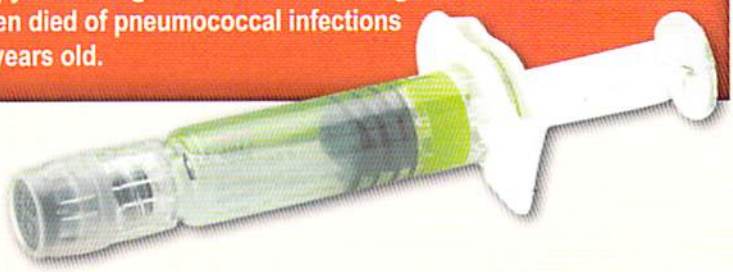
Pneumococcal Infections In Young Children : Management & Prevention

Diseases caused by the encapsulated Streptococcus pneumoniae (or pneumococcus) are a major public health problem worldwide. Pneumococcal infections are a common cause of acute otitis media, sinusitis, pneumonia, bacteremia and meningitis in young children (see figure). Pneumonia, bacteremia and meningitis constitute invasive pneumococcal diseases (IPD) that tend to occur at the extremes of age – children less than 5 years and the elderly. Infants under 1 year are at risk for pneumococcal bacteremia and meningitis, whereas children from 2 to 5 years old often develop pneumonia, empyema, acute otitis media or sinusitis. Immuno-deficient children such as those with HIV infections, receiving chronic steroid or immunosuppressant therapy are at higher risk of contracting IPD. In 2005, the World Health Organization estimated that up to 1 million children died of pneumococcal infections every year, most of whom were young children below 2 years old.



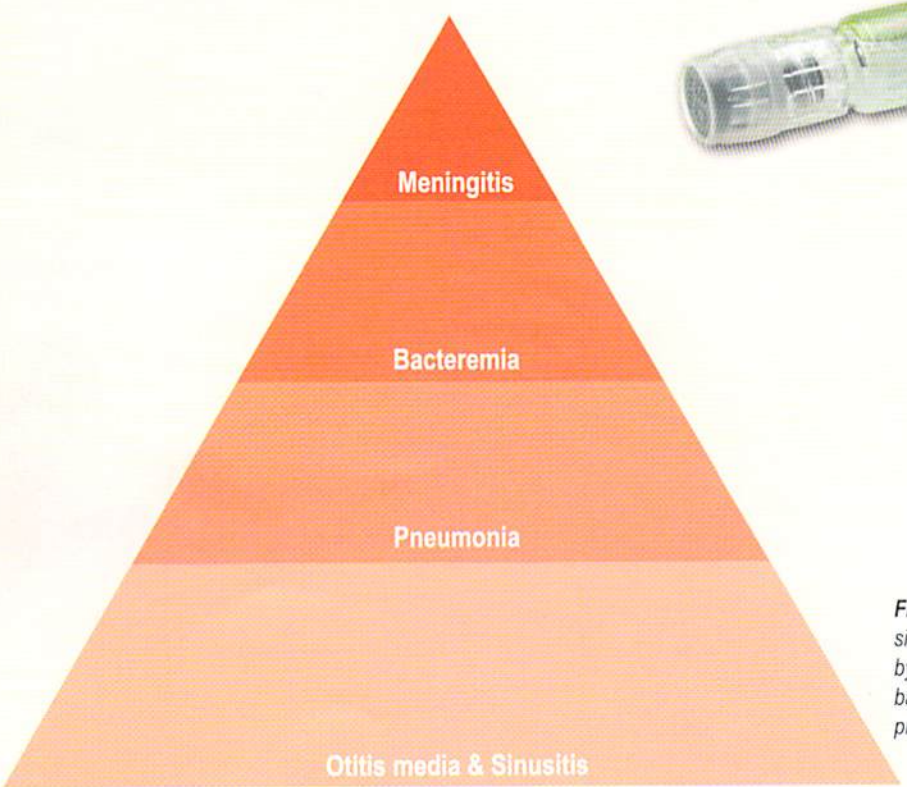


FIGURE *depicts the relative prevalence of otitis media & sinusitis, pneumonia, bacteremia and meningitis caused by Streptococcus pneumoniae (or pneumococcus). At the base of the pyramid are pneumococcal diseases of higher prevalence and lower severity.*

Disease Transmission

Pneumococci are transmitted by direct contact with respiratory secretions from patients and healthy carriers. Following incubation of up to 3 days, the infected child develops fever, cough and dyspnoea. Diagnosis of pneumococcal disease is based on bacterial identification in normally sterile sites, such as blood, cerebro-spinal fluid or tracheal aspirate. Mortality in pneumococcal meningitis is high. After recovery from IPD, the child may develop long-term sequelae such as hearing loss, neuro-developmental delay, seizures or intellectual disability.

Management

Treatment of IPD consists of a 7- to 14-day course of intravenous antibiotics, such as IV penicillins (augmentin) and macrolides. However, antibiotic resistance to the bacterium is growing over time and increasing with patient age. Hence the mortality and morbidity of pneumococcal disease is best managed by prevention through vaccination programs.

Pneumococcal conjugate vaccines (PCV) are approved for infants and toddlers. Introduction of the PCV in USA led to declining admission rates for all-cause pneumonia in children under 2 years old and lowering rates of antibiotic-resistant IPD. The "Expert Committee on Immunization" (ECI) of the Ministry of Health Singapore has recommended that PCV be included into the National Childhood Immunization Programme, since it has been shown to be safe and effective. Pneumococcal polysaccharide vaccines are not suitable for children under 2 years old because of inability to mount a response to them.

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7-Valent Pneumococcal Conjugate Vaccine (PCV7)

The currently licensed 7-valent pneumococcal conjugate vaccine (PCV7, marketed as Prevenar®) covers S. Pneumonia serotypes 4, 6B, 9V, 14, 18C, 19F and 23F. It is targeted for children from 6 weeks to 9 years. In the era before vaccination, the serotypes included in PCV7 represented about 86% of paediatric invasive strains of S. Pneumoniae in the USA.

The ECI recommends a schedule of 2 primary doses given at 3 and 5 months respectively, followed by a booster dose at age 12 to 24 months ("2 + 1" schedule). PCV7 can be concurrently administered with the other childhood vaccines (such as DTPw-polio-Hib-HBV) but in a separate syringe and at a separate intra-muscular injection site. Studies showed that co-administration of PCV with the routine DPT-polio vaccines did not affect vaccine efficacy. The efficacy, immunogenicity and safety of PCV7 administered to preterm (gestational age 32-36 weeks, birth weights 980-3320 grams) infants in an Italian study employing a "2+1" schedule (3, 5, 11 months) was similar to that for full-term infants.

In previously unvaccinated children who are under 5 years old, catch-up immunization is recommended but the number of doses depends on age. The ECI recommends that healthy children who are under 12 months old receive 2 primary doses of PCV7 eight weeks apart (minimum interval 4 weeks), followed by a booster dose given at least 8 weeks after the second dose of the primary series. In children who are 1 to 5 years old with asplenia, splenic dysfunction, compromised immunity or sub-optimal vaccine response, the ECI recommends that they receive 2 doses of PCV7, with an interval of 8 weeks between doses. In addition to PCV7, children aged 2 to 5 years in high risk groups should receive a single dose of the 23-valent pneumococcal polysaccharide vaccine (PPSV23, marketed as Pneumovax23®). The high risk groups include children with chronic heart/ lung/ kidney diseases, cochlear implants or splenic dysfunction.

While the protective efficacy of PCV7 against pneumococcal pneumonia and invasive disease has been documented in developing and developed countries, its efficacy against pneumococcal otitis media has been somewhat modest. In a study in Finland, PCV7 was shown to have efficacy against culture-confirmed pneumococcal otitis media of 34% and efficacy against any-cause otitis media of only 6 to 7%.

Children should not proceed with PCV7 vaccination if they had a serious (anaphylactic) allergic reaction to a previous dose of this vaccine or its components. The commonest adverse reactions to primary vaccination with 7-valent PCV were redness at the injection site and irritability. The duration of protection against IPD caused by vaccine serotypes is at least 2 – 3 years following primary PCV7 vaccination in infancy, although it could be longer.

10-Valent Pneumococcal Conjugate Vaccine

A 10-valent pneumococcal conjugate vaccine (PHiD-CV, marketed as Synflorix®) was developed containing 3 more serotypes (1, 5, 7F) than the PCV7 vaccine. It is a mixed carrier vaccine containing 8 capsular polysaccharides (1, 4, 5, 6B, 7F, 9V, 14 and 23F) conjugated individually to non-typeable Hemophilus influenza protein D and the remaining 2 conjugated to tetanus (serotype 18C) or diphtheria (serotype 19F) toxoids. The 10-valent PCV was found to be immunogenic against each of the 10 pneumococcal vaccine serotypes when co-administered with other childhood vaccines (such as the DTPw-polio-Hib-HBV, MMR and Rotavirus vaccines). It is given intra-muscularly.

A European study investigated the immunogenicity of a 10-valent pneumococcal conjugate vaccine that was administered as either a "2 + 1" schedule (consisting of primary doses at 3 and 5 months) or as a "3 + 1" schedule (consisting of primary doses at 3, 4, 5 months), followed by the booster dose at 11-12 months. The 10-valent vaccine was found to be immunogenic in both schedules, indicating that both regimens had elicited adequate priming. For most vaccine serotypes, a trend towards lower post-primary and post-booster immune response was observed in children primed with 2 instead of 3 vaccine doses. This trend appeared to be more pronounced for functional opsono-phagocytic activity response, but its clinical relevance was unknown.

The commonest adverse reactions to primary vaccination with the 10-valent PCV were redness at injection site and irritability, of mild to moderate severity. Children should not proceed with the 10-valent PCV if they had a serious (anaphylactic) allergic reaction to a previous dose of this vaccine or its components.

Implications of PCV immunization

Apart from the intended benefit of PCV in protecting unimmunised children against invasive pneumococcal disease, PCV is beneficial in raising herd immunity against vaccine serotypes. The result of increased herd immunity is better protection of elderly persons living in the same household as the child. This is particularly relevant in Singapore where elderly grandparents (who are often the care-givers of an asymptomatic child with pneumococcal nasal carriage) may unknowingly be at risk for IPD themselves because of age and presence of chronic conditions. PCV thus has wide-ranging effects in protecting the entire household against vaccine serotypes, not just the infant or toddler alone.

Although PCV immunization prevents colonization of the naso-pharyngeal area with particular vaccine serotypes, it does not reduce the overall rate of pneumococcal nasal carriage because of replacement of *non*-vaccine serotypes through naso-pharyngeal carriage. Factors affecting the emergence of replacement disease are multiple and are associated with persons having compromised immunity. However, replacement disease is not expected to result in vast increases in the prevalence of pneumococcal disease although it may attenuate the anticipated benefit of introducing the pneumococcal conjugate vaccine in the community.

Conclusion

Pneumococcal infections are a common cause of acute otitis media, sinusitis, pneumonia, bacteremia and meningitis in young children. Treatment poses an increasing challenge to doctors caring for the infected child because of antibiotic resistance. Prevention through vaccination is the best way to reduce its mortality and morbidity.

Reference : MOH circular MH 34:55/2, 13 Oct 09.