children have been infected with Epstein-Barr virus by the time they are 3 years old, but infection occurs after maternal antibodies have waned toward the end of the first year of life [6] rather than vertically. With HHV-8, some investigators dispute that vertical transmission is an important route at all [7, 8].

In considering postnatal transmission, we noted that, as in other studies [9–12], prevalence continues to rise in older prepubescent children, suggesting that this virus can be transmitted by nonsexual, nonvertical routes. In adolescents and young adults, sexual activity (or the salivary exchange associated with it) is likely to contribute to further spread. In Brazilian Amerindians, scarification is not widespread, and “tattooing” is typically done by staining with natural juices rather than through needle use. We are not aware of blood-letting being a common practice in Amerindians. Furthermore, transmission via blood is not an efficient route of transmission [13]. Hence, we doubt that blood exposure is an important contributor in our population.

In sum, the routes of HHV-8 transmission remain poorly understood. High-prevalence populations provide useful groups to study, since the incidence must be high. We are continuing our Amerindian investigations by studying families, groups to study, since the incidence must be high. We are continuing our Amerindian investigations by studying families, principally in the hope of better defining transmission routes. We concur that longitudinal studies may be the most definitive approaches to understanding transmission, and we look forward to seeing the results of studies now being initiated in Egypt and Africa and on high-risk European and American groups, such as homosexual men.

Robert J. Biggar,1 Frank Black,2 and Denise Whitby3
1Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland; 2Department of Epidemiology, Yale University School of Public Health, New Haven, Connecticut

Are Only Antibody Levels Involved in the Protection against Pertussis in Acellular Pertussis Vaccine Recipients?

To the Editor—In a recent report, Taranger et al. [1] demonstrate a highly significant correlation between the levels of anti–pertussis toxin (PT) IgG measured shortly (21–77 days) after completion of a primary cycle of vaccination with the PT toxoid and persistent (>2 years) protection against pertussis. This report recalls previous observations claiming that protection is related to the levels of antibodies against Bordetella pertussis antigens at the time of exposure to the infectious agent [2]. The observations by Taranger et al. [1] are clearly relevant to define the correlates of protection but do not establish that this latter is exclusively antibody mediated. In fact, anti-PT antibodies manifestly decreased 21–32 months after the third vaccine dose, yet “no decrease in vaccine efficacy” was noticed [1]. The authors interpret these findings by assuming that the “true” antibody levels ensuring actual protection at the time of vaccination. May we suggest the additional or even alternative explanation that the children with low or negligible antibody levels were protected against pertussis, because specific, long-term memory immunity, in addition to actual antibody titer, plays a role?

It has been demonstrated that, although antibodies disappear from serum, cell-mediated immunity (CMI; i.e., the actual source of memory immunity) is continuously boosted by re-
peated, disease-free exposure to the bacterium for as long as 4–5 years from the primary cycle of vaccination [3, 4]. An example, as shown in table 1, is a small cohort of children who were longitudinally followed during the Italian efficacy trial of pertussis vaccines. The data clearly show that the strong decline in anti-PT IgG levels is inversely associated with a substantial increase in the proportion and magnitude of CMI response to the same antigen ≤4 months after vaccination. Experiments with reliable animal models of B. pertussis respiratory infection also suggest that CMI must be elicited for the mouse to eventually get rid of the infectious particle [5]. Overall, the search for immunologic correlates of vaccine protection may benefit from a rigorous assessment of both arms of the immune response (i.e., humoral and cellular). Cell memory and initial priming may be very critical for long-lasting protection, since they ensure rapid antibody recall and a cytokine response favoring the activation of those phagocytic cells that elimination of B. pertussis ultimately relies upon. This might be the case of pertussis and other diseases, where antibody levels are often acritically taken to be the exclusive markers of protection.

Antonio Cassone, Paola Mastrantonio, and Clara Maria Ausiello
Department of Bacteriology and Medical Mycology, Istituto Superiore di Sanità, Rome, Italy

Table 1. Antibody and cell-mediated immunity (CMI) responses to pertussis toxin (PT) in a cohort of children ≤48 months old who were followed longitudinally (42 months after primary vaccination).

<table>
<thead>
<tr>
<th>Children’s ages, months</th>
<th>Months after vaccination</th>
<th>Immunoglobulin GMT&lt;sup&gt;a&lt;/sup&gt;</th>
<th>PBMC proliferation to PT&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No of seroresponders/total&lt;sup&gt;c&lt;/sup&gt;</td>
<td>GMT (95% CI)</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1/19</td>
<td>1.3 (0.9–1.7)</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>19/19</td>
<td>103.5 (103.1–103.9)</td>
</tr>
<tr>
<td>20</td>
<td>14</td>
<td>8/19</td>
<td>6.42 (5.7–7.1)</td>
</tr>
<tr>
<td>48</td>
<td>42</td>
<td>1/19</td>
<td>2.0 (1.5–2.6)</td>
</tr>
</tbody>
</table>

NOTE: Children were recruited, vaccinated, and followed for pertussis occurrence as in [3, 4]. No child was affected by pertussis during the study period. CI, confidence interval; GMT, geometric mean titer; PBMC, peripheral blood mononuclear cells; SI, stimulation index.

<sup>a</sup> Seroresponder was defined by serum antibody titer >4 minimal detection limit (set at 2 U/mL).
<sup>b</sup> Evaluated by thymidine incorporation as in [3]. SI is ratio between counts per minute (cpm) of PT-stimulated PBMC divided by cpm of unstimulated culture.
<sup>c</sup> CMI responder was defined as child whose PBMC had an SI >4.

References


Reprints or correspondence: Dr. A. Cassone, Dept. of Bacteriology and Medical Mycology, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy (cassone@iss.it).

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Reply

To the Editor—Our article [1] confirms reports that serum IgG anti–pertussis toxin (PT) alone confers immunity to infection with Bordetella pertussis. Although Cassone et al. [2] indicate that the mouse provides a “reliable” model, mice neither cough nor transmit B. pertussis. These 2 activities are essential components of pertussis. Furthermore, PT, either by active immunization or by passive immunization with polyclonal or monoclonal antibodies at levels that can be achieved clinically, is the only component of B. pertussis that confers 100% protection against both intracerebral and pulmonary challenge of mice [3].

Two reports show that pertussis occurs in the absence of only PT antibodies in humans [4, 5]. Further, convalescence from infection with Bordetella parapertussis induces high levels of antibodies to the filamentous hemagglutinin (FHA) and pertactin but does not confer immunity to pertussis [6, 7]. It has also been reported that antibodies to FHA and pertactin do not confer immunity to pertussis [8, 9]. The action of PT antibodies is not directly antibacterial and has been shown to be analogous to vaccine-induced antitoxin-mediated immunity to diphtheria [10]. Vaccination can only prevent disease, including pertussis, but cannot cure established infection [11].

As for T cell–mediated immunity, the authors did not demonstrate a statistically significant relation between immunity to pertussis and the degree of peripheral blood mononuclear cell (PBMC) proliferation to PT or to their description of “sero-