

described for each of these drugs, but only 1 case of *Rhodococcus* infection has been reported for a patient receiving methotrexate and none have been described for patients receiving rituximab (10).

Because of difficulties in species identification and delays in growth, non-*R. equi* infections might be underdiagnosed (9). This finding is complicated by the fact that these gram-positive bacilli may be misidentified as contaminating diphtheroids (9). It is unlikely that this organism was a contaminant, given that the fever in the patient relapsed after antimicrobial drugs were discontinued and no other cause was identified. The isolate from the patient was identified by sequencing the first ≈500 bp of the 16S rRNA gene, which is a useful molecular technique for speciation of the genus *Rhodococcus* (9). The isolate showed 99.8% identity with *R. erythropolis* type strain DSM 43066.

Antimicrobial drug susceptibility patterns in non-*R. equi* rhodococci have not been studied, and there are no established standards for treating patients with *Rhodococcus* spp. infections. This case, along with previously reported cases, represents emergence of an opportunistic pathogen in a rapidly increasing patient population, namely those with impaired local or systemic immunity.

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Factors Influencing Emergence of Tularemia, Hungary, 1984–2010

To the Editor: *Francisella tularensis*, the etiologic agent of tularemia, is a highly infectious zoonotic agent. *F. tularensis* subsp. *holarctica* (type B) is found throughout the Northern Hemisphere and is the only subspecies found in Europe (1). Lagomorphs and rodents probably serve as the primary mammalian reservoir hosts, and hematophagous arthropods, such as ticks, play a role as vectors and hosts (2,3). Although *F. tularensis* is a potential agent of biological warfare and several emergences and reemergences of tularemia have been reported around the world (1,4), the epizootiology of the disease is only partially understood. The aim of our study was to analyze factors that influence the emergence of tularemia in Hungary.

The study area (15,475 km²) included 3 counties in eastern Hungary. The analyzed data represented a period of 25 years, March 1984–February 2010. Annual *F. tularensis*-specific seroprevalence data for the European brown hare (*Lepus europaeus*) population were obtained by slide agglutination testing during the winter (December and January) screening of 2,500–25,000 animals (online Technical Appendix, wwwnc.cdc.gov/EID/article/18/8/11-1826-Techapp.xls). Population density data (animals/km²) for hares were based on February line transect counts and were obtained from the Hungarian Game Management database (www.vvt.gau.hu/vadgazdalkodasi_statistikak.htm). Common vole (*Microtus arvalis*) densities (calculated from the number of active burrows/hectare during November) for 1996–2010 were obtained from the Central Agriculture Office, Budapest, Hungary. Vole

density was scaled from 0 (absent) to 10 (peak population). The annual number of tularemia cases in humans (based on clinical history and tube agglutination test results) was obtained from the National Center for Epidemiology, Budapest.

The data were regrouped according to the yearly biologic cycle (March–February) for hares and voles (Figure), and relationships between these yearly data were quantified by using the Spearman rank correlation coefficient (5) at county and regional levels. A 2–3 year cycle was characteristic for the analyzed data. A significant positive correlation was found among the number of tularemia cases in humans and the seroprevalence of *F. tularensis* among European brown hares (Spearman $\rho = 0.73$; $p < 0.0001$) and the population density of common voles (Spearman $\rho = 0.77$; $p = 0.0081$). A significant negative correlation was found between the population density of hares and the seroprevalence of *F. tularensis* in hares (Spearman $\rho = -0.41$; $p = 0.0365$).

The comprehensive and long-term annual data used in this study provide clues regarding the factors shaping the intraannual epizootiology and emergence or reemergence of tularemia. The European brown hare

is moderately sensitive to *F. tularensis* subsp. *holarctica*. The hares produce a heterogeneous response to infection, which means that some die of overwhelming bacteremia and others survive with a protracted course of infection, thereby contributing to the maintenance of tularemia over longer periods and serving as useful sentinels of disease activity. Other studies have concluded that hares, together with infected ticks, may serve as disease reservoirs between epizootics (2,3,6,7).

However, we instead hypothesize that the 2–3 year cycling feature of the population dynamics for the common vole (2) determines the ecology of *F. tularensis* subsp. *holarctica* in eastern Hungary. The common vole is highly susceptible to *F. tularensis* subsp. *holarctica* (3,8). When population densities among voles are high, *F. tularensis* disease transmission and spillover to hares may be facilitated by stress-related aggression, cannibalism, and *F. tularensis* contamination of the environment by infectious body discharges (2). Enhanced transmission and spillover can expand local outbreaks to epizootic proportions, and infected hares may, in turn, further enhance the spread of disease through bacterial shedding in urine (6,7).

The disease in hares often results in septicemia and death (7), thus decreasing the population density of these animals. Hares and especially voles are also hosts for different stages of several tick species (2,6), so it can be expected, that higher numbers of infected rodents and lagomorphs result in an increased proportion of infected ticks and, thus, increased transmission of *F. tularensis* subsp. *holarctica*. It can be concluded that a higher number of infection sources in the environment results in elevated numbers of cases in humans, mainly through the handling and skinning of hares, but also through tick bites and, potentially, the inhalation of infectious aerosols originating from, for example, hay or grain.

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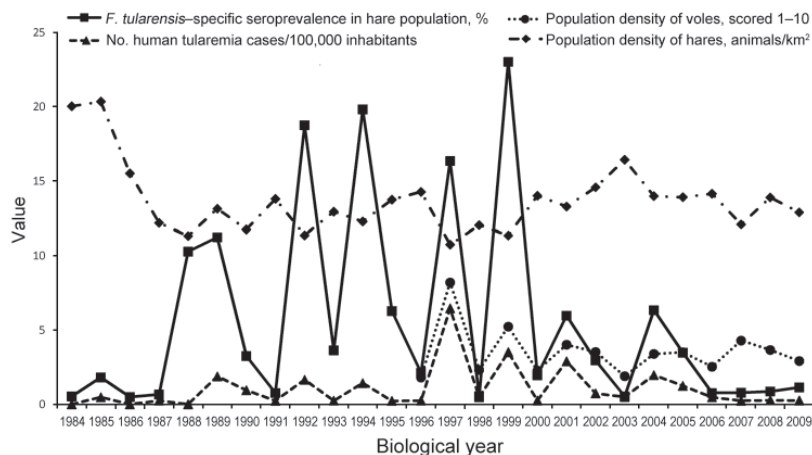


Figure. Correlation between the seroprevalence of *Francisella tularensis* in the European brown hare (*Lepus europaeus*) population, the population density of European brown hares and common voles (*Microtus arvalis*), and the number of tularemia cases in humans eastern Hungary, 1984–2010. Values were determined on the basis of biological years (March–February). Median values from the records of 3 counties were used for analysis.

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Klebsiella pneumoniae Carbapenemase-producing Enterobacteria in Hospital, Singapore

To the Editor: During the past decade, enterobacteria that produce *Klebsiella pneumoniae* carbapenemase (KPC) have become established in the United States and countries in South America and Europe (1). In Asia, KPC was reported in the People's Republic of China in 2007 (2) and subsequently in South Korea (3) and Taiwan (4). Public health agencies emphasize screening and strict contact precautions to control multidrug resistant *Enterobacteriaceae* (5). Routine testing for mechanisms of resistance facilitates detection of emerging carbapenem-resistant *Enterobacteriaceae*.

In Singapore's 1,000-bed National University Hospital during November 2010–January 2011, we identified New Delhi metallo- β -lactamase 1–producing *Enterobacteriaceae* in 2 clinical specimens but none that produced KPC (I. Venkatachalam et al., unpub. data). We conducted a laboratory screening study to determine the prevalence and nature of carbapenem-resistant *Enterobacteriaceae* in April 2011. Ethics committee approval was waived for this study.

Testing of rectal swab samples is part of an established hospitalwide program for vancomycin-resistant enterococci screening. Using a scoring system to identify patients at high risk for vancomycin-resistant enterococci (6), we found that ≈ 2.5 specimens per 100 admissions were attained each month. During our study, we also tested these samples for carbapenemase-producing *Enterobacteriaceae*.

During April–June 2011, we incubated specimens for 24 h in 10

mL tryptic soy broth containing 1 mg/L imipenem, then streaked 100 μ L of the broth onto CHROMagar KPC (CHROMagar, Paris, France). Colonies detected after 24 h incubation at 35°C were identified by using MALDI-TOF MS with a Microflex LT instrument (Bruker Daltonik GmbH, Leipzig, Germany). Imipenem and meropenem MICs for *Enterobacteriaceae* were confirmed by using Etest (bioMérieux, Marcy l'Etoile, France). Isolates with MIC ≥ 2 μ g/mL underwent analysis with Metallo- β -Lactamase Confirmative Identification Pack (Rosco Diagnostica, Taastrup, Denmark) and Etest MBL (bioMérieux) for metallo- β -lactamase production. Isolates suspected to be producers were genotypically confirmed by PCR.

Of the 201 nonduplicate samples processed, 79 microorganisms exhibited imipenem resistance and were isolated on CHROMagar KPC (Table). Among *Enterobacteriaceae*, carbapenem MIC ≥ 2 μ g/mL was present in 1 *E. aerogenes*, 2 *E. cloacae*, and 4 *K. pneumoniae* isolates. One isolate (*K. pneumoniae*) had a positive combined disk test result with a pattern suggestive of serine carbapenemase production.

We analyzed genomic DNA (DNeasy Blood and Tissue Kit, QIAGEN, Hilden, Germany) from this isolate by using PCR for transmissible carbapenem resistance markers: metallo- β -lactamases (VIM, IMP, and KHM-1), serine carbapenemases (KPC, GES1–5 and 7), and OXA-48. *bla*_{KPC}-specific primers (forward primer 5'-CGTTGACGCCAATCC-3'; reverse primer 5'-ACCGCTGGCAGCTGG-3') generated a 390-bp amplicon. Full gene sequencing of *bla*_{KPC} (forward primer 5'-ATGTCAC TGTATCGCCGTCT-3'; reverse primer 5'-CCTAAATGTGACAGTGGT TGG) revealed 100% homology to *bla*_{KPC-2} (GenBank accession no. FJ628167.2). Further analysis showed that the isolate carried extended-