bacteremia was defined as a primary laboratory-confirmed NTS bacteremia in a patient with a port at the time of (or within 48 hours prior to) the onset of symptoms in whom the infection was not related to another site. Standard definitions for healthcare-associated bacteremia (HAIs) were used.<sup>8</sup> Inappropriate use of antibiotics was defined as use of antimicrobial agents to which the clinical isolates were resistant *in vitro*.

During the study period, 4 patients were identified to have port-related NTS bacteremia: 3 infections were caused by group D *Salmonella*, and 1 was caused by group C *Salmonella*. All of the clinical isolates were susceptible to ampicillin, ceftazidime, ceftriaxone, ciprofloxacin, trimethoprim-sulfamethoxazole, and chloramphenicol. The clinical characteristics of 4 patients with port-related NTS bacteremia are summarized in Table 1. Of these 4 patients, 3 were men, and the age range of this cohort was 44–80 years. All of these patients had various cancers, and 1 patient had received chemotherapy prior to NTS infection. All of these patients had initial presentations of fever; however, none had signs or symptoms of enteritis. In addition, 1 patient had diabetes mellitus. Of these 4 patients, 3 had white blood cell counts >11,000/mm<sup>3</sup>, and none had neutropenia. In addition, 3 patients had hemoglobin <10 g/dl, and 2 patients had elevated C-reactive protein levels. None of these patients had their port removed. Although all 4 patients received appropriate antibiotics initially, 1 patient died due to NTS sepsis.

This study describes a rare cluster of NTS bacteremia in hospitalized cancer patients with ports at a single center. The immunocompromised conditions among these patients should be included as major risk factors for NTS bacteremia. Moreover, all of cases in this survey were classified as healthcare-associated, catheter-related bloodstream infections. Although rare, NTS should be considered as a possible pathogen causing intravascular catheter-related bacteremia in cancer patients in healthcare settings.

The clinical outcomes of patients with catheter-associated NTS bacteremia have not been well defined because of the

TABLE 1. Clinical Manifestations of 4 Patients with Nontyphoidal *Salmonella* Port-Related Infections

Case (year)	Age, y	Sex	Underlying disease	Healthcare-Associated Infection	Serogroup	Neutropenia	Removal of Catheter	Antibiotic	Mortality
1 (2008)	62	M	Lung cancer undergoing chemotherapy, hypertension	Yes	D	No	No	Ceftazidime	No
2 (2010)	53	M	Esophageal cancer, chronic hepatitis B	Yes	D	No	No	Ceftazidime	No
3 (2010)	44	M	Oral cancer	Yes	D	No	No	Ceftazidime	Yes
4 (2011)	80	F	Rectal cancer, ovarian cancer, diabetes mellitus, hypertension	Yes	C	No	No	Ciprofloxacin	No