Bordetella pertussis Isolates, Finland

To the Editor: Pertussis, or whooping cough, is a highly contagious respiratory disease in humans caused by *Bordetella pertussis*. Reemergence of pertussis has been observed in many countries with high vaccination coverage. In the United States, reported cases of pertussis in adolescents and adults have increased since the 1980s, despite increasingly high rates of vaccination in infants and children (1). At the same time, clinical *B. pertussis* isolates have become antigenically divergent from vaccine strains (2,3). This observation has raised the question of whether vaccination has caused selection for the variant strains, and whether the reemergence of pertussis in vaccinated populations is due to vaccination not protecting against these antigenic variants as effectively as it protects against vaccine type strains. On the other hand, vaccine-induced immunity wanes over time, and pertussis is not only a childhood disease but also a frequent cause of prolonged illness in adults and adolescents today (4).

In Finland, children are vaccinated with diphtheria-tetanus whole-cell pertussis vaccine at 3, 4, and 5 months, and from 20 to 24 months of age. The whole-cell vaccine contains 2 strains and has remained unchanged since 1976. The vaccine strain 18530 contains fimbriae 3 (Fim3), pertussis toxin S1 subunit D (PtxS1D), and pertactin 1(Prn1); the other vaccine strain, 1772, contains Fim2,3, PtxS1B, and Prn1. Ninety-six percent of Finland's population has been vaccinated with 4 doses of pertussis. The incidence of pertussis is highest in infants <1 year of age and in schoolchildren from 6 to 14 years old, although about 30% of the cases occur in adults older than 20 years. In Finland, as in many other countries with large-scale vaccination programs, several outbreaks of pertussis occurred in the 1990s. We studied prospectively 3 pertussis outbreaks in 2 elementary schools and 1 municipality in southwestern Finland (5,6). The aim of the study was to characterize the strains circulating and causing outbreaks and to track the transmission of *B. pertussis* during these outbreaks.

Sample were collected and primary cultures were done as described earlier (5,6). (See online Tables 1–3 at http://www.cdc.gov/ncidod/EID/vol11no01/04-0632.htm#table1, http://www.cdc.gov/ncidod/EID/vol11no01/04-0632.htm#table2, http://www.cdc.gov/ncidod/EID/vol11no01/04-0632.htm#table3) The outbreaks took place in 3 rural municipalities: in 1992, in Paimio with 1,400 inhabitants; in 1995, in Oripää with 3,500 inhabitants; and in 1996, in Rusko with 9,900 inhabitants. The isolates were obtained from schools and local health centers. In addition, 1 isolate was obtained from a household contact (See online Table 3 at http://www.cdc.gov/ncidod/EID/vol11no01/04-0632.htm#table3). Most of the cases occurred in schoolchildren >8 years of age and in adults.

Various DNA fingerprinting techniques, such as IS*1002*-based restriction fragment length polymorphism (IS*1002*-RFLP) and pulsed-field gel electrophoresis (PFGE) have been used to study *B. pertussis* isolates (7–10). DNA polymorphism analysis of *prn* and *ptxS1* has previously been used as a typing method for detecting antigenic shifts (2,3,8). In addition to *prn* and *ptxS1*, only tracheal colonization factor (*tcfA*), a surface–associated protein involved in the adhesion of *B. pertussis* to host cells, has been found to be polymorphic in recent *B. pertussis* isolates (3). The isolates were typed as described earlier (8,10).

Of the 46 isolates, 43 (94%) expressed Fim2, 2 (4%) expressed both Fim2 and Fim3, and 1 (2%) expressed Fim3 (See online Tables). The predominant prn allele in all 3 outbreaks was prn2, contained by 39 (85%) of the isolates. Six (13%) isolates contained prn3 and 1 (2%) isolate contained prn4. All isolates contained the ptxS1A allele. The predominant tcfA allele was tcfA2, contained by 42 (91%) of the isolates. Four (9%) isolates contained tcfA3. The tcfA3 allele was observed only in isolates with prn3. All but 1 of the 27 isolates subjected to the IS1002-RFLP analysis had the same pattern.

Seven PFGE patterns were found among the 46 isolates studied. The isolates were considered to be closely related, as the differences between the patterns were small, differing by 1 or 2 bands. Three PFGE patterns were found in both Paimio and Rusko. A major pattern was circulating in each of the schools A, B, and C, which indicates that pertussis is effectively transmitted in schools. However, in school D, the isolate from the index patient had PFGE pattern 5, whereas the rest of the isolates from patients in school D had pattern 6. In addition, the 1 isolate obtained from a household contact had a distinct PFGE pattern, 7. Similarly, in Paimio, the isolate from the index patient had a distinct PFGE pattern, 1. These findings, as well as the fact that 3 PFGE patterns were found in both Paimio and Rusko, indicate that several *B. pertussis* strains may have been circulating simultaneously in these small communities.

Our results suggest that *ptxS1* is not a useful marker in outbreaks to detect antigenic shifts. IS*1002*-RFLP was less discriminative than *Xba*I PFGE, which agree with results of previous studies (8). Most cases occurred in schoolchildren and adults, confirming epidemiologic findings from other countries with vaccination programs. Our results support the earlier observation that the recent *B. pertussis* isolates are antigenically different from vaccine strains. Several *B. pertussis* strains could circulate

simultaneously even in small communities, and only some strains, possibly with increased fitness, are capable of spreading effectively.

Acknowledgments

We thank Anna Musku and Birgitta Aittanen for technical assistance.

The Academy of Finland, the Special Governmental Fund for University Hospitals (EVO), and the European Commission Quality of Life Program (QLK2-CT-2001-01819) financially supported this work.

Johanna Mäkinen,*† Jussi Mertsola,‡ Frits R. Mooi,§ Shirley Van Amersfoorth,‡ Heikki Arvilommi,* Matti K. Viljanen,‡ and Qiushui He*

*National Public Health Institute, Turku, Finland; †Turku Graduate School of Biomedical Sciences, Turku, Finland; ‡University of Turku, Turku, Finland; and §National Institute of Public Health and the Environment, Bilthoven, the Netherlands

References

1. Tanaka M, Vitek CR, Pascual FB, Bisgard KM, Tate JE, Murphy TV. Trends in pertussis among infants in the United States, 1980-1999. JAMA. 2003;290:2968-75.
2. Mooi FR, He Q, van Oirschot H, Mertsola J. Variation in the *Bordetella pertussis* virulence factors pertussis toxin and pertactin in vaccine strains and clinical isolates in Finland. Infect Immun. 1999;67:3133-4.
3. van Loo IH, Heuvelman KJ, King AJ, Mooi F. Multilocus sequence typing of *Bordetella pertussis* based on surface protein genes. J Clin Microbiol. 2002;40:1994-2001.
4. von Konig CH, Halperin S, Riffelmann M, Guiso N. Pertussis of adults and infants. Lancet Infect Dis. 2002 Dec;2:744-50.
5. Tran Minh NN, He Q, Edelman K, Olander R-M, Viljanen MK, Arvilommi H, et al. Cell-mediated immune responses to antigens of *Bordetella pertussis* and protection against pertussis in school children. Pediatr Infect Dis J. 1999;18:366-70.
6. He Q, Viljanen MK, Ölander R-M, Bogaerts H, De Grave D, Ruuskanen O, et al. Antibodies to filamentous hemagglutinin of *Bordetella pertussis* and protection against whooping cough in school children. J Infect Dis. 1994;170:705-8.
7. van der Zee A, Vernooij S, Peeters M, van Embden J, Mooi FR. Dynamics of the population structure of *Bordetella pertussis* as measured by IS1002-associated RFLP: comparison of pre- and post- vaccination strains and global distribution. Microbiology. 1996;142:3479-85.
8. Mooi FR, Hallander H, von Konig CH, Hoet B, Guiso N. Epidemiological typing of *Bordetella pertussis* isolates: recommendations for a standard methodology. Eur J Clin Microbiol Infect Dis. 2000;19:174-81.
9. de Moissac YR, Ronald SL, Peppler MS. Use of pulsed-field gel electrophoresis for epidemiological study of *Bordetella pertussis* in a whooping cough outbreak. J Clin Microbiol. 1994;32:398-402.
10. Mäkinen J, Mertsola J, Soini H, Arvilommi H, Viljanen MK, Guiso N, et al. PFGE and pertactin gene sequencing suggest limited genetic variability within the Finnish *Bordetella parapertussis* population. J Med Microbiol. 2003;52:1059-63.

Address for correspondence: Johanna Mäkinen, Mycobacterial Reference Laboratory, National Public Health Institute, Kiinamyllynkatu 13, 20520 Turku, Finland; fax: 358-2-331-6699; email: johanna.makinen@ktl.fi

Correction Vol. 10, No. 12

In the article entitled "Wildlife as Source of Zoonotic Infections" by Hilde Kruse et al., errors occurred in the 2nd paragraph under Factors Influencing the Epidemiology of Zoonoses with a Wildlife Reservoir on page 2068. The first sentence incorrectly identified deer as a main reservoir for *Borrelia burgdorferi*. The corrected sentence appears below:

The spirochete *Borrelia burgdorferi*, which causes Lyme borreliosis, has its main reservoir among small rodents and uses various *Ixodes* species as vectors (13).

Instructions for Authors

Letters

Letters commenting on recent articles as well as letters reporting cases, outbreaks, or original research are welcome. Letters commenting on articles should contain no more than 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article's publication. Letters reporting cases, outbreaks, or original research should contain no more than 800 words and 10 references. They may have one Figure or Table and should not be divided into sections. All letters should contain material not previously published and include a word count.