New Childhood Immunisation Programme in Hong Kong

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Introduction

In Feb 2006, the Department of Health in Hong Kong started to implement a new universal immunisation programme for children. The old and new immunisation schedules are shown in Table 1. In the new programme, oral polio vaccine (OPV) is replaced by inactivated polio vaccine (IPV) and whole cell pertussis vaccine (wP) is replaced by acellular pertussis vaccine (aP). In addition, vaccines against diphtheria, tetanus, pertussis and poliovirus are given as a combined quadruple vaccine (DTaP-IPV) instead of separate DTaP and IPV vaccines. In this article we shall review the rationale behind and evidence supporting the change in the immunisation programme. We shall also briefly review other combination vaccines widely used in private sector in Hong Kong, as well as the differences between our local childhood immunisation programme and that of the United States and the United Kingdom.

IPV vs OPV

The Salk formalin-inactivated polio vaccine and the Sabin live-attenuated oral polio vaccine were licensed in the US in 1955 and 1961 respectively. Though developed later, OPV soon replaced IPV in most countries as it is inexpensive, requires no needle, produces mucosal immunity and herd immunity. More than 95% of recipients develop long-lasting immunity to all 3 types of poliovirus after 3 doses of OPV. On the other hand, the immunogenicity of the original IPV was low and was replaced in 1988 by enhanced-potency IPV which has greater antigenic content. Both IPV and OPV induce mucosal immunity of the gastrointestinal tract, but that induced by OPV is superior, though pharyngeal mucosal immunity is comparable for both vaccines. Herd immunity induced by the spread of the live polioviruses of OPV offers distinct advantage and contributes to the global eradication of poliomyelitis. Routine and mass administration of OPV in the past 40 years has markedly reduced the incidence of paralytic poliomyelitis in most parts of the world as well as in Hong Kong; and OPV is still the type of polio vaccine recommended by WHO for eradication of polio in endemic countries. Although the public health benefit of OPV is enormous, there is a trend in the switch of OPV to IPV in many developed countries because OPV is associated with a severe adverse effect, namely vaccine-associated paralytic poliomyelitis (VAPP), which occurs in approximately 1 per 1.4 million OPV doses in England and 1 per 2.5 million doses in the US. Apart from VAPP, vaccine-derived poliovirus can be excreted in faeces and cause outbreaks of poliomyelitis.

After eradication of poliomyelitis in the US since 1979, the risk for VAPP is considered to outweigh its benefits. Consequently, in 1997, the US Advisory Committee on Immunization Practices (ACIP) recommended replacing the all-OPV schedule with a sequential schedule of IPV followed by OPV to decrease the risk for VAPP while maintaining the benefits of OPV. This sequential schedule was accepted with no decline in immunisation coverage despite the need for additional injections. In 2000, ACIP went on to recommend exclusive use of IPV to eliminate the risk of VAPP. However, ACIP reaffirms OPV as the only vaccine recommended to eradicate polio from endemic countries. Based on similar circumstances and rationale, Hong Kong has now switched to IPV for universal childhood immunisation.

Studies have confirmed that 99%-100% of children develop protective antibodies after administration of three doses of IPV. The response is not inferior to OPV in a randomised controlled trial. In addition, more than 90% of vaccinated persons have serum antibodies 25 years after the fourth dose. Although there is no direct evidence that IPV is equally effective as OPV in preventing outbreaks of poliomyelitis, switching from OPV to IPV is considered unlikely to result in resurgence of poliomyelitis given the current eradication of polio in our locality. Furthermore, an extensive review has not found any serious adverse event caused by IPV. Therefore, switching from OPV to IPV in Hong Kong is likely to have a good risk-benefit ratio, and experience from the US has shown that vaccine uptake is unlikely to be compromised by the switch.

Acellular vs Whole cell pertussis vaccine

Vaccines made from killed whole Bordetella pertussis organisms have been available since the 1950s. However, whole cell pertussis vaccines have many adverse effects which include reactions such as fever, irritability and injection site pain commonly, and transient severe reactions such as hypotonic-hyporesponsive episodes, convulsions and acute encephalopathy rarely. Acellular pertussis vaccines containing purified or recombinant Bordetella pertussis antigens instead of intact organisms have been...
developed hoping that they would be as effective as wP but less reactogenic. Introduction of aP in Japan in the 1980s was followed by a steady decline in the incidence of pertussis, and a variety of different aP has been developed since then.

A recent systematic review including 6 efficacy and 45 safety trials found that aP with three or more pertussis antigens were more effective than those with one or two antigens. They were also more effective than one type of wP, but less effective than two other types of wP. However, differences in trial design precluded pooling of the efficacy data and results should be interpreted with caution. Nevertheless, most systemic and local adverse events were significantly less common with aP than with wP. In conclusion, aP is probably not inferior to wP in efficacy, but shows fewer adverse effects in general. However, in areas where pertussis is endemic and highly fatal, the most effective types of wP might be preferable despite its higher toxicity. As the incidence of pertussis in Hong Kong is not high in recent years (5-32 cases reported annually) and most cases can be treated effectively, aP with better toxicity profile is now considered more appropriate for universal childhood immunisation.

### Combination vaccines

Combination vaccines are developed to avoid multiple injections during single clinic visits and its use may improve immunisation uptake and compliance. Other benefits include reduction in pain for the infant and anxiety for the parents, decreased costs as a result of fewer office visits, storage of fewer vials, decreased risk of needle sticks as a result of handling fewer syringes, and potentially improved record keeping and tracking.

A combined DTaP-IPV vaccine is now recommended for universal childhood immunisation in Hong Kong. In a randomised controlled trial involving 400 healthy children aged 4-6 years, non-inferiority of the DTaP-IPV vaccine to separate DTaP and IPV vaccines was demonstrated. No significant differences were observed in adverse events between the two groups. In addition, the DTaP-IPV vaccine had no negative effect on the response to co-administered MMR vaccine. Another randomised controlled trial also demonstrated that DTaP-IPV is comparable to DTaP + OPV in immunogenicity and reactogenicity.

### Table 1: Immunisation schedules in Hong Kong, United States and United Kingdom

<table>
<thead>
<tr>
<th>Age</th>
<th>Hong Kong before Feb 2007</th>
<th>Hong Kong after Feb 2007</th>
<th>United States</th>
<th>United Kingdom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>BCG&lt;sup&gt;a&lt;/sup&gt;</td>
<td>HBV&lt;sup&gt;b&lt;/sup&gt;</td>
<td>OPV&lt;sup&gt;c&lt;/sup&gt; type 1</td>
<td>BCG</td>
</tr>
<tr>
<td>1 month</td>
<td>HBV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-4 months</td>
<td>DTwP&lt;sup&gt;d&lt;/sup&gt; OPV</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5 months</td>
<td>DTwP</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>DTwP OPV</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>HBV</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>MMR</td>
<td>MMR</td>
<td>MMR</td>
<td>Hib&lt;sup&gt;f&lt;/sup&gt; MCV&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>13 months</td>
<td></td>
<td></td>
<td></td>
<td>MMR PCV</td>
</tr>
<tr>
<td>18 months</td>
<td>DTwP OPV</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td>DTaP&lt;sup&gt;e&lt;/sup&gt; HAV&lt;sup&gt;j&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>3 years 4 months - 5 years</td>
<td>DTwP OPV</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td>DTaP&lt;sup&gt;e&lt;/sup&gt; HAV&lt;sup&gt;j&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>6 years (Primary 1)</td>
<td>MMR DT OPV</td>
<td>MMR DTaP&lt;sup&gt;e&lt;/sup&gt; OPV</td>
<td>MMR DTaP&lt;sup&gt;e&lt;/sup&gt; IPV Varicella</td>
<td></td>
</tr>
<tr>
<td>11-12 years (Primary 6)</td>
<td>Td&lt;sup&gt;k&lt;/sup&gt; OPV</td>
<td>DTaP-IPV&lt;sup&gt;e&lt;/sup&gt;</td>
<td>MCV&lt;sup&gt;l&lt;/sup&gt; IPV&lt;sup&gt;mm&lt;/sup&gt;</td>
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</tr>
<tr>
<td>13-18 years</td>
<td></td>
<td></td>
<td></td>
<td>Td-IPV</td>
</tr>
</tbody>
</table>

- **a.** BCG
- **b.** HBV-hepatitis B vaccine
- **c.** OPV - oral polio virus vaccine
- **d.** DTwP - combined diphtheria, tetanus, whole cell pertussis vaccine
- **e.** DTaP - combined diphtheria, tetanus, acellular pertussis vaccine
- **f.** Hib - conjugated Haemophilus influenzae type b vaccine
- **g.** OPV - trivalent oral polio virus vaccine
- **h.** DTwP - combined diphtheria, tetanus, whole cell pertussis vaccine
- **i.** IPV - inactivated polio vaccine
- **j.** IPV - inactivated polio vaccine
- **k.** DTwP - combined diphtheria, tetanus, whole cell pertussis vaccine
- **l.** DTwP - combined diphtheria, tetanus, whole cell pertussis vaccine
- **m.** Td - combined tetanus and reduced dose diphtheria vaccine
- **n.** MCV - meningococcal group C vaccine
- **o.** HPV - human papillomavirus vaccine
- **p.** PCV - conjugated pneumococcal vaccine
- **q.** MCV4 - tetravalent conjugate meningococcal vaccine
- **r.** HPV - human papillomavirus vaccine
- **s.** Hib - conjugated Haemophilus influenzae type b vaccine
burden of invasive pneumococcal and Hib diseases should be performed so that public health and economic impact of universal immunisation against these infections can be more accurately estimated for policy formulation. Considerations should be given to make pneumococcal and Hib infections notifiable. Those vaccines universally provided in the Western developed countries with success should be seriously and carefully considered to be included in childhood immunisation programme in Hong Kong.

References

13. Black S, Friedland LR, Schuind A, Howe B. Immunogenicity and safety of a combined DTap/IPV vaccine compared with separate DTap and IPV vaccines when administered as pre-school booster doses with a second dose of MMR vaccine to healthy children aged 4-6 years. Vaccine. 2006;24:6163-6171.