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ACIP Update: Prevention of Haemophilus influenzae Type b Disease

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ACIP UPDATE: PREVENTION OF HAEMOPHILUS INFLUENZAE TYPE B DISEASE*

Haemophilus influenzae type b (Hib) is the most common cause of bacterial meningitis in the United States. It also causes other serious invasive illnesses, including epiglottitis, sepsis, celulitis, septic arthritis, osteomyelitis, pericarditis, and pneumonia. By 5 years of age, one of every 200 children in the United States will have had a systemic infection due to Hib. A polysaccharide vaccine against systemic Hib disease was licensed in the United States in April 1985. Information on the vaccine and Immunization Practices Advisory Committee (ACIP) guidelines for its use should be consulted. The purpose of this statement is to update these recommendations and to provide guidelines for the prevention of secondary cases of Hib disease.

CHEMOPROPHYLAXIS

Risk of Secondary Disease. Secondary disease, defined as illness within one to 60 days following contact with a child who has Hib disease, accounts for less than 5% of all invasive Hib disease. However, six studies of household contacts of Hib patients found a secondary attack rate of 0.3% in the month following disease onset in the index patient, which is about 600-fold higher than the age-adjusted risk in the general population. Among these studies, the attack rate among household contacts varied markedly with age: 4% for children under 2 years of age; 2% for children 2 to 3 years of age; 0.1% for children 4 to 5 years of age; and 0% for those over 6 years of age. Among these household contacts, 64% of secondary cases occurred within the first week (excluding the first 24 hours) of disease onset in the index patient; 20%, during the second week; and 16%, during the third and fourth weeks.

The risk of secondary disease among children who were exposed to a primary case in day-care and who did not receive rifampin prophylaxis has been examined in four studies. A national collaborative study that calculated secondary attack rates for household and day-care classroom contacts found that one (1%) of 91 children under 4 years of age in day-care acquired disease in the month following the index patient, compared with three (2%) of 125 household contacts under 4 years of age. A multicenter study in Seattle-King County, Washington; Oklahoma; and Atlanta, Georgia, found that the risk of secondary Hib disease among day-care classroom contacts was age-dependent; 10 (3%) cases occurred among the 376 contacts 0 to 23 months old, whereas none of the 379 classroom contacts older than 23 months of age acquired secondary disease. No cases occurred among children who attended day-care for fewer than 25 hours per week. In this study, classroom contacts were defined as children who spent more than half their day-care time in the same classroom as a child with primary Hib disease in the week before disease onset of the primary case. The over-all risk for classroom contacts was 0.7% (10/1,388), 20 times higher than the risk for other children in the center (0.04% [2/5,639]). Thirty-three percent of the secondary cases occurred within three weeks of onset of the index case; 13%, between days 21 and 40; and 53% between days 41 and 60. Meningitis and other systemic Hib infections were equally likely to result in secondary cases.

Two prospective studies have examined the risk of subsequent Hib disease in day-care facilities. In Dallas County, Texas, follow-up for 60 days of classroom contacts revealed no cases of secondary disease in 361 children under 2 years old, and a secondary attack rate of 0.5%

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(1/213) in those 2 to 3 years of age. Other cases of Hib disease occurred but could not be classified as secondary cases because these children enrolled in the day-care facility after the index patient became ill. Since it is known that rates of asymptomatic transmission are elevated in day-care classrooms with children with Hib disease, some of these cases may have been associated with the index case.

A similar surveillance study was conducted in Minnesota. No cases of secondary Hib disease were found among 370 day-care contacts under 2 years of age; 263 (71%) were classroom contacts. These were defined as children who spent more than eight hours in the same classroom as the primary case in the week before the patient with primary disease became ill. Similarly, secondary cases were not seen in 716 children 2 to 3 years of age, of whom 421 (59%) were classroom contacts.

The disparities in the risk of day-care-associated secondary Hib disease in Minnesota; Dallas County, Texas; and the two multicenter studies remain unexplained. Possible reasons include differences among the several study areas in day-care characteristics, such as classroom size and age distribution of children, which might affect intensity and duration of contact. There may be further unrecognized differences in epidemiologic factors or invasiveness of prevalent Hib strains.

Efficacy of Rifampin Prophylaxis. Most children at risk of secondary disease are too young to respond to the Hib polysaccharide vaccine. Therefore, the main preventive measure presently available is rifampin administration. Currently available data from several studies indicate rifampin in a dosage of 20 mg/kg per dose once daily (maximum daily dose 600 mg) for 4 days eradicated Hib carriage in 95% or more of contacts of primary cases, including children in day-care facilities. In a randomized placebo controlled trial, rifampin in the currently recommended dosage administered to all household and day-care classroom contacts, including adults, significantly decreased secondary Hib disease among household and day-care contacts (none of 303 rifampin-treated contacts under 4 years of age had secondary disease, compared with four of 216 placebo-treated contacts under 4 years of age [$p = 0.03$]); the number of cases was insufficient to evaluate efficacy in the household or day-care setting alone. However, the collaborative study of day-care centers cited above found that among classroom contacts of Hib patients, children aged 0 to 23 months who received rifampin prophylaxis were significantly less likely to develop secondary disease than children who did not take rifampin (none of 232, compared with 10 [3%] of 376 [$p < 0.02$]). Secondary disease did not develop in day-care classes in which over 75% of the class received rifampin. However, rifampin prophylaxis is unlikely to be 100% effective, and a day-care center in which rifampin prophylaxis failed to prevent subsequent disease has been reported.

Implementation of Chemoprophylaxis. Rifampin is available in 150-mg and 300-mg capsules. For those unable to swallow capsules, rifampin may be mixed with several teaspoons of applesauce immediately before administration, resulting in acceptable serum and salivary levels. Although there has been more experience with the applesauce mixture, a suspension of rifampin may also be freshly prepared in United States Pharmacopeia syrup; the preparation should be vigorously shaken before use. Side effects of rifampin in the recommended dose include nausea, vomiting, diarrhea, headache, or dizziness, which occurred among 20% of those taking rifampin and 11% of placebo recipients. No serious reactions occurred. Those taking rifampin (including parents and day-care staff) should be informed that orange discoloration of urine, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives can occur.

In implementing chemoprophylaxis in day-care centers, it is important to ensure that all classroom contacts receive rifampin during the same period. Some local and state health departments have facilitated the timely implementation of chemoprophylaxis by coordinating rifampin administration following consultation with private physicians or by providing information to parents of day-care contacts.

VACCINE

Effect of Hemophilus b Polysaccharide Vaccine on Nasopharyngeal Carriage. Limited data are available on the effect of the Hemophilus b polysaccharide vaccine on nasopharyngeal carriage of the organism. By analogy to carriage studies after serogroups A and C meningococcal polysaccharide vaccination, some reduction in acquisition of carriage may occur shortly after immunization, but no long-term effect has been noted.

Use of Hemophilus b Polysaccharide Vaccine in Children with Preceding Hib Disease. Studies have shown that the development of anticapsular antibodies following invasive Hib disease is largely age-dependent. A study of acute and convalescent sera from 125 patients with meningitis, septicemia, or epiglottitis due to Hib determined that, among those who acquired disease when they were younger than 18 months, 41 (85%) of 48 failed to develop an adequate antibody response, in contrast to 18 (23%) of 77 of those older than 18 months. Cases have been reported in which children who do not mount an antibody response after an invasive episode of Hib have developed a second systemic infection with the organism.

RECOMMENDATIONS

The primary strategy for preventing Hib disease is immunization. Children should be vaccinated at 24 months of age. Those at high risk for Hib disease, including children attending day-care, may be given the vaccine at 18 months of age. ACIP guidelines for use of the vaccine should be consulted. This update addresses chemoprophylaxis (recommendations 1 to 7) and additional vaccine issues (recommendations 8 and 9).

Chemoprophylaxis. Although unexplained disparities in available data prevent a precise estimate of the magnitude of risk among day-care contacts, it is likely that the increased risk of disease observed among young household contacts is also present among day-care classroom contacts under 2 years of age. Since rifampin prophylaxis is effective in preventing subsequent cases in this high-risk group, the ACIP recommends that:

1. Contacts of all ages who develop symptoms suggestive of invasive Hib disease, such as fever or headache, be evaluated promptly by a physician.

2. In any household in which a case of invasive Hib disease has occurred and in which another child under 4 years of age resides, all members of the household, including adults, should receive rifampin according to the following regimen: **rifampin in a dosage of 20 mg/kg per dose once daily (maximal daily dose 600 mg) for 4 days; the dose for neonates (under 1 month of age) is 10 mg/kg once daily for 4 days.**

3. In day-care classrooms in which a case of Hib disease has occurred and in which another child under 2 years of age has been exposed, all parents should be notified (preferably in writing) regarding the occurrence of the case and the possibility of increased risk to their children. They should be informed about the symptoms and the need for prompt medical evaluation if symptoms occur. They should also be notified of the availability of rifampin prophylaxis. Although the data on which to base recommendations are not optimal, and some authorities disagree, the consensus of the ACIP is as follows: **In a day-care classroom in which a case of systemic Hib disease has occurred, and in which one or more children under 2 years old have been exposed, strong consideration should be given to administering rifampin prophylaxis to all children and staff in the classroom, regardless of age.**

4. Rifampin should not be used in pregnant women, as its effect on the fetus has not been established, and it is teratogenic in laboratory animals.

5. Chemoprophylaxis should be instituted as rapidly as possible. If more than 14 days have passed since the last contact with the index patient, the benefit of chemoprophylaxis is likely to be decreased.

6. All children convalescing from systemic Hib disease who are anticipated to resume close contact with other young children, at home or in day-care, should receive rifampin immediately after completing treatment for their illness. Therapy for systemic disease does not reliably eradicate respiratory carriage of Hib, and some physicians may wish to give rifampin to all index patients.

7. In day-care classrooms in which children are to receive chemoprophylaxis, children who have received the Haemophilus b polysaccharide vaccine should also receive rifampin. Although these children are felt to be at decreased risk for disease, the vaccine probably does not affect carriage of the organism, which they may pass on to susceptible classmates.

8. Children who have had invasive Hib disease when they were under 24 months of age should still receive the vaccine according to previous recommendations, since most children under 24 months of age fail to mount an immune response to the clinical disease.

9. Satisfactory response to the vaccine is not consistent among children 18 to 23 months of age, and most authorities believe that these children should be revaccinated. Although data on the precise timing of this second dose are not currently available, it would be reasonable to reimmunize 2 to 12 months after the initial dose but not before 24 months of age. Previous immunization does not change the immune response or adverse reaction to a subsequent dose of the vaccine.

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