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in the United States

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Epidemiology of Pertussis

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This review addresses the epidemiology of pertussis based on: (1) reported pertussis; (2) the increase in reported cases during the last 22 years; and (3) the data supporting the endemicity of *Bordetella pertussis* infection in adolescents and adults. This topic has been addressed previously^{1–6} as well as covered briefly in the Pertussis Update in *Concise Reviews of Pediatric Infectious Diseases* in September 2005.⁷

REPORTED PERTUSSIS

It is common knowledge that pertussis has been and is presently under-reported. Rates of reported pertussis depend on how carefully cases are sought. For example, in Switzerland and 3 bordering countries (Germany, Italy and Austria), the rates of reported pertussis for the period 1998–2002 varied by as much as 70-fold.⁸ The rates per 100,000 were: Switzerland, 123.9; Germany, 10.1;

Italy, 6.1; and Austria, 1.8. Because the 4 countries have similar immunization practices in addition to close proximity, these differences in pertussis rates are explained by the rigorosity of the respective surveillance programs and not unique epidemiology by country. Similarly, in the United States in 2004, the rate per 100,000 of reported pertussis in infants younger than 6 months of age was 126.5, whereas it was 3.8-fold higher in Wisconsin where an intensive surveillance program was conducted (J. Davis, unpublished data; CDC/NIP/ESB/BVPDB).

In spite of the fact that reported pertussis is only the “tip of the iceberg,” it is clear that a cyclic disease pattern occurs and that this pattern has continued in the vaccine era.³

RESURGENCE OF PERTUSSIS

During the last 2 decades, there has been an increasing trend in reported pertussis which reached a rate of 8.9 per 100,000 in 2004 (CDC/NIP/ESD/BVPDB). Several possible causes of this resurgence have been suggested.^{1–3} Mutations in the pertactin and pertussis toxin genes have been documented and may be vaccine-driven in some instances. However, there is no clinical or laboratory evidence that these are playing a role. Most cases in persons older than 10 years of age are due to waning vaccine-induced immunity, and even disease-induced immunity does not appear to last much longer than that from vaccination. The use of less immunogenic

vaccines in the 1990s may have contributed to this “resurgence,” but the most important cause is increased awareness by public health personnel and pediatricians and the resulting enhanced surveillance and diagnostic programs in many states.

B. PERTUSSIS INFECTION

The available data indicate that *B. pertussis* infections in adolescents and adults of all ages are endemic.¹ This conclusion is based on 3 types of studies in adolescent and adult populations: (1) studies of prolonged cough illnesses; (2) studies of antibody titer rises to pertussis toxin (PT) in populations over time; and (3) determination of rates by studying cough illnesses in defined populations. The significant factor which made all of these studies possible was the development of enzyme-linked immunosorbent assay (ELISA).^{3,4} In general, all *B. pertussis* infections in adolescents and adults occur in previously primed persons (by either previous infection or vaccination) so that antibody responses are early and brisk and shedding of bacteria in the nasopharynx is short-lived.^{9,10} Because adolescents and adults with cough illnesses due to *B. pertussis* infection do not usually seek care until the third or fourth week of illness, nasopharyngeal cultures and PCR are most often negative.^{4,11} However, single serum testing for significantly high antibody values to PT can confirm the diagnosis of pertussis.^{4,12}

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Since 1983, there have been a number of studies of prolonged cough illnesses in adolescents and adults in which *B. pertussis* infections were diagnosed by ELISA.¹ Of these, 8 were done during nonpertussis outbreak periods, and diagnosis depended on titer rises or high titers to PT, or in 2 instances, to fimbriae (FIM).^{1,13} The results of these studies were remarkably similar. The data suggested that 7–17% of the prolonged cough illnesses studied were due to *B. pertussis* infection (median, 13%; mean, 12.4%). Because at least 10% of infected persons (S. A. Halperin, unpublished data) do not have an antibody response to PT or FIM, the median rate of 13% is an underestimate. These studies span a time period of 16 years (1983–1998), and it should be noted that cases were found throughout the 16-year period. This indicates that *B. pertussis* infections with cough illnesses are endemic in adolescents and adults.

Five studies have examined populations with stored sera for titer rises. The first of these studies involved 51 health care workers followed for 5 years. The determined average annual rate was 8%.¹ If antibody titer rises to FIM as well as PT are examined, the average annual rate was 15% (J. D. Cherry, unpublished data). In contrast, the other 4 studies had more modest annual rates of 1–3%. These studies, which also span 16 years, suggest frequent unrecognized *B. pertussis* infections.

Recently, de Melker et al¹⁴ published the results of a very extensive population based study in the Netherlands. Using antibody decay curves of patients with pertussis, they calculated population-based ELISA antibody cut-off values to PT. From this, they esti-

mated an overall yearly incidence of infection of 6.6% for persons 3–79 years of age. The incidence was highest in those 20–24 years old (10.8%). It decreased to 6.5% in those 25–55 years of age and then further decreased to ~4% in those 56–79 years of age.

Six studies conducted in defined adolescent and adult populations have calculated the rates of *B. pertussis* infections with cough illnesses.¹ All of these studies have 1 or more limitations. In my opinion, the 3 studies with the least limitations suggested the following rates: 0.37%, 0.5%, and 1.5%. When the rate of infection study data are compared with the rate of symptomatic infection data, it appears that most of infections are asymptomatic or trivial illnesses. The ratio of asymptomatic to symptomatic infections varies from 3.5:1 to 21.6:1. PT IgA antibody data in children suggest that unrecognized infections in children are also common.¹⁰

In summary, *B. pertussis* infections in adolescents and adults are very common and endemic in the present vaccine era. Data from Germany in the 1990s when few children were being immunized and pertussis was epidemic as well as early observations in the United States suggest that infections in adolescents and adults were also common and endemic in the prevaccine era.^{3,5,6,11} Rates of reported pertussis are 40- to 160-fold less than actual illness rates, and asymptomatic infections are 4–22 times more common than symptomatic infections. Although no data exist, it is likely that the duration of time between infections in individual people determines the clinical outcome of an infection (ie, the longer the time between infections, the greater is the likelihood of

clinical disease). Today symptomatic adolescents and adults are the major source of infection in unvaccinated children.

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