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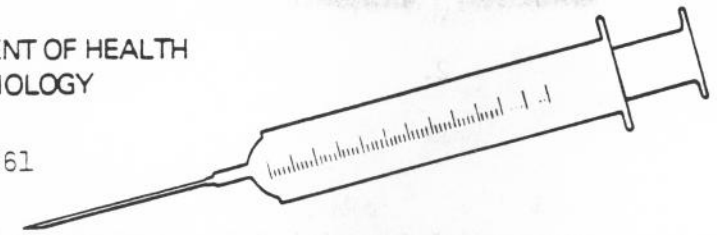

EPIDEMIOLOGY BULLETIN

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PREVENTION OF SECONDARY CASES OF HAEMOPHILUS INFLUENZAE TYPE B DISEASE*

Haemophilus influenzae type b is the leading cause of meningitis in the United States, resulting in an estimated 8,000-11,000 cases per year (1,2). Age-specific incidence rates are highest among children less than 1 year of age and decrease steadily thereafter. The case-fatality ratio is approximately 3%-7%, and neurologic sequelae are common. In addition, H. influenzae type b causes an estimated 6,000 cases a year of other invasive diseases, including epiglottitis, pneumonia, cellulitis, and bacteremia (3).

An experimental vaccine composed of the polysaccharide capsule of the organism has been shown to be effective in children over the age of 18 months (4). However, the vaccine is poorly immunogenic and not protective in children under this age, the group at highest risk of disease. Work is continuing on development of an efficacious vaccine for this age group.

Recent studies have shown an increased risk of disease among close contacts of persons with H. influenzae disease, suggesting a need to consider chemoprophylaxis for prevention of secondary cases, pending development of a satisfactory vaccine.

Risk of secondary disease: Six studies have estimated the risk of disease among household contacts of cases in the month following onset of disease in the index case (3,5-9). Attack rates varied substantially with age; the rate was 3.8% among children under 2 years of age, 1.5% among children 2-3 years of age, 0.1% among children 4-5 years of age, and 0% among contacts over the age of 6 years. The attack rate for all ages was 0.3%. This represents approximately a 600-fold increase in risk, compared with the risk in the population at large. Fifty percent of associated cases occurred within 3 days of onset in the index case and 75% within 7 days (Figure 1) (3,5-9).

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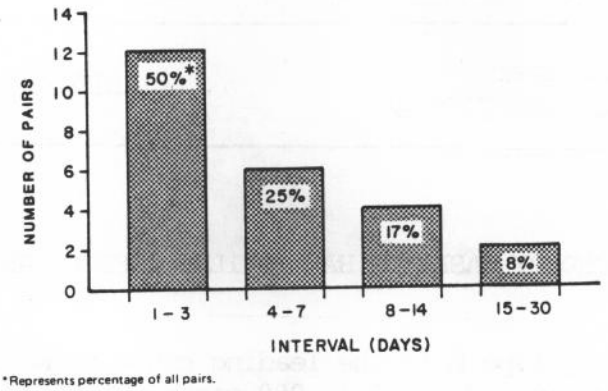
*These recommendations were developed by CDC in consultation with James Chin, MD, Chief, Infectious Diseases Section, California Department of Health Services; Vincent A. Fulginiti, MD, Chairman, Committee on Infectious Diseases, American Academy of Pediatrics; Gregory R. Istre, MD, Acting State Epidemiologist, Oklahoma State Department of Health; Arnold L. Smith, MD, Chief, Division of Infectious Diseases, Children's Orthopedic Hospital and Medical Center, Seattle, Washington; and Joel I. Ward, MD, Director of Medical Epidemiology and Assistant Professor of Pediatrics and Medicine, Harbor-UCLA Medical Center, Torrance, California. Reprinted from MMWR 1982; 31: 672-680.

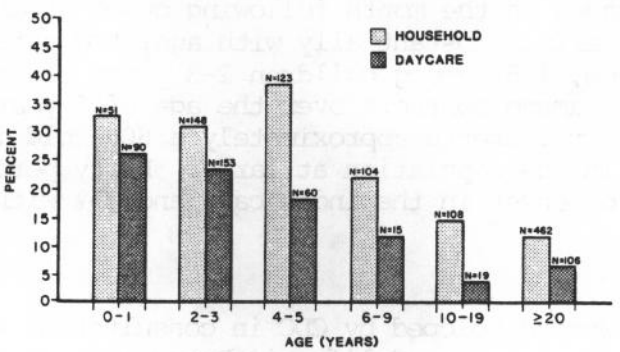
FIGURE 1. Interval Between Onset of Primary and Associated Cases of Haemophilus influenzae Type b Disease



*Represents percentage of all pairs.

Whether increased risk of disease occurs in day-care center contacts of children with invasive H. influenzae disease has not been resolved. Numerous clusters of cases in day-care centers have been reported, but only one study has looked systematically at attack rates in day-care centers contacts; in that study, 1% (1/91) of day-care center contacts less than 4 years of age acquired invasive disease in the month after the index case, compared with 2% (3/131) of household contacts less than 4 years of age (9). Carriage rates among contacts were only slightly higher in households than in day-care centers (Figure 2) (9). This study looked only at contacts in the same classroom as the index case.

FIGURE 2. Carriage Rates of H. influenzae Type b in Contacts, by Age of Contact and Setting Exposed



It is not known whether the risk of secondary cases is different for persons in contact with a case with meningitis than for those in contact with cases with epiglottitis or other invasive H. influenzae diseases. Carriage rates among contacts of meningitis patients have been reported as lower than carriage rates among contacts of patients with other clinical syndromes (9), and secondary cases have been reported among both groups. At this time, all index cases with invasive H. influenzae disease are considered to increase the risk for contacts.

Efficacy of Chemoprophylaxis: Initial studies focused on usefulness of various antimicrobial agents to eliminate nasopharyngeal carriage of H. influenzae type b. Ampicillin, trimethoprim-sulfamethoxazole, erythromycin-sulfisoxazole, and cefaclor were shown to eliminate carriage in fewer than 70% of culture-positive contacts. Also, in persons with H. influenzae disease, pharyngeal carriage of the organism has been shown to persist following intravenous therapy with chloramphenicol or ampicillin.

Rifampin in a dosage of 10 mg/kg per dose* administered twice a day for 2 days, the regimen currently recommended for meningococcal chemoprophylaxis, failed to eradicate carriage in as many as 36% of culture-positive individuals (9,10). However, rifampin in a dosage of 20 mg/kg per dose* once daily for 4 days (maximum dose 600 mg) eradicated carriage in 90%-100% of contacts treated (9, 11, 12).

A recent multicenter, randomized, placebo-controlled trial among both household and day-care center contacts has evaluated the efficacy of rifampin chemoprophylaxis in preventing secondary cases of H. influenzae disease. The study included day-care centers in which at least 75% of those present received chemoprophylaxis. Pilot studies had demonstrated that, if fewer than 75% participated, rates of new acquisition of H. influenzae carriage among those receiving either rifampin or placebo were similar. Four secondary cases occurred among the 800 placebo-treated contacts in contrast to no cases among the 1,166 rifampin-treated contacts ($p = 0.03$). Analysis of attack rates among children under 4 years old by place of exposure showed a trend toward efficacy in both households (3/131 placebo recipients vs. 0/173 rifampin recipients, $p = 0.08$) and day-care centers (1/91 placebo recipients vs. 0/264 rifampin recipients, $p = 0.26$), but the small number of secondary cases precluded detailed analysis of subgroups (9). Anecdotal reports have appeared about the failure of rifampin to prevent secondary cases (13).

Implementation of chemoprophylaxis: Mixing rifampin with applesauce results in peak serum and salivary concentrations that are not significantly different from those obtained with a specially prepared suspension (14). The applesauce mixture is the formulation used in the multicenter trial examining the prevention of secondary cases (9). A suspension of rifampin can also be prepared in United States Pharmacopeia (USP) syrup.

Side effects of rifampin in the 20 mg/kg dosage occurred in 20% of recipients, compared with 11% of placebo recipients. Side effects included nausea, vomiting, diarrhea, headache, and dizziness. The rate was similar to the 24% rate of adverse effects in recipients of rifampin at a dosage of 10 mg/kg. No serious adverse reactions occurred (9). Orange discoloration of urine was noted in 84% of rifampin recipients. Rifampin usage may also cause discoloration of soft contact lenses or ineffectiveness of oral contraceptives.

Concern has been raised about the possibility of developing rifampin-resistant H. influenzae isolates. None of the isolates from index patients or contacts was rifampin-resistant in the multicenter chemoprophylaxis trial (9), although an occasional rifampin-resistant strain has been reported. Monitoring strains causing invasive disease for development of rifampin resistance will be important for assessing the continued usefulness of rifampin as a chemoprophylactic agent.

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*Dose is halved for neonates--see below.

Questions have been raised about the difficulties of coordinating and implementing chemoprophylaxis in a day-care center. These concerns are especially relevant in view of the observation noted previously that chemoprophylaxis is unlikely to be effective if fewer than 75% of contacts actually receive rifampin. Several approaches have been successfully used. The local health department in Sarasota, Florida provided rifampin following consultation with private physicians. The Oklahoma State Health Department distributed a letter from the health department to contacts containing information about the disease and the risk of secondary spread, and recommending that parents contact their physicians for a rifampin prescription. State and local health departments should collaborate with private practitioners to monitor the completeness and timeliness of participation in chemoprophylaxis. Studies to document the risk of secondary cases with and without chemoprophylaxis and to evaluate the rifampin sensitivity of isolates causing invasive disease should also be considered. As such data become available, appropriate changes in these recommendations can be made.

Recommendations: In view of the increased risk of disease in household contacts less than 4 years of age and the efficacy of rifampin in eliminating carriage of H. influenzae organisms and preventing secondary cases of disease, it is recommended that:

1. Contacts who develop symptoms suggestive of H. influenzae type b disease, such as fever or headache, should be evaluated promptly by a physician.

2. In any household in which a case of invasive H. influenzae disease has occurred and in which another child less than 4 years of age resides, all members of the household, including adults, should receive rifampin in a dosage of 20 mg/kg per dose once daily (maximum dose 600 mg/day) for 4 days; dose for neonates (<1 month) is 10 mg/kg once daily for 4 days.

3. In day-care center classrooms in which a case of H. influenzae disease has occurred and in which children less than 4 years of age are present, all parents should be notified (preferably in writing) regarding occurrence of a case and the possibility of increased risk to their children. The symptoms to look for, the usefulness of rifampin chemoprophylaxis, and the need for prompt medical evaluation if symptoms occur should be stated. All students and staff in the classroom should be considered for chemoprophylaxis according to the above regimen. It should be noted, however, that the data on risk of secondary spread and efficacy of chemoprophylaxis in day-care centers are less complete than for household contacts.

4. Chemoprophylaxis should be instituted as rapidly as possible following onset of disease in the index case. If more than 7 days have passed since the last contact with the index case, chemoprophylaxis is probably not indicated.

5. The index case should be treated with the same rifampin regimen before discharge from the hospital.

6. Nasopharyngeal carriage studies should not be employed as a guide for chemoprophylaxis because of the lack of correlation of carriage with risk of disease and because the time required to complete such studies would delay implementation of chemoprophylaxis.

7. Rifampin should not be used in pregnant women, because it is teratogenic in laboratory animals.

Editor's Comment: Chemoprophylaxis of day-care center contacts presents more of a logistic problem than prophylaxis of household contacts. Given the current controversy surrounding the indications for chemoprophylaxis (15) and the differences among individual situations, no uniform approach to this problem by all local health departments can be expected. Physicians, or their offices, and hospitals must report promptly every case of invasive H. influenzae in a child attending a day-care center to the local health department. If this report is not from a physician, the local health department will confirm the diagnosis with the attending physician and then coordinate with day-care center management the notification of parents. In most situations a decision will be made to offer rifampin chemoprophylaxis, and to that end, it would be most appropriate to refer day-care staff members and children to their private physicians. In such a situation, however, the local health department should act to ensure that all who seek chemoprophylaxis can indeed obtain it in a timely fashion.

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MONTH: January, 1983

DISEASE	STATE					REGIONS				
	THIS MONTH	LAST MONTH	TOTAL TO DATE 1983	TOTAL TO DATE 1982	MEAN 5 YEAR TO DATE	THIS MONTH N.W.	N.	S.W.	C.	E.
CHICKENPOX	105	92	105	67	98	12	38	37	2	16
MEASLES	1	0	1	8	15	0	1	0	0	0
MUMPS	5	5	5	4	12	3	1	0	0	1
PERTUSSIS	1	1	1	0	1	0	1	0	0	0
RUBELLA	0	0	0	5	3	0	0	0	0	0
MENINGITIS – ASEPTIC	21	15	21	4	10	2	2	2	3	12
BACTERIAL	27	18	27	9	22	5	3	4	6	9
ENCEPHALITIS – INFECTIOUS	6	5	6	1	2	0	0	3	1	2
POST-INFECTIOUS	1	0	1	0	1	0	0	0	0	1
HEPATITIS A (INFECTIOUS)	17	13	17	14	19	1	2	4	3	7
B (SERUM)	46	33	46	31	37	5	7	12	15	7
SALMONELLOSIS	75	89	75	78	62	8	15	9	24	19
SHIGELLOSIS	13	10	13	21	15	2	3	8	0	0
TUBERCULOSIS – PULMONARY	15	52	15	32	–	–	–	–	–	–
EXTRA-PULMONARY	6	11	6	2	–	–	–	–	–	–
SYPHILIS (PRIMARY & SECONDARY)	53	60	53	50	45	1	9	2	10	31
GONORRHEA	1719	1638	1719	1599	1660	–	–	–	–	–
ROCKY MOUNTAIN SPOTTED FEVER	0	0	0	0	–	0	0	0	0	0
RABIES IN ANIMALS	52	94	52	16	4	6	46	0	0	0
MENINGOCOCCAL INFECTIONS	7	6	7	4	6	1	1	1	2	2
INFLUENZA	7	16	7	9	967	0	0	3	1	3
MALARIA	1	2	1	1	2	0	0	0	1	
OTHER: Hepatitis Unspec.	10	8	10	6	16	1	4	2	1	2

COUNTIES REPORTING ANIMAL RABIES: Arlington 1 raccoon; Augusta 1 raccoon; Fairfax 1 skunk 28 raccoons; Fauquier 1 raccoon; Frederick 1 cat, 1 skunk, 1 raccoon; Highland 1 raccoon, Loudoun 1 fox; 10 raccoons; Prince William 1 fox, 4 raccoons.

Occupational illnesses: Occupational pneumoconiosis 13; Occupational hearing loss 15; Asbestosis 5.

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