



UPDATE ON THE CURRENTLY AVAILABLE VACCINES IN HONG KONG

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Streptococcus Pneumoniae

Streptococcus pneumoniae (over 90 serotypes) is a ubiquitous bacteria colonizing many healthy people in their upper respiratory tracts. Illness occurs in 15% of young children who acquire a new serotype in the nasopharynx, and this usually takes place within 1 month of acquisition. Disease spectrum includes occult bacteremia, fulminant septicemia, meningitis, otitis media, sinusitis, pneumonia, conjunctivitis and primary bacterial peritonitis.

Patients at greatest risk are all children especially 6-24 months old, children with immune defect like asplenia, and nephrotic syndrome/chronic liver disease, and

asplenia. Other risk factors for invasive disease are children with sickle cell disease, in day care attendance, and with history of frequent otitis media.

The invasive pneumococcal disease (IPD) rate (incidence per 100,000 population) reported in the literature are 18 among children 0-2 years old (fatality rate of 5%), 12.5 in 3-5 years group (fatality rate of 5.9%), 18 in the age group of 3-5 years, and 16 in adults of 75 years or more (fatality rate of 50.6%). In Hong Kong the IPD rate is similar (15-18/100,000).

Two vaccines are available: polysaccharide pneumococcal vaccine (P23, 23-valent) and conjugated pneumococcal vaccine (CP7, 7-valent). The former is traditionally used

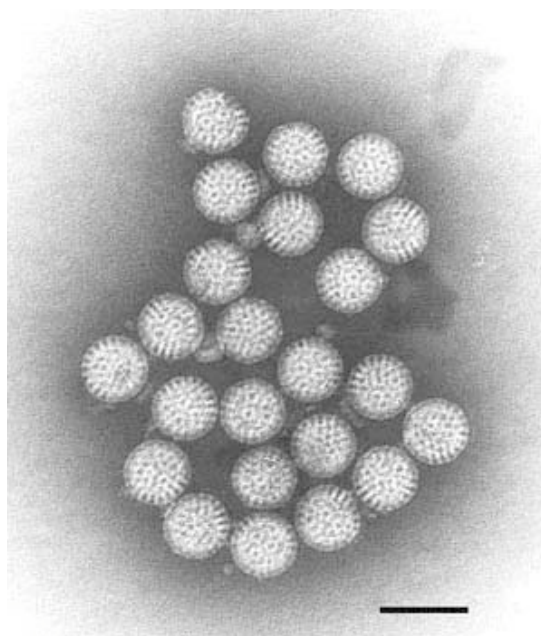


in immuno-compromised or asplenic children of older than 2 years of age. However CP7 has a potential worry of non-vaccine type replacement (i.e. colonization or infection by other serotypes not included in the vaccine), whereas PS23 does not seem to have this problem (see Table).

Is CP7 suitable for Hong Kong children? Vaccination can prevent 73-97% (vaccine type) of invasive disease, 80% of which is caused by the 7 serotypes included in the vaccine. So the currently available vaccine is considered effective. Our serotype data also showed that addition of further serotypes (e.g. 11-valent) does not confer additional protection. Vaccination would provide significant "personal protection" for children under 5-year old and those over 65 years. The real issue is financing, i.e. whether the Hong Kong Government is willing to shoulder the burden of a universal vaccination programme.

Rotavirus (RV)

It belongs to the Reoviridae genus, a ds-RNA virus with 11 gene segments, affecting both human and animal RVs.



Its gene segments are capable of spontaneous re-assortment in nature or in experiments. It is transmitted via faecal-oral route (air-borne spread is a definite possibility) and even a very small dose (<100 virus particles) can cause infection. The incubation time is 18-36 hours, and patients shed more than 10^{12} viruses per gram of stool. Two natural infections will confer 100% protection against moderate/severe disease regardless of serotype.

Worldwide 110 million episodes take place every year with a total of 610000 deaths, occurring mostly in Asia and Africa (*Lancet 2006;368:323*); rotavirus disease thus represents an enormous disease burden and risk to the world.

In a study a 30% positive rotavirus detection rate is found in 7391 Hong Kong children hospitalized with gastroenteritis; and it is deduced that the incidence of hospitalization for RV would be 8.8 per 1000 children of less than 5 years of age, not an insignificant figure (*Nelson et al. JID. 2005;192:S71-79*)

Serologically the rotavirus is classified according to the inner-core structural protein (A-E), and major glycosylated outer capsid protein (responsible for the G serotype), and the protease-sensitive outer capsid protein (responsible for the P serotype). Four rotavirus strains, G1, G3, G4 and G2, make up 96% of the globally identified strains. Recently, previously rare G serotypes, such as G9, have emerged. It should be noted that predominant serotypes vary from year to year, and from region to region. Natural infection or immunization with one RV serotype may induce protection against another serotype (heterotypic protection).

The first rotavirus vaccine (4-valent vaccine) was introduced in 1998 but had to be withdrawn in 1999 due to a possible association with intussusception. Two newer vaccines were introduced in the market recently. Rotarix™ (GSK), an attenuated live oral vaccine of

Table.

	In children < 24 m	Reduction of invasive diseases	Carriage rate reduction	Local reaction
CP 7	Effective	73-97% (same serotype as vaccine) 11-89% (all serotype) Pneumonia 11-73% Acute otitis media only 6-7%	Yes	10-20%
PS 23	Not effective	38-78% protection in adult	No	30-50%

G1P [8] human RV replicates well in gut, and provides cross-reactions against most other serotypes (like natural RV infections). Two oral doses are given to 2 and 4 months old infants. It can be given together with oral polio vaccine RotaTeq™ (Merck) is a pentavalent human-bovine WC3 RV with 5 human-bovine reassortant viruses G1, G2, G3, G4 and P1A[8]. It is also a live oral vaccine naturally attenuated for human but not broadly cross-reactive, and grows less well in human intestine. Three oral doses are given to infants from 6 to 12 weeks old at 4-10 weeks' interval (all 3 doses to be completed by 32 weeks of age). It can be combined with IPV. (*NEJM 2006;354:11-12 and 23-33*)

The efficacy of both vaccines has been shown to be good, resulting in significant decrease of hospitalization, even in malnourished children. Intussusception rate is not increased when compared with placebo-group; this favourable finding may be related to the early start of vaccination as infants of less than 3 months old are naturally less susceptible to intussusception.

Human Papillomavirus (HPV)

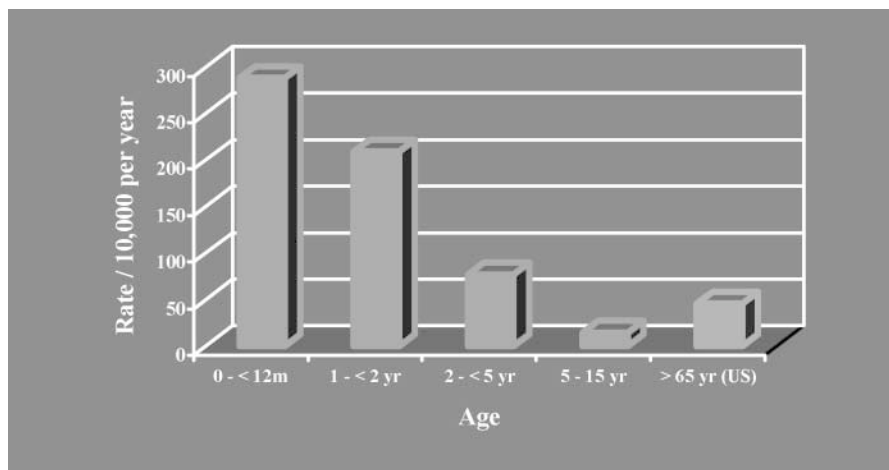
There are at least 100 types of HPV that infect human, 35 of which targeting human genitalia in sexually active men and women. Some types may cause external genital warts or respiratory papillomatosis (usually low risk types 6 and 11). Persistent infection causes cervical cancer, which is the second most common cancer in women resulting in 233,000 deaths per year worldwide.

Human papillomavirus vaccine, a quadrivalent (types 6, 11, 16, 18) recombinant vaccine, was approved by the US FDA in June 2006 and aimed at 9-26 years old girls and women to prevent cervical cancer, vaginal and vulvar pre-cancerous lesions, and genital warts. It consists of 3 injections at 0, 2, 6 months. In women not already infected, HPV vaccine was almost 100% effective in preventing precancerous cervical, vaginal and vulvar lesions, and genital warts. Immune response of girls 9-15 years is shown to be as good. So far immunity efficacy shows no breakthrough 5 years after immunization. The long-term effectiveness study is still ongoing.

The most effective strategy is to immunise girls by 12 years before they become sexually active. There is concern about waning immunity, and some may have the added concern over the unwanted message condoning sexual promiscuity. Whether boys need vaccination is debatable; the advantage of providing herd immunity and protection against genital warts from some HPV types should be weighed against the cost (US\$ 300+ for one set). Local epidemiology is unknown and a working group is set up to study the situation in Hong Kong.

Is There Anything New with Influenza in Children?

Influenza should not be taken lightly; a report (*Bhat et al. NEJM 2005*) shows high mortality in the 2003-2004 season (new drift strain 'Fujian' H2N2) causing 153 deaths in children with a median age of 3 years, 63% of which are less than 5 years of age and 40% less than 2 years of age.



Excess hospitalization for acute respiratory disease due to influenza, 1998-1999 (HK): -
0-12 m = 270/10,000 per year; 1-2 yr = 200; 2-5 yr = 55
(*Chiu et al. N Engl J Med 2002*)

What is 'new'? High mortality has been documented with new drift strain in previously healthy children in young children <5 years and especially <6 months of age who are currently not recommended for vaccination. Most at risk are those children with chronic illness, neurological disorders, genetic disorders and prematurity.

A 'New' Side Effect – Oculorespiratory Syndrome (ORS)

In the 2000-01 season a constellation of symptoms associated with Fluviral S/F (Shire Biologicals) marketed only in Canada was reported. It includes bilateral red eyes, respiratory symptoms (cough, wheeze, chest tightness, shortness of breath or sorethroat) or facial swelling beginning 2-24 hours after vaccination. Fortunately complete resolution takes place within 48 hrs. Similar effect was also reported in other influenza vaccines and in Europe.

Other Update on 'Old' Vaccines in Hong Kong

BCG

It is now known that BCG protects from TB related deaths (disseminated and meningitis) in the neonatal period but

offers only 50% protection against TB infection. There is no convincing reason for repeating vaccination in older children and the second BCG in primary school is now discontinued.

New US Recommendation for Varicella Vaccine

CDC and ACIP in June 2006 recommend that children 4-6 years of age receive a second dose of varicella vaccine, and adolescent or adults who received only 1 dose to receive a second one due to waning of immunity. A 10-year observation of 2216 vaccinated children that had 2 doses showed a 3.3-fold lower risk for chickenpox when compared with those who had only 1 dose. The duration of protection of the two-dose regime is still not known.

Varicella Vaccination – The Recommended Practice

Both Varivax (Merck) and Varilrix (GSK) are available in HK. The US recommendation was made on Varivax, the varicella vaccine used there: children 12 months to 12 years – 2 doses, 2nd dose given at minimum of 3 months later; adolescents (≥ 13 years) and adults – 2 doses 4-8 weeks apart. There is no similar recommendation from GSK at the time of the lecture.