UNIT NO. 5

CHILDHOOD VACCINATIONS

A/Prof Lee Bee Wah, A/Prof Goh Lee Gan, Dr Lee Kheng Hock

ABSTRACT

The prevention of infectious diseases in children by immunisation is one of the greatest achievements of research in the history of medicine. Five particular diseases share two outstanding features in common: they kill young children; and young children can be protected against them by immunization. These are measles pertussis, diphtheria, tetanus (neonatal tetanus), poliomyelitis and probably, also tuberculosis. WHO recommends that each country determines its own schedule to best fit its own needs. Catch up programmes are required for children who are delayed or missed their immunization dates. To reduce the number of injections needed, combination vaccines have been introduced and the two well-known ones are DPT and MMR. There is now the five-in-one vaccine that contains DPT, inactivated polio vaccine and Hib which could be given all in one injection. In addition, vaccines have been introduced into the childhood immunization schedules of several countries as options where relevant – meningococcal C conjugate vaccine, pneumococcal conjugate vaccine, varicella vaccine, influenza vaccine, and Hepatitis A vaccine. Finally, parental concerns on the safety of vaccines need to be addressed. Their individual supports of the immunization programme are essential in the creation of herd immunity.

INTRODUCTION

Childhood vaccine development has been a combination of serendipitous discoveries, contributions of basic research, and the threats posed by litigation and economic factors. The prevention of infectious diseases in children by vaccination, has been one of the greatest achievements of research in the history of medicine[1].

In this study unit, the following aspects are reviewed:

- Principles of childhood vaccination.
- National childhood immunisation schedules.
- Catch-up programmes for unimmunised or partially immunised children.
- Combination vaccines for childhood immunisation.
- Other childhood vaccines.
- Contraindications and adverse reactions; and
- Parental concerns.

LEE BEE WAH, The Child & Allergy Clinic, Mount Elizabeth Medical Centre

GOH LEE GAN, Senior Consultant Family Physician, Department of Community, Occupational and Family Medicine, National University of Singapore

LEE KHENG HOCK, Executive Director, College of Family Physicians Singapore

PRINCIPLES OF CHILDHOOD VACCINATION

Definition

Immunisation may be defined as the process that converts an individual from a susceptible to an immune status. The purpose of vaccination is to induce protection (immunity) from subsequent disease, similar to that induced by natural infection, with minimal or no systemic symptoms[2].

What is the difference between vaccination and immunisation?

The terms 'vaccination' and 'immunisation' are often used interchangeably, but their meanings are not equivalent. Vaccination originally referred to the inoculation of vaccinia virus to render individuals immune to smallpox. Today, the term 'vaccination' means the administration (by injection, mouth or any other route) of a vaccine. Vaccination and/or suffering from the disease do not always result in immunisation. Immunisation is the process of converting to an immunised state[2].

How does immunisation work?

There are several types of vaccines, but immunisation works in the same general way, by preparing the immune system to attack the infection. A vaccine 'looks like' the infecting organism and the immune system responds as it would to an infection of that disease. The immune system has a memory and is prepared (primed) by the vaccine for a faster and better response to the infection.

The first exposure to a vaccine stimulates the immune response (known as priming). The immune system recognises the antigen, and antibodies are produced, initially IgM and then IgG. Priming can take more than one dose. For example, many infants will need at least two doses of pertussis vaccine for priming to occur.

A subsequent injection with the same vaccine stimulates the secondary response. The secondary response is much brisker than the primary response and is predominantly IgG rather than IgM. The aim is to generate enough antibodies to provide long lasting protection against the disease. The primary and secondary responses constitute the primary series of a vaccine.

If a further dose (booster) is given some months or years later, a greater and longer lasting secondary response is stimulated, reinforcing the immunologic memory for that antigen.

The immune response to vaccines involves both the production of antibodies and 'cell memory', but it is much easier to measure circulating antibodies in the laboratory, so this tends to be the focus. One exception is Bacillus Calmette-Guérin (BCG), where antibodies are not relevant, and the cell mediated immunity is measured by the tuberculin skin test (Mantoux test)[2].

Serological confirmation of immunity

Serological confirmation of immunity following vaccination, if necessary, can be done by requesting disease specific IgG (except BCG) not less than one month after completion of the vaccine course.

Preventing mortality and morbidity

We immunize children to prevent mortality and morbidity from specific infections. Six particular diseases across the world share two outstanding features in common: they kill young children; and young children can be protected against them by immunization. The six killer diseases of children are measles pertussis, diphtheria, tetanus (neonatal tetanus), poliomyelitis and tuberculosis.

Some idea of the contribution of childhood vaccines to the reduction of morbidity and morbidity are given by the following information:

- Prior to the introduction of the diphtheria vaccine in 1939, around 45,000 notifications were recorded annually in the UK, with over 2,000 deaths. In 1957, only 37 notifications were recorded with six deaths[3];
- *Haemophilus influenzae* Type B (Hib) infection has the potential to cause complications such as epiglottitis and meningitis which occur in 40 per cent of cases. Since the Hib vaccine was introduced in 1992 in UK, infections due to this bacterium have become rare, although recent indications are that the incidence of Hib in the UK is starting to rise once more[4]. Possible reasons are: random variation in Hib disease occurrence; decreasing population immunity; or the fact that the UK schedule provides Hib vaccination at two to four months of age with no booster[5].

Importance of population immunity

When an individual is immunized against a disease, say poliomyelitis, he is protected against getting it. The incidence of poliomyelitis in the community is unlikely to fall very much if only a small proportion of newborn children receive their vaccine. This is because there are still enough susceptibles (people who have no resistance to the organism because they have not been immunized or have not had the natural infection) for the natural infection to keep on passing around in the community.

If immunization by vaccines is to be an effective means of controlling communicable diseases, then at least 80% of the whole population and 80% of the newborns have to be successfully vaccinated. This is the condition for creating herd immunity (Table 1).

When there are very few susceptibles left, the natural infection cannot keep going in the community and the incidence of disease will gradually get less and less until it reaches a very low level. When a high proportion of people are immunized, even those few people who have not been vaccinated also get some protection because the disease becomes so uncommon. This mechanism of control is mainly effective for those diseases that pass from man to man such as measles, poliomyelitis, and pertussis.

Table 1: Immunisation coverage required for herd immunity (population immunity)

Disease/vaccine	% coverage required for population immunity
Diphtheria	80 – 85
Tetanus	Not applicable as no person to person spread
Polio	80 – 85
Pertussis	92 – 95
Measles	92 – 95
Mumps	90 – 92
Rubella	85 – 87

Source: Moxon E R (ed) (1990) Modern vaccines. A Lancet review. Current practice and new approaches. Edward Arnold, London.

There is a need to guard against public pressure that immunisation be stopped in a community because the susceptibles have been immunised and the incidence of a particular disease has fallen to a low level. Once immunization is stopped, there is a real danger of an epidemic occurring amongst all the new susceptibles being born. This is why it is so important to keep vaccination programmes going from year to year once they have been started, despite the low incidence. There is a need to explain this to the public.

NATIONAL CHILDHOOD IMMUNISATION SCHEDULES

WHO Recommendations

No immunization schedule is ideal. The World Health Organization (WHO)'s Expanded Programme of Immunization recommends that each country determine its own schedule to best fit its own needs. A guiding strategic principle of any immunization programme is that protection must be achieved prior to the time infants are at high risk from a disease. For example, form one quarter to one half of all new poliomyelitis cases occur in infants from 12 months of age with some cases occurring in those as young as 3 months. Infants are susceptible to pertussis soon after birth.

The Singapore Childhood Immunization Programme

The childhood immunisation programme in Singapore[6] offers vaccination against tuberculosis, hepatitis B, diphtheria, pertussis, tetanus (DPT), poliomyelitis, measles, mumps and rubella (MMR). Only diphtheria and measles immunisations are compulsory by law (Table 2).

Since 1 Jan 1990, the monovalent measles vaccine given to one-year-old children, was replaced by the trivalent measles, mumps and rubella (MMR) vaccine. As of 1 Jan 1998, the monovalent rubella vaccine given to primary school leavers is replaced by the second dose of MMR vaccine[7].

Hepatitis B vaccination for infants born to carrier mothers was incorporated into the national childhood immunisation programme in October 1985. This was extended to all newborns through the use of Medisave since 1 September 1987. To protect those who were born before 1987, a 4-year hepatitis B immunization programme was implemented for students in secondary 3, junior college year 2, centralised institute year 3,

institutes of technical education, polytechnics and universities in Jan 2001. In addition, full-time national servicemen who were non-immune are also offered hepatitis B immunization[8].

Notes on Hepatitis B (HepB) vaccine

All infants should receive the first dose of hepatitis B vaccine soon after birth and before hospital discharge; the first dose may also be given by age 2 months if the infant's mother is hepatitis B surface antigen (HBsAg) negative.

Only monovalent HepB can be used for the birth dose. Monovalent or combination vaccine containing HepB may be used to complete the series. Four doses of vaccine may be administered when a birth dose is given. The second dose should be given at least 4 weeks after the first dose, except for combination vaccines which cannot be administered before age 6 weeks. The third dose should be given at least 16 weeks after the first dose and at least 8 weeks after the second dose. The last dose in the vaccination series (third or fourth dose) should not be administered before age 24 weeks (6 months).

Table 2. National Childhood Immunisation Schedule – Singapore (2003)

Age	Vaccine	Immunisation against
At Birth	BCG Hepatitis B - 1st Dose	Tuberculosis Hepatitis B
1 month	Hepatitis B - 2nd Dose	Hepatitis B
3 months	DPT/DT - 1st Dose Oral Sabin - 1st Dose	Diphtheria, Pertussis & Tetanus Poliomyelitis
4 months	DPT/DT - 2nd Dose Oral Sabin - 2nd Dose	Diphtheria, Pertussis & Tetanus Poliomyelitis
5 months	DPT/DT - 3rd Dose Oral Sabin - 3rd Dose	Diphtheria, Pertussis & Tetanus Poliomyelitis
5-6 months* 1 year	Hepatitis B - 3rd Dose Hepatitis B - Booster dose for children born to Hepatitis B carrier mothers only	Hepatitis B Hepatitis B
1-2 years	MMR - Primary dose	Measles, Mumps & Rubella
18 months	DPT/DT - 1st Booster Oral Sabin - 1st Booster	Diphtheria, Pertussis & Tetanus Poliomyelitis
6-7 years	DT - 2nd Booster Oral Sabin - 2nd Booster	Diphtheria & Tetanus Poliomyelitis
11-12 years	DT - 3rd Booster Oral Sabin - 3rd Booster MMR - Booster dose	Diphtheria & Tetanus Poliomyelitis Measles, Mumps & Rubella

Source: Health Promotion Board, 2003 (http://www. HPB_childimm2003.htm)
*Footnote: * The 3rd dose of Hepatitis B vaccination can be given with the 3rd dose of DPT and Oral Sabin for the convenience of parents.*

Infants born to HBsAg-positive mothers should receive HepB and 0.5 mL of Hepatitis B Immune Globulin (HBIG) within 12 hours of birth at separate sites. The second dose is recommended at age 1-2 months. The last dose in the immunization series should not be administered before age 24 weeks. These infants should be tested for HBsAg and antibody to HBsAg (anti-HBs) at age 9-15 months.

Infants born to mothers whose HBsAg status is unknown should receive the first dose of the HepB series within 12 hours of birth. Maternal blood should be drawn as soon as possible to determine the mother's HBsAg status; if the HBsAg test is positive, the infant should receive HBIG as soon as possible (no later than age 1 week). The second dose is recommended at age 1-2 months. The last dose in the immunization series should not be administered before age 24 weeks.

MISSED DOSES AND CATCH-UP PROGRAMMES FOR UNIMMUNISED OR PARTIALLY IMMUNISED CHILDREN

Missed doses

If the immunization schedule is interrupted e.g., by an acute febrile illness, what steps are required? There is no need to repeat prior doses. Simply continue the vaccine schedule as if no interruption had occurred. Note however, that children who miss a vaccine dose may do so again and close follow-up may be required.

Catch-up programmes

The objective of a catch-up programme is to complete a course of vaccination and provide adequate protection. Catch-up programmes should be based on documented evidence of previous vaccination. When children have missed many vaccine doses, it is important to bring them up to date as quickly as possible. This may require more than two injections at some visits.

The following is a guide in deciding what immunizations need to be given and the timing:

- Where more than one vaccine is overdue, it is preferable to give the maximum possible at the first visit.
- For children 12 months of age and over, MMR should be the priority because these diseases pose the greatest immediate risk.
- Determine the total number of antigens required and subtract the number of previous documented doses. Complete the primary programme using the minimum intervals of one month between doses. When a fourth dose is required, give it not less than six months after the third dose (for the booster response to occur).
- Hib and PCV are generally not recommended for children of 5 or more years (CDC, 2005). After the seventh birthday, Td (DT booster dose) should be used. At present pertussis vaccine is not recommended after the seventh birthday, unless a vaccine with reduced dose of components of acellular pertussis is used.

Children from another country

For a child who has arrived from another country and will be staying in Singapore for 6 months or more, a change to the local recommended schedule may have to be considered

with due account being taken of prior vaccine administration. If the vaccination history is uncertain, it is important to err on the side of giving rather than withholding vaccines. If there is doubt about which immunizations have been given, consider starting on a complete catch up immunization programme.

A point to reiterate is if the child has not had any immunizations and is aged 12 months or more, the priority is to give MMR first. Polio and DPT can be given at the same time as MMR immunization, in separate injection sites or allow an interval of 4 weeks. However, the total number of doses of diphtheria and tetanus toxoid vaccines should not exceed 6 doses before the 4th birthday otherwise there is a risk of large local reactions.

COMBINATION VACCINES FOR CHILDHOOD IMMUNISATION

To reduce the number of injections needed for the child, combination vaccines have become important solutions to the increasing number of diseases that children need to be protected against. The first combination vaccines are the DPT and MMR vaccines. Various other combination vaccines are now available[9].

Advantages

The use of combination vaccines has several advantages[9]:

- They form a practical way to overcome the constraints of multiple injections, especially for starting the immunization series for children behind schedule.
- The use of combination vaccines might improve timely vaccination coverage.
- Some immunization providers and parents object to administering more than two or three injectable vaccines during a single visit because of a child's fear of needles and pain and because of unsubstantiated concerns regarding safety.
- Cost and convenience factors – (a) reducing the cost of stocking and administering separate vaccines, b) reducing the cost for extra health-care visits, and c) facilitating the addition of new vaccines into immunization programs, and (d) The combination vaccine might represent a better economic value if one considers the direct and indirect costs of extra injections, delayed or missed vaccinations, and additional handling and storage.

Drawbacks

Combination vaccines have some drawbacks[9]:

- Chemical incompatibility or immunologic interference may result when different antigens are combined into one vaccine and this has to be excluded;
- Vaccine combinations that require different schedules might cause confusion and uncertainty when children are treated by multiple vaccine providers who use different products.

Combination vaccines that have been available for many years

These include:

- diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP);
- measles-mumps-rubella vaccine (MMR); and
- trivalent inactivated polio vaccine (IPV).

Combination vaccines made available in recent years

These include:

- diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP),
- DTP-*Haemophilus influenzae* type b vaccine (DTP-Hib),
- DTaP-Hib where accellular pertussis antigen take the place of the whole cell pertusis organism.
- Hib-hepatitis B vaccine (Hib-Hep B).

Combining Separate Vaccines

- Immunization providers should not combine separate vaccines into the same syringe to administer together unless such mixing is allowed as specified in the product label inserts[9].
- In general, vaccines from different manufacturers that protect against the same disease may be administered interchangeably in sequential doses in the immunization series for an individual patient (eg, hepatitis A vaccine [HepA], HepB, and Hib).
- Until data supporting interchangeability of acellular pertussis vaccines (eg, DTaP) are available, vaccines from the same manufacturer should be used, whenever feasible, for at least the first three doses in the pertussis series.

Vaccines For Diseases With Serologic Correlates of Immunity

- Studies of serologic responses that have been correlated with protection against specific diseases support the interchangeability of vaccines from different manufacturers for HepA, HepB, and Hib.
- Hepatitis B vaccine products (ie, HepB and Hib-HepB if age-appropriate) also may be interchanged for any doses in the hepatitis B series.
- Different Hib vaccine products from several manufacturers may be used interchangeably for sequential doses of the vaccination series.

Vaccines For Diseases Without Serologic Correlates of Immunity

- No data are available regarding the interchangeability of acellular pertussis products from different manufacturers for the first three pertussis doses scheduled at ages 2, 4, and 6 months. Thus, use of the same manufacturer's acellular pertussis vaccine product(s) is preferred for at least the first three doses in the series[9].

Safety of Extra Doses Of Vaccine Antigens

The following have been determined[9]:

- An extra dose of live, attenuated virus vaccines to immunocompetent persons who already have vaccine-induced or natural immunity has not been demonstrated to increase the risk of adverse events. Examples of these include MMR, varicella, rotavirus, and oral polio vaccines.

- An extra dose of Hib or HepB vaccines has not been found to be harmful.
- However, the risk of adverse reactions might increase when extra doses are administered earlier than the recommended interval for certain vaccines (eg, tetanus toxoid vaccines and pneumococcal polysaccharide vaccine). Examples of such vaccines include DTaP, DTaP-Hib, diphtheria and tetanus toxoids for children (DT), tetanus and diphtheria toxoids for adolescents and adults (Td), and tetanus toxoid.

The DTaP/IPV/Hib – 5 in 1 Vaccine

The 5 in 1 new combination vaccine, called DTaP/IPV/Hib, protects against diphtheria, tetanus, pertussis (whooping cough), poliomyelitis and Hemophilus influenza b (Hib) has been introduced for routine use in the UK as from 2004, where it is given to babies when they are two, three and four months old. The polio vaccine is in the same injection as polio inactivated vaccine. Also, acellular whooping cough antigen is used. This will conveniently replace the current hassle of a DTP injection, Oral polio and separate Hib injection.

What are the benefits of this new vaccine?

- As the polio vaccine is inactivated (that is, it is not live), it does not carry the slight risk of causing vaccine-associated paralytic polio (that is, when the vaccine itself causes paralysis) that the previous live oral vaccine carried.
- The acellular pertussis vaccine is as effective as the whole cell pertussis vaccine used previously.
- The new vaccine is likely to cause fewer minor reactions such as swelling or redness where the injection is given, particularly in older children.
- It does not contain thiomersal, a preservative that contains mercury.

Measles, mumps, and rubella vaccine (MMR)

MMR protects against Measles, Mumps and Rubella (German measles). This is a live vaccine. The first dose is given to children at around 13 months of age. A second dose is given at around 11-12 years in the Singapore immunization schedule but earlier in other schedules.

Children who are 'immunosuppressed' should not, in general, receive live vaccines. These include those:

- whose immune system is suppressed because they are undergoing treatment for a serious condition such as a transplant or cancer, or
- who have any condition which affects the immune system, such as HIV or AIDS.

What are the side effects from the vaccine?

The three different viruses in the vaccine act at different times and may produce the following side effects after the first dose. Side effects after the second dose are even less common and usually milder.

- Six to ten days after the immunisation, some children may become feverish (this happens to about one in ten children).
- Some develop a measles-like rash and go off their food as the measles part of the vaccine starts to work.
- About one in every 1000 immunised children may have a febrile fit. However, if a child who has not been immunized gets measles, they are five times more likely to have a fit.
- Rarely, children may get mumps-like symptoms (fever and swollen glands) about three weeks after their immunization as the mumps part of the vaccine starts to work.
- Very rarely, children may get a rash of small bruise-like spots in the six weeks after the vaccination. This is usually caused by the measles or rubella parts of the vaccine.
- Fewer than one child in a million develops encephalitis (swelling of the brain) after the MMR vaccine, and there is very little evidence that it is caused by the vaccine. As a comparison, if a child catches measles, the chance of developing encephalitis is between one in 200 and one in 5,000.

OTHER CHILDHOOD VACCINES

Several childhood vaccines have been introduced into the childhood immunization programme across the world in recent years.

Haemophilus influenzae type b (Hib) conjugate vaccine

Haemophilus influenzae Type B (Hib) caused 95 percent of *Haemophilus influenzae* invasive disease in infants and children. Hib causes meningitis, pneumonia, epiglottitis, septic arthritis, bacteraemia, cellulitis, and empyema in infants and young children. The vaccine is available as a monovalent vaccine (eg. Hiberix) or as a combination vaccine (eg. Infanrix-Hib). Three doses need to be given at the time DTP are given. These vaccines will not protect against infection with non-encapsulated strains of Haemophilus influenzae, and therefore do not protect against otitis media, recurrent upper respiratory tract infections, sinusitis, or bronchitis[2].

Varicella vaccine

Chickenpox is usually but not invariably a mild, self limited disease in otherwise healthy children, but the severity of disease and risk of complications are usually greater in adolescents and adults. Varicella can also cause severe and even fatal disease in immune suppressed individuals (eg. children with acute leukaemia), in whom the mortality may be as high as 7-10 percent. Mortality in normal children is less than 2 per 100,000 cases, increasing up to 15 fold in adults. Varicella vaccine is recommended at any visit at or after age 12 months for susceptible children (i.e., those who lack a reliable history of chickenpox). Susceptible persons aged >=13 years should receive 2 doses, given at least 4 weeks apart[10].

Meningococcal vaccine

Routine immunisation with meningococcal vaccine is not recommended as the usual risk of vaccine preventable meningococcal disease is very low. Individuals with a high risk of invasive meningococcal infection should be offered

meningococcal vaccine. These include those suffering from:

- actual or functional asplenia – individuals scheduled for splenectomy should be immunised at least two weeks before the operation.
- sickle cell anaemia.
- deficiencies of the terminal complement components
- individuals with HIV infection, who may be safely immunised with meningococcal polysaccharide vaccines.

Close contacts of cases of meningococcal meningitis are at increased risk of developing disease over subsequent months, despite appropriate chemoprophylaxis. Immediate family or close contacts of cases of proven invasive meningococcal disease (if disease is due to a group included in the vaccine) should be considered for meningococcal vaccine as well as chemoprophylaxis. For those two years of age and over the vaccine is administered as a single dose of 0.5 ml, given by subcutaneous injection. In an epidemic the group C conjugate vaccine may be considered for those less than two years of age, and two doses will be required. The introduction of an infant programme has reduced the incidence of meningococcal meningitis in the UK. Specific recommendations will be made, depending on the situation.

There are areas of the world where the risk of acquiring meningococcal infection is increased. Nevertheless, the risk to travellers to the developing world as a whole has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan 'meningitis belt', from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world and occurred recently in Saudi Arabia (during a Haj pilgrimage), Kenya, Tanzania, Burundi, Mongolia and Nepal.

Pneumococcal vaccine

Pneumococcal polysaccharide vaccine should be considered for all patients, two years of age and over, if they are at special risk. These include:

- individuals with actual or functional asplenia – where possible the vaccine should be administered at least 14 days before splenectomy.
- immune competent persons at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic cardiac, renal or pulmonary disease, and diabetes).
- patients with chronic CSF leaks.
- immune compromised patients at increased risk of pneumococcal disease (eg, those with HIV infection, nephrotic syndrome, multiple myeloma, lymphoma, and Hodgkin's disease, or those who are immune suppressed following organ transplantation).

Re-immunisation should be considered after three to five years in children younger than 10 years of age when first immunised, and after five years in older children and adults belonging to particularly high risk groups, which frequently exhibit a poor immune response. Examples of such high risk individuals include those with functional or anatomic asplenia, sickle cell anaemia, nephrotic syndrome, renal failure and transplant recipients. Expert advice should be sought in such situations.

Because of the relatively poor response to vaccination with pneumococcal vaccine in splenectomised children and individuals with nephrotic syndrome or sickle cell disease, it is recommended that such patients receive continuous penicillin prophylaxis in addition to pneumococcal vaccine. The age at which prophylaxis can be discontinued must be decided empirically since no studies on this question have been performed. Some experts continue prophylaxis throughout childhood, and into adulthood for particularly high risk patients.

Influenza vaccine

Influenza vaccine is recommended annually for children aged >=6 months with certain risk factors (including but not limited to asthma, cardiac disease, sickle cell disease, HIV, and diabetes), In addition, healthy children aged 6-23 months and close contacts of healthy children aged 0-23 months are recommended to receive influenza vaccine, because children in this age group are at substantially increased risk for influenza-related hospitalizations.

Children receiving trivalent inactivated influenza vaccine (TIV) should be administered a dosage appropriate for their age (0.25 mL if 6-35 months or 0.5 mL if >=3 years). Children aged <=8 years who are receiving influenza vaccine for the first time should receive 2 doses (separated by at least 4 weeks for TIV and at least 6 weeks for live, attenuated influenza vaccine (LAIV).

Individuals who have had an anaphylactoid reaction to hens' eggs or egg protein should not be given influenza vaccine, as it contains minute quantities of residual egg protein. Anaphylactoid hypersensitivity to polymyxin or neomycin or any other vaccine component is a contraindication, as traces of these antibiotics may also be present in the vaccine.

Hepatitis A vaccine

Hepatitis A vaccine is recommended for children and adolescents Begin the hepatitis A immunization series during any visit. The 2 doses in the series should be administered at least 6 months apart.

CONTRAINDICATIONS AND ADVERSE REACTIONS

General contraindications to immunization in childhood are shown in Table 3.

Intercurrent Illness

Do not immunize a child if the child has an acute febrile illness. Any child who is currently ill should not receive any vaccine. However if the child is clearly in the recovery phase of an illness then immunisation may be carried out.

Anaphylaxis

An anaphylactic reaction to previous dose of vaccine, is an absolute contraindication to further doses of that vaccine. This is rare, but as with the injection of all foreign proteins is a real and significant risk. Anyone administering vaccines should be able to recognise anaphylaxis and if they cannot deal with it themselves, should have someone on site who can. These reactions may be delayed by a few minutes so it is advisable that children stay in the clinic for 20 to 30 minutes after immunisation. This is particularly important with measles immunisation.

Immunosuppression

Children with poor immune responses. such as – those with leukaemia or other cancers who are receiving chemotherapy should not receive live vaccines. Children receiving high doses of corticosteroids or those on prolonged courses of oral steroids should not be immunised with live vaccines until three months after completion of treatment.

Local administration of steroids including inhaled steroids is not a contraindication to vaccination, nor are short courses of systemic steroids.

Table 3. General Contraindications To Immunization In Childhood

- Current illness - usually febrile
- Anaphylactic reaction to previous dose
- Immunosuppression - relative contraindication
- Does not include local steroids or short courses of systemic steroids.

PUBLIC CONCERNS

Public concern about whether vaccines have been thoroughly tested prior to general release needs to be addressed. Despite extensive research, vaccines, like all pharmaceutical products, are not entirely risk-free[12,13]. Therefore, it is imperative that that the public is aware and reassured of ongoing surveillance programmes to monitor vaccine safety. Methodological difficulties associated with the study of rare, delayed or insidious vaccine safety allegations, combined with anti-vaccine lobbyists and media eagerness for controversy, means that vaccine safety concerns are likely to remain prominent.

Bedford & Elliman have identified five key concerns of parents and suggested helpful responses to these concerns[14] (Table 4).

Concerted action may be needed to dispel the concerns. The following are examples of such instances:

Multiple vaccines and the effect on immune system. Public concern about the effect on the immune system of giving a number of vaccines simultaneously and the possible long term effects such as asthma[15] has not been substantiated by the available evidence. In a double blind randomised controlled trial involving 9,829 children, three quarters were given the DTP vaccine containing one of three different types of pertussis vaccine. The other quarter were given DT vaccine only. There were no significant differences between groups in the proportions of children with wheezing, itchy rash, or sneezing at two and a half years old[16].

Table 4. Public concerns and response needed to placate the concerns

Concern	Response
The disease is not serious.	Healthy children can still die from these diseases.
The disease is uncommon.	The disease is common in unimmunised populations and can easily recur and spread if immunisation rates drop.
The vaccine is ineffective.	Studies showing the effectiveness of a vaccine are needed before introduction of a vaccine.
The vaccine is unsafe.	As with effectiveness, the safety of a vaccine is rigorously tested before, and after, its introduction.
Other methods of disease prevention, such as homoeopathy are preferable to immunisation.	There is no body of scientific evidence that supports homoeopathy or other methods for supports homoeopathy or other methods for

Source: Bedford & Elliman, 2000

MMR and autism/irritable bowel syndrome. Parental concern about MMR arose as a result of press coverage following the publication of a paper by Wakefield and others in the *Lancet* in 1998[17]. The authors speculated about a possible link between MMR and autism and/or inflammatory bowel disease (IBD). The authors said: 'We did not prove an association between MMR vaccine and the syndrome described.' Nevertheless, there was much concern generated that had to be resolved.

In 1998, in response to concerns about MMR vaccine, the Chief Medical Officer (CMO) in England asked the Medical Research Council (MRC) to consider the available data regarding a possible link. The group concluded that there was no evidence of any link. In 1999, a study was published in the *Lancet*, reviewing the cases of nearly 500 children born in north London between 1979 and 1994 who had been diagnosed with autism. The authors examined possible associations between their condition and the MMR vaccine[18].

The study found:

- no increase in autism associated with the introduction of MMR in 1988
- no difference in age of diagnosis of autism between MMR immunised and unimmunised children
- no difference in MMR immunisation rates between children with autism and the rest of the population
- no link between the timing of MMR and the onset of autism.

REFERENCES

1. Baker JP & Katz SL. Childhood vaccines development: an overview. Paediatric Research 2004; 55(2): 347-56.
2. MOH. Immunisation Handbook. MOH:New Zealand, 2002. *Informative handbook that could be downloaded from the Internet in full-text. URL:www.moh.govt.nz/publications/ immunisationhandbook2002*

3. British Medical Association. Childhood immunisation: a guide for healthcare professionals, June 2003.
4. Garner D & Weston V. Effectiveness of vaccination for *Haemophilus influenzae* type b. *The Lancet* 2003; 361: 395-9.
5. Steinhoff M & Goldblatt D. Conjugate Hib vaccines. *The Lancet 2003;* 361: 306-1.
6. Childhood immunization schedule for Singapore, 2003. Source: http://www.nir.hpb.gov.sg/nir/sv/eservices/eservicesv?ACTION=DISPLAY_IMMUNSCH (accessed 22 Apr 2005)
7. Goh KT. The childhood Immunisation Programme in Singapore, 1999. Epid News Buletin Sep 2000, 26:9:53-7.
8. School Health Service, Singapore Report, 2002.
9. American Academy of Paediatrics. Combination Vaccines for Childhood Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP). Paediatrics 5 May 1999; 103:1064-7.
10. CDC. Recommended Immunisation Schedule for Children & Adolescents Who Start Late or Who are more than 1 month behind. United States, 2005. http://www.cdc.gov/nip/recs/child-catchup.pdf (downloaded 22 Apr 2005).
11. Recommended Childhood and Adolescent Immunization Schedule – United States, July-December 2004. MMWR April 30, 2004 / 53(16);Q1-Q3.
12. Chen RT & Hibbs B. Vaccine safety: current and future challenges. *Pediatr Ann* 1998; 27: 445-64.
13. Freed GL *et al.* Vaccine safety policy analysis in three European countries: the case for thiomersal. *Health Policy* 2002; 62: 291-307.
14. Bedford H, Elliman D. 2000. Concerns about immunisation. *BMJ* 2000 320: 240-3.
15. Odent MR, Culpin EE & Kimmel T. Pertussis vaccination and asthma: is there a link? *JAMA* 1994; 272: 592-3.
16. Nilsson L *et al* (1996) Lack of association between pertussis vaccination and symptoms of asthma and allergy. *JAMA* 275: 760.
17. Wakefield AJ *et al* (1998) Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *The Lancet* 351: 637-41.
18. Taylor B *et al* (1999) Autism and measles, mumps and rubella vaccine: no epidemiological evidence for a causal association. *The Lancet* 353: 2026-9.

LEARNING POINTS

- **The prevention of infectious diseases in children by immunisation is one of the greatest achievements of research in the history of medicine.**
- **Six particular diseases share two outstanding features in common: These are measles pertussis, diphtheria, tetanus (neonatal tetanus), poliomyelitis and tuberculosis.**
- **WHO recommends that each country determines its own schedule to best fit its own needs.**
- **Catch up programmes are required for children who are delayed or missed their immunization dates.**
- **To reduce the number of injections needed, combination vaccines have been introduced and the two well-known ones are DPT and MMR.**
- **There is now the five-in-one vaccine that contains DPT, inactivated polio vaccine and Hib which could be given all in one injection.**
- **In addition, vaccines have been introduced into the childhood immunization schedules of many countries as options where relevant – meningococcal vaccine, pneumococcal vaccine, varicella vaccine, influenza vaccine, and Hepatitis A vaccine.**
- **Parental concerns on the safety of vaccines need to be addressed. Their individual supports of the immunization programme are essential in the creation of herd immunity.**