EPIDEMIOLOGY SECTION

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HAEMOPHILUS INFLUENZAE DISEASE: PREVENTION OF SECONDARY CASES

Haemophilus influenzae is the most common cause of bacterial meningitis in the United States, accounting for an estimated 8,000 - 11,000 cases per year (1). The mean incidence rate for the disease in Connecticut from 1979 through 1982 was 2.0 cases/100,000 population/year. This rate is consistent with those found among other population groups in the U.S. Age specific attack rates are highest among children less than one year of age and decrease steadily thereafter. Ninety-two percent of cases in Connecticut occurred in the two month to five year age group. Rare cases were also reported in individuals greater than 50 years of age.

Meningitis due to ampicillin-resistant strains of H. influenzae type b were first reported in 1972. Such resistance, due to plasmid-mediated B-lactamase production, has increased in frequency since that time. In Connecticut, 4.6% of isolates tested in 1979 were resistant to ampicillin, increasing to 15.2% in 1980 and 41.8% in 1981. Such increases have been documented in other states and nationally. Colorado reported that the percentage of resistant isolates in that state had increased from 4% in 1977 to 25% in 1980 (2). National rates range from 5-20% (3,4,5). Because of this increasing resistance to ampicillin, initial treatment with chloramphenicol is recommended either alone or in conjunction with ampicillin until antibiotic susceptibility test results are available.

The case fatality rate (CFR) for meningitis due to H. influenzae ranges from 5 to 14%. In Connecticut, the CFR for H. influenzae was 5-8% (1979-1981). Neurologic sequelae are common. In addition, at the national level, approximately 6,000 cases a year of other invasive diseases are attributed to H. influenzae. These include epiglottitis, pneumonia, cellulitis, and bacteremia.

RISK OF SECONDARY DISEASE

Recent studies have identified an increased risk of disease among close contacts of persons with H. influenzae disease. While an experimental vaccine has been shown to be effective in children over the age of 18 months, it is poorly immunogenic and not protective in children under this age, that group at greatest risk of disease (6). Work is continuing on developing a vaccine which is efficacious for this age group. Until such time, there is a need to consider chemoprophylaxis for prevention of secondary cases.

Six studies have estimated the risk of disease among household contacts of cases in the month following onset of disease in the index case. Attack rates varied substantially with age: 3.8% among children less than two 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 overall attack rate was 0.3%. This represents approximately a 600 fold increase in risk, compared to the population at large (7). Fifty percent of associated household cases occurred within three days of onset of the index case and 75% within seven days (7).

The issue of whether or not day-care center exposures are associated with increased risk of disease has not been resolved. While numerous clusters of cases have been reported in the day care setting, only one study has looked systematically at attack rates in day-care center contacts (8). One percent of day care center contacts (1/91) less than four years of age acquired invasive disease within one month after the index case compared with 2% (3/131) of household contacts in the same age group.

Also unanswered is the question of whether or not the risk of secondary cases is different for persons in contact with a case of meningitis than for those in contact with other types of invasive disease due to H. influenzae. At this time, all index cases with invasive H. influenzae disease are considered to increase the risk for contacts.

EFFICACY OF PROPHYLAXIS

Initial studies evaluated the usefulness of various antimicrobial agents in eliminating nasopharyngeal carriage of H. influenzae type b. Ampicillin, trimethoprim-sulfamethoxazole, erythomycin-sulfisoxazole, and cefaclor were shown to eliminate carriage in fewer than 70% of culture positive contacts. Pharyngeal carriage has also been shown to persist in persons with H. influenzae disease following intraveneous therapy with chloramphenicol or ampicillin.

Rifampin, in a dosage of 10 mg/kg per dose administered twice a day for two days (the regimen recommended for meningicoccal chemoprophylaxis), successfully eradicated carriage only 64% of the time (8,9). 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 (7).

A multicenter, randomized, placebo-controlled trial among both household and day-care contacts has evaluated the efficacy of rifampin prophylaxis in preventing secondary cases of H. influenzae disease. The study included only those 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. In this study, four secondary cases occurred among the 800 placebo-treated contacts compared with no cases among the 1,166 rifampin treated contacts ($p=0.03$). The small number of secondary cases precluded further analysis by subgroup (9).

RECOMMENDATIONS

In view of the increased risk of disease in household contacts less than four years of age and the efficacy of rifampin in eliminating carriage of H. influenzae and preventing secondary cases of disease, the Centers for Disease Control and the American Academy of Pediatrics Committee on Infectious Diseases have developed recommendations for chemoprophylaxis of contacts (7,10):

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 four 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 four days; the dose for neonates (less than one month) is 10 mg/kg once daily for four days.

3. In day-care center classrooms in which a case of H. influenzae disease has occurred and in which children less than four 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 evalution 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 seven days have passed since the last contact with the index case, chemoprophyalxis 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.

IMPLEMENTION

Mixing rifampin with applesauce results in peak serum and salivary concentrations that are not significantly different from those achieved with a specially prepared suspension (11). A suspension of rifampin can also be prepared by the pharmacy mixing simple syrup and fractional doses calibrated from the suspension concentration.

Side effects, including nausea, vomiting, diarrhea, headache, and dizziness, occurred in 20% of rifampin recipients of the 20 mg/kg dosage versus 11% in placebo recipients. No serious adverse reactions occurred. Orange discoloration of urine is common. Rifampin may also cause discoloration of soft contact lenses or ineffectiveness of oral contraceptives.

There are concerns that the use of rifampin for prophylaxis will encourage the development of rifampin-resistant H. influenzae. Occasional rifampin-resistant strains have been reported; however, none of the isolates from index patients or contacts in the CDC multicenter study was resistant to rifampin (7). Monitoring strains for development of rifampin resistance will be important for assessing the continued usefulness of this agent for chemoprophylaxis.

As more data become available documenting the risk of secondary cases with and without chemoprophylaxis, appropriate changes in these recommendations can be made.

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ERRATA

HEPATITIS B VACCINE
Vol. 1, No. 2, 1982
Table 1, column 4, line 4 annual incidence 1-10** should have no asterisks Table 1, column 4, line 9 annual incidence 13-20 should read 13-20**

RABIES PREVENTION IN CONNECTICUT
Vol. 1, Nos. 3 & 4, 1982
Figure 1, column 3, line 2 "0.06 ml (9IV)[b] should read "0.06 ml (9IU)[b] per lb. body weight"

p. 4, Question 7, Comments line 10 "after hours and weekends 566-2779" should read "after hours and weekends 566-2279"

REPORTED MORBIDITY - DECEMBER, 1982

	AMEBIASIS	BOTULISM	BRUCELLOSIS	ENCEPHALITIS (TOTAL)	Primary	Post	FOODBORNE OUTBREAKS	GONORRHEA	HEPATITIS A	HEPATITIS B	HEPATITIS NON A NON B	HEPATITIS UNSPECIFIED	LEGIONELLOSIS	LEPROSY	MALARIA	MEASLES	MENINGITIS (All Types)	Aseptic	Hemophilus influenzae	Meningococcal	Other	MUMPS	PERTUSSIS	PSITTACOSIS	RABIES IN ANIMALS	REYE'S SYNDROME	ROCKY MT. SPOTTED FEVER	RUBELLA	SALMONELLA	SHIGELLA	SYPHILIS	TUBERCULOSIS (TOTAL)	Pulmonary	Other	TYPHOID FEVER
TOTAL FOR DEC	8	0	0	3	3	0	1	843	18	119	3	5	4	1	2	0	44	10	12	8	14	6	0	0	0	0	1	1	87	26	17	27	21	6	0
CUMULATIVE 1982*	40	1	3	30	25	5	21	8830	87	513	25	45	39	2	18	6	261	84	55	58	64	29	5	2	6	1	3	6	909	955	152	151	112	39	2
CUMULATIVE 1981	34	0	1	39	34	5	25	9687	190	516	NR	70	51	1	26	10	295	93	68	71	63	53	2	2	6	4	3	13	841	436	141	163	132	31	10

*Subject To Change When Final Report Is Submitted To CDC

REFUGEE HEALTH PROGRAM

In the fall of 1980, the Department of Health Services received federal funds to establish a Refugee Health Program. The program complements the State's Refugee Resettlement Plan by assuring that health problems do not impede a refugees' progress toward self-sufficiency. The program also assures that refugees' personal health problems are addressed expeditiously, decreasing the likelihood of any adverse efferts on the public health.

The program provides annual and quarterly reports on identified health problems of refugees to the Centers for Disease Control, coordinates health assessment activities for all refugees in Connecticut, and provides information to those involved in refugee health care.

Address inquiries about the program to:
Joseph Marino
Department of Health Services
Preventable Diseases Division
Refugee Health Program
79 Elm Street
Hartford, CT 06106
566-3099

HERPES SYMPOSIUM PLANNED

A symposium on Herpes simplex virus (HSV) will be held on March 30, 1983 from 8:30 a.m. to 3:45 p.m. at the Lord Cromwell Inn, Cromwell, Connecticut. It is designed for physicians, nurses and concerned health care professionals. Continuing education units (CEUs) have been applied for. Topics and speakers include: "HSV Precautions for Health Care Professionals: Facts and Figures on HSV", - James Goodrich, M.D., Centers for Disease Control; "Current Research in HSV, and Care of the Ob/ Gyn Patient" - Michael Baggish, M.D., Mt. Sinai Hospital; "Psychological Responses to Genital Herpes", Oscar Gillespie, Ph.D., Fordham University; "Nursing and the Herpes Patient: Coordinating H.E.L.P. Group" - Pamela McKinnon, P.H.N.; "Laboratory Diagnosis of Herpes", - Douglas Moore, Ph.D., State of Connecticut.

The cost will be $56.00 for physicians and $40.00 for nurses. If you want an application, contact David Fuller, STD Program, State of Connecticut Department of Health Services, 79 Elm Street, Hartford, CT 06106.

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