**Very Early Pertussis Vaccine Confers Protection**

**BY PATRICE WENDLING**

**Chicago Bureau**

CHICAGO — Monovalent acellular pertussis vaccine given at birth and 1 month results in immunogenicity in infants by 2 months of age, according to data presented in a late-breaking poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The finding is important because most cases of severe pertussis disease occur in infants less than 4 months of age, before they are fully vaccinated. The currently recommended vaccination schedule for U.S. children aged 0-6 months calls for diphtheria, tetanus, and acellular pertussis (DTaP) vaccinations at 2, 4, and 6 months of age.

Two doses of acellular pertussis are thought to be crucial for protection, but are typically delayed until at least 6 weeks of age because of concerns that the newborn’s immature immune systems may not recognize the vaccine and respond by making antibodies, and that maternal antibodies may interfere with vaccine efficacy, lead investigator Dr. Nicolas Wood told reporters at a press briefing at the conference, which was sponsored by the American Society for Microbiology.

“We think it’s an important study because we were able to show that the early doses at birth and 1 month could get you higher antibody at a time [when] if you do get pertussis infection you are more likely to get severe disease,” said Dr. Wood, a pediatrician and clinical fellow at the Children’s Hospital at Westmead, New South Wales, Australia.

Dr. Wood and his associates at the Women’s and Children’s Hospital, in Adelaide, Australia, examined the immunogenicity of birth and 1-month acellular pertussis (Pa) vaccination in a cohort of 76 children. Serology and pertussis vaccine were provided by GlaxoSmithKline. Each dose contained pertussis toxin 25 mcg, filamentous hemagglutinin 25 mcg, and pertactin 8 mcg. The children were divided into three groups. (See accompanying chart for vaccination schedules.)

At 2 months of age, infants who received pertussis vaccine at birth and 1 month had significantly higher antibody levels against pertussis toxin and pertactin (an antigenic protein in most pertussis vaccines) than infants who received pertussis just at birth or who did not receive any pertussis before 2 months of age.

The infants were followed for 4, 6, and 8 months, and at all time points, the infants who received pertussis vaccine at birth and 1 month had higher antibody levels against pertussis toxin and pertactin than infants on the other two schedules.

The difference in antipertussis response was significant at 2, 4, and 6 months for group 1 vs. groups 2 and 3 (P < .05), and at 2 and 4 months for group 2 versus group 3 (P < .05).

By the end we were able to show that giving the early doses had given them earlier antibody protection, and by the time they’d finished the schedule, the antibodies were equivalent to those [in] babies [who] started later,” Dr. Wood said. “So it didn’t result in the suppression of the immune system, which was one of our concerns.”

Among the 75 evaluated children, there were no serious adverse reactions.

One child was exposed to pertussis, which resulted in a mild case. Because there was only one exposure, Dr. Wood said no conclusions could be made about how protective the early schedule is against disease. Unlike hepatitis B, there is no specific antibody level cutoff point at which protection can be guaranteed.

Larger trials are needed to consider the combination of pertussis with hepatitis B vaccine at birth and different schedules, said Dr. Wood, who received research support from the Financial Markets Foundation for Children in Australia.

Dr. Claire Anne Siegrist of the Centre for Vaccinology and the Neonatal Immunology, University of Geneva, said in an interview that the findings confirm results reported previously by her and her colleagues. “What all of our studies have shown is that you can give the first dose of pertussis at birth and already have a significant immune response much earlier than if you wait until the age of 2 months, which is the regular timing,” she said.

Further studies are needed to define the best dosing schedule, she said, and to entice vaccine manufacturers to create a monovalent acellular pertussis vaccine, which currently is not commercially available.

A third study, reported by Dr. Natasha Halasa at the Interscience Conference on Anti­microbial Agents and Chemotherapy in 2005, supports the use of a monovalent pertussis vaccine, as antibody suppression was demonstrated by a pertussis dose given in combination with diphtheria. “One of the theories with the diphtheria added in it is that there may be some intolerance early on that is interfering with the antigen presentation with pertussis,” Dr. Halasa of Vanderbilt Children’s Hospital, Nashville, Tenn, said in an interview.

### Schedules for Study of Early Pertussis Vaccination

<table>
<thead>
<tr>
<th>Ages</th>
<th>Group 1 (n = 27)</th>
<th>Group 2 (n = 23)</th>
<th>Group 3 (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>P*</td>
<td>P*</td>
<td>None</td>
</tr>
<tr>
<td>1 month</td>
<td>B</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2 months</td>
<td>Prevenar</td>
<td>Prevenar</td>
<td>Prevenar</td>
</tr>
<tr>
<td>4 months</td>
<td>Infanrix Hexa</td>
<td>Prevenar</td>
<td>Infanrix Hexa</td>
</tr>
<tr>
<td>6 months</td>
<td>Infanrix Hexa</td>
<td>Prevenar</td>
<td>Infanrix Hexa</td>
</tr>
<tr>
<td>8 months</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*Monovalent acellular pertussis measured by GlaxoSmithKline, Belgium.

Note: All vaccines are Australian formulations. Infanrix Hexa vaccine contains diphtheria, tetanus toxoids, acellular pertussis, Haemophilus influenzae type b, hepatitis B, and polymyxin (inactivated) antigens. Prevenar is a formulation of Prevenar.

Source: Dr. Wood

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**Tuberculosis Infection Growing Among International Adoptees**

**BY MICHELE G. SULLIVAN**

**Mid-Atlantic Bureau**

Mycobacterium tuberculosis infection is becoming increasingly common among children adopted from foreign countries, Dr. Anna Mandaklas and her colleagues reported.

Because of this risk, international adoptees should receive tuberculin screening as soon as possible after their arrival in their new country, wrote Dr. Mandaklas of Case Western Reserve University, Cleveland, Ohio, and her coauthors (Pediatrics 2007;120:610-6).

“In addition, because of the risk of a false-negative [screen] after recent exposure to M. tuberculosis or secondary to malnutrition, clinicians should consider repeat screening 4-6 months after children arrive in their adoptive countries and when nutrition has improved,” they said.

The team performed a retrospective review of 86 adoption (median age 26 months) who presented to the International Adoption Clinic at the University of Minnesota, Minneapolis, from 1986 to 2001. In addition to receiving a tuberculin skin test, each child underwent a nutritional assessment that included measurements of weight, height, length, and body mass index.

Twenty-eight percent of the group had evidence of chronic malnutrition, and 5% had evidence of acute malnutrition.

Based on a previously published analysis of a subset of this group, the investigators expected to find M. tuberculosis infection in about 12% (15 of 869) of the children. The rate of infection was much higher, with 12% of the group (102) showing a tuberculin skin test (TST) induration of at least 10 mm.

The frequency of a positive skin test did not differ among birth countries nor was it related to the presence of malnutrition. However, the proportion of children with a positive skin test decreased that a significant portion of children who live in orphanages are exposed to infected adults with active tuberculosis. In children with exposure to an active adult, the TST should instead be interpreted as positive when TST indurations are greater than or equal to 5 mm. Therefore, our study likely underestimates the number of children who would receive a diagnosis of M. tuberculosis infection if the history regarding tuberculin exposure were available. In addition, children with recently acquired M. tuberculosis infection may not have fully developed their immune response and associated TST response,” the investigators said.

“They suggested that adding screening such as chest x-ray and a repeat TST 3-6 months after arrival may be a good idea in internationally adopted children with TST indurations greater than or equal to 5 mm.”

Although our study did not demonstrate a statistically significant association between nutritional status and TST reactivity, this lack of association reflects the small number of children defined as severely malnourished in our study and the Financial Markets Foundation for Children in Australia, Dr. Mandaklas and her associates said.

Previous studies have shown that malnourished children are at an increased risk of developing positive TST responses—those who have an associated impairment in T-cell function may not be responsive to the TST.

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**Infectious Diseases**