This statement updates previous information and recommendations regarding *Haemophilus influenzae* type b conjugate vaccines. The four vaccines that have received extensive clinical investigation and/or licensure by the United States Food and Drug Administration (FDA) are listed in the Table. Previously, the Committee recommended that all infants be immunized at 18 months of age with one of the two conjugate vaccines, designated PRP-D and HbOC, that were licensed at that time.\(^1\)\(^2\) A third conjugate vaccine, designated PRP-OMP and consisting of the capsular polysaccharide of *H influenzae* type b complexed with outer membrane proteins of *Neisseria meningitidis*, was licensed by the FDA in December 1989. Currently, the FDA has approved labeling for PRP-OMP, HbOC, and PRP-D vaccines that states “Administration of *Haemophilus b* Conjugate Vaccine may be considered for children as young as 15 months of age when it is expected that the child will not return at 18 months for *Haemophilus b* immunization.” After review of the data available on immunogenicity for PRP-D, HbOC, and PRP-OMP administered to children at 15 months of age, the Committee concludes that all children should be immunized at 15 months of age.

**BACKGROUND**

Before the introduction of immunization against *H influenzae* type b, it was estimated that annually approximately 16,000 cases of invasive infection occurred in the United States in children 5 years of age or younger.\(^3\) About 26.6% of cases occurred in children 18 months of age or older, and approximately an additional 9.3% occurred in children 15 to 17 months of age. Thus, about 35.9% of the disease burden is potentially preventable by an effective vaccine administered at 15 months of age.

Preliminary data suggest that PRP-D and HbOC each have been highly effective when administered to children in the United States at 18 months of age (M. Osterholm, PhD, oral communication, April 1990).\(^4\)\(^-\)\(^7\) In Minnesota (M. Osterholm, personal communication, April 1990)\(^4\) and Los Angeles County, CA,\(^5\) two locales where the “plain” capsular polysaccharide vaccine (PRP) was found to be ineffective, vaccine efficacies of greater than 95% (95% confidence interval, 72% to 100%) and 86% (95% confidence interval, 59% to 95%), respectively, have been documented among children who have received PRP-D vaccines. High efficacy estimates for PRP-D were also reported in Dallas County, Texas,\(^6\) in Connecticut, and in Pittsburgh, PA.\(^7\) A somewhat lower efficacy of 77% (95% confidence interval, 31% to 93%) in children 18 to 59 months of age was found in preliminary analysis of a case control study in four states coordinated by the Centers for Disease Control (C. Broome, MD, oral communication to the Committee, March 1990).

The previous decision to approve the use of PRP-D and HbOC in 18-month-old children was based on data then available on immunogenicity. Review of new unpublished data on immunogenicity in 15-month-old children immunized with the three licensed conjugate vaccines leads us to believe that the immunogenicity of all three vaccines is sufficient to recommend immunization of all children at 15 months of age.

Because of conflicting efficacy data on PRP-D used in infants as young as 2 to 3 months of age,\(^8\)\(^9\)
TABLE. Conjugate Vaccines

<table>
<thead>
<tr>
<th>Vaccine Manufacturer</th>
<th>Abbreviation for Vaccine</th>
<th>Carrier Protein</th>
<th>Saccharide</th>
<th>Spacer</th>
<th>Licensed by the FDA* as of May 1990</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connaught Praxis (Lederle)</td>
<td>PRP-D</td>
<td>Diphtheria toxoid</td>
<td>Poly</td>
<td>6 carbon</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>HbOC</td>
<td>CRM97 (a nontoxic mutant diphtheria toxin)</td>
<td>Oligo</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>Merck, Sharp &amp; Dohme</td>
<td>PRP-OMP</td>
<td>OMP (an outer membrane protein complex of Neisseria meningitidis)</td>
<td>Poly</td>
<td>Complex, involving a thioether</td>
<td>Yes</td>
</tr>
<tr>
<td>Pasteur Merieux</td>
<td>PRP-T</td>
<td>Tetanus toxoid</td>
<td>Poly</td>
<td>6 Carbon</td>
<td>No</td>
</tr>
</tbody>
</table>

* FDA, United States Food and Drug Administration.

Additional studies will be required before *H influenzae* conjugate vaccines can be recommended for administration at an age earlier than 15 months.

RECOMMENDATIONS

1. All children should receive a single dose of an *H influenzae* type b conjugate vaccine at 15 months of age or as soon as possible thereafter, rather than at 18 months of age as recommended previously. Although there are differences in the chemical structure of the three licensed vaccines (PRP-D, HbOC, or PRP-OMP) and the recipients’ antibody responses to those vaccines, data available on efficacy are insufficient to recommend one more than the others.

2. For those children 18 months of age or older who have not yet been immunized against *H influenzae* type b disease, immunization continues to be recommended up to the fifth birthday (ie, up to 59 months of age) after which the risk of invasive disease is small in healthy children.

3. Children immunized with PRP-D, HbOC, or PRP-OMP at 15 months of age or older need not be reimmunized.

4. Any of the *H influenzae* type b conjugate vaccines may be administered simultaneously with polio vaccines (IPV or OPV), measles-mumps-rubella vaccines, or diphtheria-tetanus-pertussis vaccines, although not all combinations have been studied.

5. Children who have experienced *H influenzae* type b disease before 24 months of age should receive a dose of an *H influenzae* type b conjugate vaccine, because the disease may not have rendered them immune. The vaccine should be administered at least 2 months after illness and after the child has reached at least 15 months of age. Unimmunized children whose disease occurred at 24 months of age or later do not need immunization, because the disease probably rendered them immune.

6. Irrespective of immunization status, as recommended previously, rifampin prophylaxis is indicated for all appropriate child or adult contacts exposed to an individual with *H influenzae* type b disease (see reference 1, recommendation 10). For further recommendations concerning rifampin administration, see reference 10.

7. As recommended previously, children 5 years of age or older with a chronic illness known to be associated with an increased risk for *H influenzae* type b disease, eg, immune deficiency states, should be given a single dose of an *H influenzae* type b conjugate vaccine (see reference 1, recommendation 11).

8. *H influenzae* conjugate vaccines have been well tolerated. In addition, no increased incidence of *H influenzae* type b disease has been demonstrated during the first 2 weeks after the administration of an *H influenzae* type b conjugate vaccine. However, these vaccines cannot be expected to be protective until anticapsular antibody synthesis occurs, approximately 2 weeks after immunization. Cases of invasive *H influenzae* type b disease and/or important adverse reactions to the vaccine occurring at any time following immunization should be reported promptly to state and local health departments, the manufacturer, the FDA, or the Centers for Disease Control.

9. *H influenzae* type b conjugate vaccines are not recommended for infants younger than 15 months of age. Efficacy trials involving HbOC, PRP-OMP, and PRP-T are being conducted in American infants in this very young age-group. It is hoped that one or more of these vaccines will prove effective in immunizing younger infants, and that their use in young infants can be recommended in the near future.

COMMITTEE ON INFECTIOUS DISEASES, 1989–1990
Stanley A. Plotkin, MD, Chairman
Neal A. Halsey, MD
Martha L. Lepow, MD
Edgar K. Marcuse, MD
George H. McCracken, Jr, MD
George A. Nankervis, MD
Carol F. Phillips, MD
Gwendolyn B. Scott, MD

AMERICAN ACADEMY OF PEDIATRICS 795
REFERENCES

4. Osterholm MT. Efficacy of Haemophilus b plain polysaccharide (PRP) vaccine and conjugate vaccine (PRP-D) in Minnesota. Abstracts of the 29th Interscience Conference on Antimicrobial Agents and Chemotherapy; September, 1989; Houston, TX. Abstract
6. Murphy TV, Herrin-Kane CM, Coury S, Medley F. Protective efficacy of Haemophilus influenzae type b vaccines in Dallas County, Texas. Clin Res. 1990;38:183A
Haemophilus influenzae Type b Conjugate Vaccines: Immunization of Children at 15 Months of Age

Pediatrics 1990;86;794

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/86/5/794

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pediatrics.aappublications.org/content/reprints
Haemophilus influenzae Type b Conjugate Vaccines: Immunization of Children at 15 Months of Age

Pediatrics 1990;86;794

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/86/5/794