Bacterial Respiratory Infections and Otitis Media

EUGENE D. SHAPIRO, MD

Children who attend group day care are at increased risk of a number of bacterial infections of the respiratory tract. This article focuses on three such infections that are particularly important because of either their potential severity (infections caused by *Haemophilus influenzae* type b or by *Neisseria meningitidis*) or their frequency and associated morbidity (otitis media).

**HAEMOPHILUS INFLUENZAE TYPE B Colonization, Pathogenesis, and Risk of Disease**

*Haemophilus influenzae* type b (Hib) is the most common cause of serious invasive bacterial infections (such as meningitis and epiglottitis) among children who attend group day care. Hib is part of the normal flora of the upper respiratory tract. Strains of Hib are asymptptomatically carried in from 1% to 5% of the population at any given time. The carriage rate is lowest in adults and very young children and highest in preschool-aged children. However, under certain conditions, such as in day-care centers, carriage rates may be much higher. For example, in day-care facilities in which a case of invasive Hib disease occurred, point-prevalence rates of colonization with Hib among other children in the group have been as high as 58% in day-care centers and 91% in smaller day-care homes.\(^1\)

Rates of colonization with Hib also may be high in some day-care centers where no cases of invasive disease occurred, which indicates that the organism is periodically introduced by and transmitted among asymptomatic children. The point-prevalence of colonization with Hib at such centers has been reported to be as high as 15% to 25% at times. In one prospective, longitudinal study conducted at a day-care center in Dallas where no invasive infections occurred, the average rate of colonization with Hib
The risk of Hib infection associated with attendance of group day care diminishes with increasing age so that there is no longer a statistically significant increased risk by 2 years or, in some studies, by 3 years of age.

was 10%.\(^2\) Seventy-one percent of the children 18 to 35 months of age and 48% of the children 36 to 71 months of age were colonized at some time during the 18 months of the study.

Person-to-person transmission of Hib occurs via respiratory droplets or via direct contact with oral secretions. Close contact among individuals (as occurs in day-care centers) potentiates transmission. There is some evidence that concomitant viral infections also may potentiate both colonization and invasive disease. Relatively prolonged, asymptomatic colonization with the organism is the rule. It is not known at what point after initial colonization by the organism that invasive disease may occur. Given infection of a susceptible host, the organism invades the bloodstream from the nasopharynx and disseminates to cause meningitis and other systemic illnesses.

The risk of acquiring Hib infection in day-care centers can be divided into the risk of primary infection and the risk of secondary infection. Primary Hib infections are infections that occur in children who are not known to have had direct exposure (within the preceding 30 days) to another person with an invasive Hib infection. Secondary Hib infection refers to an invasive Hib infection that occurs in a close contact of another person with invasive Hib infection. A case is arbitrarily defined as secondary if it occurs more than 24 hours but less than 31 days after the onset of the disease in the index case, although in the setting of group day care, most investigators have extended the interval for secondary cases to 60 days. Cases that occur within 24 hours of each other are referred to as "co-primary" cases.

There is evidence from several different studies that the attendance of group day care is associated with a substantially increased risk of primary Hib infection.\(^3,4\) Most of these studies found that children who attended group day care were at a two to five times greater risk of acquiring Hib infection than children who did not attend group day care. Most studies found that the youngest children (those under 1 year of age) in day care were at the greatest risk, with a 10 to 280 times increased risk of Hib infection compared to infants not in group day care. The risk associated with attendance of group day care diminishes with increasing age so that there is no longer a statistically significant increased risk by 2 years or, in some studies, by 3 years of age. In most of these studies, a "dose-response" effect was found, with the risk increasing as the time spent in day care and the number of children in the day care group increased.

Secondary Hib Disease

Close contacts of children with Hib infections have been demonstrated to have very high rates of Hib colonization. Because of the high prevalence of colonization and the frequent and relatively intimate contact among children who attend group day care, there is an increased likelihood that uncolonized members of the group will encounter and become colonized with Hib. In susceptible individuals, invasive disease may follow colonization. Thus, it may not be contact with the index patient per se that puts contacts at increased risk. Rather, the index patient serves as a marker that there is a high prevalence of colonization with Hib in the group of which the index case is a member. Although it is commonly assumed that the index case transmits the organism to the secondary case, it is more likely that both have acquired the infection from common exposure to one or more asymptomatic carriers.

The major risk factors for secondary spread of Hib infection are the nature of the exposure and the age of the contacts. The risk of secondary disease is greatly elevated among children who are household contacts of an index case. Household contacts of an index case who are less than 6 years of age have a 585 times greater age-adjusted risk of developing invasive Hib infection than the general population. In a large national study, the risk of secondary infection among household contacts was 6% for those under 1 year of age, 2% for those 1 to 3 years of age, and 0.5% for those 4 to 5 years of age.\(^3\) Older children and adult contacts are at little or no increased risk. The risk of secondary infection for contacts is similar regardless of the clinical manifestations of Hib infection in the index case (e.g., meningitis vs epiglottitis). The risk is greatest in the first week after the onset of illness in the index case and diminishes thereafter.

It might be expected that rates of secondary illness among contacts of an index case who attends group day care would be similar to those of household contacts because of the increased opportunity for exposure in the day-care setting. On the other hand, unrelated children in group day care may be less likely than siblings of an index case to share susceptibility factors that increase the risk of Hib infection. In fact, the data on the risk of secondary Hib infections in group day care have been conflicting. In one retrospective study conducted by the Centers for Disease
Control in three different regions of the country, the risk of secondary infection among children in the same day-care classroom as an index case was 2.7% for children under 2 years of age who were not given chemoprophylaxis with rifampin. There was no increased risk for older children or for children who were in a different classroom than the index case. In addition to age, risk was directly related to the number of hours per week that a child attended day care. In a different prospective study conducted in Oklahoma, of children who did not receive rifampin prophylaxis, 1% of classroom contacts under 2 years of age of an index case developed secondary Hib infections.

By contrast, in two other prospective studies on the risk of secondary Hib infection in day-care facilities, the risk among untreated classroom contacts under the age of 2 was 0% in Minnesota (0/370) and 0% in Dallas, Texas (0/361). The rates of secondary Hib infection among untreated classroom contacts 24 months of age and older were 0% (0/716) and 0.3% (1/313), respectively, in Minnesota and in Dallas. These data suggest that there is variability in the risk of secondary Hib disease among children who attend group day care.

Prevention

When a child who attends group day care develops an invasive Hib infection, it is generally impossible, without conducting molecular analyses of the bacteria, to tell whether the infection was acquired in the day-care center or elsewhere. Regardless of where the infection was acquired, it must be assumed that other children in the group are at increased risk of Hib infection. Rifampin, an antimicrobial agent, which, after oral administration, reaches high concentrations intracellularly and in saliva and tears, is effective in eradicating colonization with Hib. Consequently, it may be possible to prevent some cases of secondary Hib infection through rifampin chemoprophylaxis of groups that are at risk. The goal of chemoprophylaxis is to protect the susceptible child from acquiring Hib from contacts by eliminating colonization with Hib in all members of the group of close contacts (i.e., the day-care group). Adults and older children in such groups may transmit Hib to susceptible children even though they are at little risk of developing invasive infection themselves. Consequently, if it is decided to initiate chemoprophylaxis, rifampin should be administered to all members of the group, even to older children and to adults.

While recommendations for chemoprophylaxis to prevent secondary Hib infections in households have been widely accepted, there has been disagreement about the use of rifampin for children enrolled in day-care centers. First, because the data on the risk of secondary Hib infection among children who attend group day care are conflicting, some believe that the risk is too low to justify the effort of getting all the children in a day-care classroom to take rifampin. Furthermore, because there are usually many different physicians involved, it often is difficult to institute a uniform policy. Also, in the day-care setting, children who are treated may soon become recolonized with Hib from untreated siblings.

When deciding whether chemoprophylaxis to prevent secondary infections is indicated, the potential benefits and risks need to be weighed. The potential benefits of chemoprophylaxis are likely to be greatest when the risk of secondary Hib infection is greatest (i.e., when the other children in the group are young [<18 to 24 months of age] and attend the day-care center for many hours each day) and when it is deemed likely that most members of the group will take the rifampin. The potential risks of rifampin are relatively few; it is quite safe when administered in a brief prophylactic regimen. It may, however, cause gastrointestinal distress, it is quite expensive, and it turns the urine and tears a reddish-orange color. Pregnant women should not take rifampin. The appropriate dosage of rifampin for prophylaxis of contacts is 20 mg/kg/dose (maximum dose 600 mg/dose) once a day for 4 days for preventing Hib secondary infections.

The most effective weapon to prevent Hib infections in group day care is vaccination. Now that highly effective conjugate Hib vaccines are available, all infants and young children should receive the recommended regimen of one of the licensed vaccines. Because it usually takes at least 1 to 2 weeks after vaccination before concentrations of antibodies against Hib rise substantially (and much longer for younger children who require multiple doses of the vaccine), the use of vaccines for postexposure prophylaxis for unimmunized children is not an optimal strategy. Rather, universal immunization of children at the earliest recommended age (i.e., beginning at 2 months) may prevent most Hib disease in group day care.

NEISSERIA MENINGITIDIS

Like Hib, N meningitidis may cause serious invasive infections such as meningitis and septic shock. There are nine different serogroups of meningococci (A, B, C, D, 29E, W-135, X, Y, and Z) that are classified based on their specific capsular polysaccharides. Approximately half of the infections in the United States are caused by serogroup B. The presumed pathogenesis of disease
Acute and chronic effusions of the middle ear are common complications of upper respiratory infections in young children, particularly among children under the age of 2. Otitis media is the most common cause of acquired hearing loss in children and is responsible for a tremendous amount of less severe morbidity. The bacteria that commonly cause otitis are *Streptococcus pneumoniae*, *H influenzae* (non-typable), and *Moraxella catarrhalis*.

Children who attend group day care are at increased risk of developing otitis media. Most studies suggest that compared to their peers who do not attend group day care, children less than 2 years of age who attend group day care experience about 50% more episodes of otitis media. The reason for the increased frequency of otitis media in these children presumably is simply the well-documented increased frequency of viral infections of the upper respiratory tract among children who attend group day care. These infections predispose children to otitis media because they cause eustachian tube dysfunction, which leads to impaired ventilation of the middle ear. The viral infection also alters the normal function of the epithelial cells that line the upper respiratory tract.

Transmission and Prevention

Unlike with infections caused by Hib and *N meningitidis*, there is no evidence that otitis media can be transmitted from person to person. On the other hand, the viral infections that predispose children to otitis media clearly are transmitted from child to child. Unfortunately, however, there are no effective interventions available to prevent the spread of common viral respiratory infections among children in group day care.

Prophylactic antimicrobials have been shown to be effective in reducing the number of recurrences in children with recurrent acute otitis media. Prophylaxis with sulfisoxazole (50 mg/kg), amoxicillin (20 mg/kg), or trimethoprim (40 mg)/sulfamethoxazole (200 mg), each in a single daily dose, may be initiated in children with three documented episodes of acute otitis media in 6 months or four episodes in 12 months. Chemoprophylaxis usually is continued daily during the period of peak frequency of viral respiratory infections (generally the winter and spring months), but it may be extended for a longer period if necessary. It is important to distinguish children with recurrent episodes of acute otitis media (for whom chemoprophylaxis may be effective) from those with chronic effusions of the middle ear. Chemoprophylaxis will not be of benefit to the latter group. Pneumococcal polysaccharide vaccine has not been demonstrated to be efficacious in preventing otitis media.

**STREPTOCOCCUS PNEUMONIAE AND GROUP A STREPTOCOCCI**

Children who attend group day care have not been shown to be at increased risk of invasive infections...
caused by S pneumoniae (although S pneumoniae is responsible for many episodes of otitis media, for which children in group day care are at increased risk). However, there have been a number of reports of the isolation, from children with invasive infections as well as from asymptomatic carriers, of pneumococci that are resistant to or relatively resistant to antimicrobials such as penicillin or trimethoprim/sulfamethoxazole. Physicians should be aware of this problem if they are faced with a child who does not respond appropriately to conventional antimicrobial therapy.

Although generally a disease that affects older children, some outbreaks of respiratory infections caused by group A streptococci have been reported among children who attend group day care. In one study, during a 3-month period, 26% (55/214) of the children and adult staff members of a day-care center developed symptomatic infections of the upper respiratory tract associated with a throat swab that was positive for group A streptococci. Physicians should be aware that group A streptococci may be a significant pathogen in the day-care setting.

**SUMMARY**

Bacterial infections of the respiratory tract are an important potential problem for children who attend group day care. Immunization (for Hib) or chemoprophyaxis, when appropriate, should lessen the risk and help to control or prevent the problem in many instances.

**REFERENCES**


