Serologic Response and Antibody-Titer Decay in Adults with Pertussis

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Pertussis is a frequent and significant illness in adults. Because acellular pertussis vaccines for use in adolescents and adults have now been developed, it is important to compare serologic responses in adults after infection with serologic responses in adults after vaccination. We measured IgG and IgA antibodies to 4 Bordetella pertussis antigens at ~6-month intervals for 28 months in 11 adults with pertussis. After reaching peak levels, titers of antibody to pertussis toxin decreased more than did titers of antibodies to filamentous hemagglutinin, pertactin, and fimbriae type 1 and type 2. Although studies of adults who have been vaccinated with acellular pertussis vaccines have had shorter follow-up periods than studies of adults with pertussis infection, the antibody decay patterns are similar in both groups.

In recent years, there has been an increased awareness among health care professionals of pertussis in adolescents and adults [1–16]. In fact, the data of Strebel et al. [10] suggest that there are ~1 million cases of pertussis in adolescents and adults in the United States annually. In addition, it is recognized that the major source of pertussis in infants is infection by adults with cough illnesses due to Bordetella pertussis infection [3–5, 17–20].

Because B. pertussis illnesses in adolescents and adults are a significant problem, acellular pertussis vaccines for adults have been developed and are being evaluated [20–25]. For comparative purposes, it is important to examine patterns of antibody decay following vaccination and compare them with patterns of antibody decay following natural infection. In this report, we present patterns of antibody decay over a 28-month period in 11 adults with pertussis and compare these findings with available data on antibody decay following vaccination.

Methods. Informed consent was obtained from study subjects, and the human experimentation guidelines of the US Department of Health and Human Services and those of the trial site in Germany were followed. Adults with culture-proven and/or serologically proven B. pertussis infection were identified in households during a large pertussis vaccine efficacy trial conducted in Germany from 1991 to 1995 [3, 26]. These subjects were asked to provide follow-up serum samples approximately every 6 months for 28 months to monitor their anti-pertussis antibody values.

IgG and IgA antibodies to 4 B. pertussis antigens (pertussis toxin [PT], filamentous hemagglutinin [FHA], pertactin [PRN], and fimbriae type 2 and type 3 [FIM]) were measured by ELISA using standard techniques, as described elsewhere [3, 4, 12, 13, 15, 16, 27–29]. We used human reference serum from US Food and Drug Administration lots 3, 4, and 5. ELISA units were calculated by comparison of the response curve of the test specimen with that of the human reference serum, with use of the reference line method.

Results. Data for 11 adults with proven B. pertussis cough illnesses for whom multiple serum samples were available over a period of ~28-months are included in this report. The times at which serum samples were obtained, in relation to onset of disease, were as follows: 1 week (range, 0–8 days), 2 months (range, 0.5–3.5 months), 6 months (range, 5.6–8.2 months), 12 months (range, 9.0–14.3 months), 18 months (range, 15.3–22.6 months), and 28 months (range, 24.5–35.7 months). Serum samples were not available from all subjects at each time point. Because serum samples were available from only 3 subjects at the 24-month time point, no data are expressed for this time point. A minimum of 6 serum samples were required at each time point for that time point to be included in the study.

The characteristics of the subjects are presented in table 1. There were 9 women and 2 men, and their age range was 24–51 years. The median duration of cough was 7 weeks, and 10 (90%) of 11 subjects had paroxysmal cough, 4 (36%) had whooping, and 4 (36%) had posttussive vomiting. Only 1 woman did not have paroxysms, whooping, or vomiting. None of the subjects recalled having had a previous illness thought
Table 1. Characteristics of 11 adults with cough illnesses due to Bordetella pertussis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age in years, sex</th>
<th>Date of onset of illness</th>
<th>Duration of illness in weeks</th>
<th>Symptoms</th>
<th>Method of diagnosis</th>
<th>History of pertussis</th>
<th>History of pertussis vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37, F</td>
<td>27 Nov 1993</td>
<td>5</td>
<td>P, W</td>
<td>Culture, serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>33, F</td>
<td>20 Jan 1994</td>
<td>7</td>
<td>P, W</td>
<td>Culture, serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>40, M</td>
<td>24 Feb 1994</td>
<td>7</td>
<td>P, V</td>
<td>Culture, serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>31, F</td>
<td>25 Mar 1994</td>
<td>12</td>
<td>P, W, V</td>
<td>Serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>27, F</td>
<td>16 May 1994</td>
<td>11</td>
<td>P</td>
<td>Serology</td>
<td>None</td>
<td>3 doses of DTP</td>
</tr>
<tr>
<td>6</td>
<td>24, F</td>
<td>5 Aug 1994</td>
<td>4</td>
<td>P, V</td>
<td>Serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>36, F</td>
<td>10 Sep 1994</td>
<td>7</td>
<td>None</td>
<td>Culture, serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>31, M</td>
<td>9 Oct 1994</td>
<td>8</td>
<td>P, W, V</td>
<td>PCR, serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>24, F</td>
<td>12 Oct 1994</td>
<td>6</td>
<td>P</td>
<td>PCR, serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>34, F</td>
<td>17 Oct 1994</td>
<td>4</td>
<td>P</td>
<td>Serology</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>11</td>
<td>51, F</td>
<td>21 Apr 1995</td>
<td>6</td>
<td>P</td>
<td>Serology</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

NOTE. DTP, diphtheria and tetanus toxoids and pertussis vaccine; P, paroxysmal cough; W, whooping; V, posttussive vomiting.

to be pertussis, and only 1 subject had received 3 doses of whole-cell pertussis vaccine in childhood.

The geometric mean titers (GMTs) of specific anti-pertussis antibodies at the various time points, as determined by ELISA, are presented in table 2 and figure 1a and 1b. The kinetics varied substantially by antigen.

Two months after the onset of illness, the GMT of IgG antibodies to PT was 11-fold greater than in the acute-phase serum samples. It was 5-fold greater at 6 months and 2-fold greater at 28 months. The GMT of IgG antibodies to FHA increased 5-fold, and it was still 2.5-fold greater 28 months after the onset of illness than at the baseline. The GMT of IgG antibodies to PRN increased 9.3-fold, and it was 4.4-fold greater than the baseline at 28 months after the onset of illness. The IgG response to FIM was similar to the response to FHA, but was less pronounced.

The GMT of IgA antibodies to PT increased 3-fold between 1 week and 2 months, and it had returned to baseline at 1 year. IgA antibodies to FHA and PRN increased 12-fold and 4-fold, respectively, and were still 6-fold and 3-fold greater, respectively, at 28 months after onset of illness than at baseline. The IgA response to FIM was minimal.

**Discussion.** The magnitude of IgG and IgA antibody responses to PT, FHA, and PRN in the 11 subjects in the present study (median age, 33 years) was greater than that noted in an earlier study involving 48 subjects in Cleveland aged ≥65 years [13]. However, the response pattern and slope of decay for titers of IgG antibody to PT was similar in both studies. This comparison should be reviewed with some caution, because it is likely that some of the infections identified in the Cleveland study were due to other Bordetella species or to other agents that elicit cross-reacting antibodies to FHA and PRN [12, 13, 16, 26].

The apparent low titer of antibody in response to FIM is noteworthy. It is attributable to the fact that 6 of the 11 subjects had no antibody response to FIM. The other 5 subjects had typical antibody responses to FIM, similar to their antibody responses to PT, FHA, and PRN. The lack of a response in

Table 2. Geometric mean titers (GMTs), as determined by ELISA, of IgG and IgA antibodies to pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN), and fimbriae type 2 and type 3 (FIM) in serum samples obtained from 11 adults with cough illnesses due to Bordetella pertussis.

<table>
<thead>
<tr>
<th>Time point* (range)</th>
<th>No. of serum samples obtained</th>
<th>GMT in U/mL (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PT</td>
</tr>
<tr>
<td>1 week (0–8 d)</td>
<td>6</td>
<td>22 (3–169)</td>
</tr>
<tr>
<td>2 mo (0.5–3.5 mo)</td>
<td>11</td>
<td>242 (99–592)</td>
</tr>
<tr>
<td>6 mo (5.6–8.2 mo)</td>
<td>8</td>
<td>104 (40–268)</td>
</tr>
<tr>
<td>18 mo (15.3–22.6 mo)</td>
<td>9</td>
<td>46 (13–156)</td>
</tr>
<tr>
<td>28 mo (24.5–35.7 mo)</td>
<td>10</td>
<td>45 (18–114)</td>
</tr>
</tbody>
</table>

NOTE. D, days; mo, months.

* Time since onset of illness.
Figure 1. Geometric mean titers (GMTs), as determined by ELISA, of antibodies to pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN), and fimbriae type 2 and type 3 (FIM) in serum samples obtained at selected times after the onset of illness in 11 adults with pertussis. A, IgG antibody; B, IgA antibody.

These 6 subjects is probably due to the fimbrial serotype of the infecting organism. In our ELISA, we used a reagent that was prepared from both fimbriae type 2 and fimbriae type 3 strains. However, the fimbriae type 3 antigen is weak. Subjects infected with type 1; 1,3 or untypable organisms would not produce a measurable antibody response. During the course of this study, we performed serotyping of 209 B. pertussis isolates, and the majority (52%) of those isolates were type 1,3; 1 or untypable strains (S. Ramakrishnan, P. Newland, D. S. L. Xing, U. Heininger, J. D. Cherry, M. J. Corbel, unpublished data).

There have been a number of immunogenicity studies of acellular pertussis vaccines in adults, but the longest follow-up periods to date are 1 year (in 2 studies) and 18 months (in 1 study) [20, 24] (T. Le, J. D. Cherry, S.-J. Chang, M. D. Knoll, M. L. Lee, S. Barenkamp, D. Bernstein, R. Edelman, K. M. Edwards, D. Greenberg, W. Keitel, J. Treanor, J. I. Ward, unpublished data). The 18-month values reported for IgG antibody to PT, FHA, and PRN are very similar to our findings. However, the values for IgA antibodies to FHA and PRN were different, with less decay observed in samples obtained 18 months after illness than in those obtained 18 months after vaccination.

The finding of persistently high titers of IgA and IgG antibodies to FHA and PRN 28 months after onset of illness, in conjunction with the absence of similarly high values for antibody to PT, suggests the possibility that the sustained titers of antibodies to FHA and PRN may be the result of cross-stimulation caused by other Bordetella species and/or other infectious agents, as has been noted in other studies [12, 13, 16, 26].

Acknowledgments

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References


26. Stehr K, Cherry JD, Heininger U, et al. A comparative efficacy trial in Germany in infants who received either the Lederle/Takeda acellular pertussis component DTP (DTPa) vaccine, the Lederle whole-cell component DTP vaccine, or DT vaccine. Pediatrics 1998; 101:1–11.

