Haemophilus Influenza: ***What's the Hubbub About?***

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There are many strains of *Haemophilus influenza* (*H. influenza*), but the most virulent strain is capsular Type B. This strain is responsible for invasive disease in humans and was the most common cause of early childhood meningitis prior to the introduction of the *Haemophilus influenza* Type B (Hib) vaccine in the late 1980s. It is for this reason that the *H. influenza* is our **Bug of the Month**.

What is H. influenza?

H. influenza is a gram-negative coccobacillary pathogen of humans that is found mainly in the upper respiratory tract. Since it requires a growth factor that is supplied by erythrocytes, it has acquired the name *haemophilus*, meaning blood-loving. Some strains of *H. influenza* produce a polysaccharide capsule, which allows it to evade phagocytosis and enhance its invasive potential. The most notable of these strains is *H. influenza* Type B (Hib).

Strains that lack the polysaccharide capsule are referred to as non-typeable because they do not react with the typing antiserum capable of identifying each of the six capsular types.

The respiratory tract of humans is colonized by *Haemophilus spp*, of which *H. parainfluenza* and non-encapsulated strains of *H. influenza* comprise 25% to 75% of isolates in approximately 3% to 5% of people that are carriers of Hib. The use of conjugate Hib vaccine results in reduced rates of nasopharyngeal colonization by Hib in infants.

Why the concern about Hib?

The Type B capsule is a main virulence factor in the pathogenesis of invasive disease. The capsule allows the organism to evade the host's immune mechanisms and allows it to successfully invade the bloodstream after it has colonized in the respiratory tract. While both typeable and non-typeable strains of *H. influenza* can lead to similar infections, the invasive infections, such as meningitis and epiglottis, are mainly caused by Hib. Non-typeable strains are responsible for non-invasive infections, such as otitis media, sinusitis, conjunctivitis and acute exacerbations of chronic bronchitis.

The clinical manifestations of Hib include the following:

- Meningitis
- Epiglottitis
- Pneumonia and empyema
- Cellulitis
- Bacteremia

How does H. Influenza Spread?

H. influenza is a commensal organism of the nasopharynx, colonizing up to 5% of children at any given time. It is transmitted by airborne droplets and direct contact with respiratory secretions. Individuals may be asymptomatically colonized for months, but an intercurrent viral illness may enhance local invasion and transmission of *H. Influenza*.

What are the risk factors for Hib?

Hib disease has an age-dependent susceptibility. Passive immunity is acquired transplacentally and through breast milk by passage of maternal antibodies to the infant. This immunity persists for the first six months of life. Peak attack rates have been observed at six months of age, declining thereafter, to the extent that the Hib disease is uncommon after the age of five.

The risk factors for invasive Hib disease include both host and exposure factors and are summarized in Table 1.

How can Hib be prevented?

Vaccination is the key to protect against Hib. Although a pure polysaccharide vaccine became available in 1985, it was not

effective among children < 18 months of age. The response to the vaccine was age dependent, it had poor immunogenicity in children < two years and did not boost antibody titre with repeated doses. To overcome these deficiencies, polysaccharide-protein conjugate vaccines were created.

Conjugation is the process whereby a polysaccharide is chemically bonded to a protein carrier. This turned the polysaccharide from a T-independent to a T-dependent antigen which greatly enhanced immunogenicity, particularly in young children. Conjugation also results in repeat doses of the Hib vaccine which elicit booster responses.

A number of Hib conjugate vaccines are licensed for use and their vaccination schedules vary; however, the general recommendation is that vaccinations start at two months of age. After two to three preliminary doses, more than 95% of infants will develop protective antibody levels with clinical efficacy ranging from 95% to 100%. As a result, Hib invasive disease has been nearly eradicated. The Hib vaccine is immunogenic in persons who are at increased risk of invasive disease (Table 1). Vaccination response varies according to the individual's level of immunodeficiency.

Table 1

Risk factors for haemophilus influenza Type B disease

Exposure related factors	Host factors
Household crowding	Race/ethnicity (elevated risk in African American and Aboriginal people)
Large household size	Chronic disease (sickle cell anemia, antibody deficiency syndromes, malignancies and chemotherapy)
Daycare attendance	Possibly gender (male > female)
Low socioeconomic status	
Low parental education levels	
School-age siblings	

What are the precautions of the Hib vaccine?

The Hib conjugate vaccine is contraindicated in patients known to have experienced anaphylaxis following a prior vaccination. Furthermore, it is important to delay vaccination in children with moderate to severe acute illnesses. Children under six weeks of age should not be vaccinated because an immunologic tolerance may occur.

How is Hib treated?

Proper diagnosis of Hib invasive disease is difficult because many agents may cause similar clinical manifestations. Therefore, it is prudent to treat conditions, such as meningitis, pneumonia and septic arthritis, based upon the clinical manifestation, availability of preliminary gram stain results and ultimately the final cultures and susceptibility profiles for the pathogens recovered. It is also important that local epidemiology be guided by antimicrobial choices because some strains of *H. influenza* are beta lactamase producers.

Any child under the age of four, who is not immunized and has been in contact with an individual with Hib (spent more than four hours a day, for at least five to seven days) is at an increased risk of acquiring the disease.

Rifampin prophylaxis, 20 mg/kg once daily, maximum dose 600 mg, for four days, eradicates the carrier state in approximately 95% of cases and significantly reduces the incidence of secondary cases in household members.

Rifampin prophylaxis is recommended for all household members including adults, excluding pregnant females, contacts younger than 48 months whose immunization with conjugate vaccine is incomplete, or immunocompromised children of any age. The rifampin must be given within seven days after the individual with Hib is hospitalized.

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