CURRENT CHILDHOOD IMMUNIZATIONS

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INTRODUCTION

Vaccines are considered one of the greatest achievements of biomedical science and public health, and immunization probably is the most cost-effective intervention against infectious diseases to date. Despite recent public concerns about vaccine safety, immunization is much safer than accepting the risks for the diseases these vaccines prevent. Although not all vaccines are equally effective, immunization has already enabled the eradication of smallpox. Other previously devastating diseases such as polio, neonatal tetanus and measles may soon also be eliminated by use of existing vaccines, assisted by international governmental commitment to immunization.

In this article practical aspects of immunization are discussed, providing the General Practitioner with comprehensive, but easy to use reference. *(SA Fam Pract 2003;45(9): 25-31)*

INTRODUCTION

The World Health Organization introduced its Expanded Programme on Immunization (EPI) in 1974 and reached its initial goal of achieving full vaccination of 80% of the world's children by 1990 in most but not all countries. This, together with the development of the "cold chain" annually saved about 3-4 million children, especially in developing countries. WHO/EPI goals have since been increased to full immunization of 90% of all children less than one year of age, but many developing countries have even failed to sustain the previously attained 80% rate of immunization.[1] New initiatives such as the Children's Vaccine Initiative[2] and the WHO/UNICEF strategy of Integrated Management of Childhood Illness (IMCI) were introduced in the 1990s to strengthen effective vaccine delivery and development, and to decrease the morbidity and mortality due to vaccine preventable causes, especially in developing settings. Active immunization is the administration of either a live (attenuated) or killed (inactivated) microorganism, a modified product of that organism (toxoid), or a purified or a genetically engineered antigen. This then evokes an immunological response similar to the natural infection but with little or no clinical risk to the patient. The effectiveness of a vaccine, determined by the measure of protection it gives against the natural disease, differs amongst vaccines. Some, especially the inactivated and component vaccines, require booster doses for maintenance of long-lasting immunity. Health care professionals should be aware that some constituents of vaccine products might cause adverse events in some individuals. These will be discussed under contraindications.

Anti-vaccination movements

Parents may question the need for or the safety of immunizations and some may even refuse certain or all immunizations for their child. These concerns could be based on religious or philosophical objections, incorrect information or deliberate one-sided information about possible problems that vaccines may cause. The latter is often found on anti-vaccine websites.[3] No immunization is currently mandatory in South Africa, but the benefit of the EPI vaccines outweigh the risks in by far the majority of children, with a few exceptions that will be addressed.

The response to parents who resist immunization should not be aggressive, but health care professionals should aim to effectively and empathetically communicate the true benefits, safety and possible risks of vaccine(s) to them, as well as the risks encountered by unimmunized children. Many vaccine-preventable conditions are more severe in adults and parents who have withheld immunization from their children are obligated to inform them once they reach adulthood. If, after discussion, parents still refuse immunization for

their child, this should be documented in the patient's record to reduce any future liability should a vaccine-preventable disease occur in the unimmunized child.

Storage and handling of vaccines (Cold chain)[4]

Inattention to vaccine storage and handling (cold chain) from the time of manufacture until administration to the individual can contribute to vaccine failure. Most vaccines should be transported and stored at 0-8° Celsius. Vaccines such as measles and measles-mumps-rubella (MMR), oral poliovirus (OPV), Bacille Calmette-Guérin (BCG), varicella and yellow fever vaccines, all live attenuated vaccines, are very sensitive to increased temperatures. Other, such as diphtheria-tetanus-pertussis vaccines (DPT and DTacellularP), diphtheria and tetanus toxoids (DT and dT), *Haemophilus influenzae* type b (Hib) conjugate, inactivated polio vaccine (IPV), hepatitis A virus, hepatitis B virus, polyvalent pneumococcal vaccine, and influenza vaccines are damaged by freezing. Vaccines should not be frozen in the freezer compartment unless otherwise stated. The two that do require storage below 0°C are OPV and varicella vaccines. Parents who purchase vaccines from other sources should be advised that vaccines should be administered immediately or transported on ice and not left lying around in the motor vehicle or at home.

The national Expanded Programme on Immunization (EPI SA)

The national immunization schedule gives coverage for polio, tuberculosis, diphtheria, pertussis, tetanus (including immunization of pregnant women in high incidence areas to prevent neonatal tetanus), hepatitis B, Haemophilus influenzae type b disease and measles. The recommended times of immunization are summarized in table1. Every visit of an infant or child to a health care professional or health facility calls for screening of immunization and, if appropriate, to immunize to avoid missed opportunities.

Contraindications for EPI SA scheduled immunizations and problems encountered immunizing children

Problems commonly encountered by health care professionals about immunizations are summarized in table 2. One of the problems is to decide what contraindications there are for specific vaccines. A few of the more commonly asked questions will be addressed briefly.

Anaphylaxis and allergy to egg

Health care professionals have been reluctant to immunize infants or children with measles or MMR vaccine if there is a history of allergy to egg, whether it be a skin rash or anaphylactic response, or even if they have not yet had egg before. In a review of the literature, Khakoo and Lack found that the majority of life threatening (cardio respiratory) allergic reactions to measles or MMR vaccine have been reported in children who were *not* allergic to egg.[5] The amount of ovalbumin, derived from the chicken egg embryo tissue in which the vaccine is produced, is probably insufficient to cause an allergic response. The allergic response is more due to gelatin or neomycin present in greater quantities than the albumin.

Allergy to egg should therefore not delay measles vaccination. Any vaccine can cause anaphylactic reactions and adrenaline (epinephrine) should always be available where vaccines are administered. Skin testing for reactions and desensitization are both associated with a risk of allergic reaction and should not be done. Children with milder forms of allergy to egg, even urticarial skin reaction, can be safely vaccinated without additional precautions. The only children that need to be vaccinated under conditions where they could be observed for about two hours and be effectively resuscitated are those with an allergy to egg in whom previous exposure led to cardio respiratory reactions and those with egg allergy and coexisting asthma (mainly older children).

Other vaccines not included in the EPI schedule but derived from chicken egg embryo tissue are influenza and yellow fever vaccines. Influenza vaccine is usually recommended in patients with asthma, but if such patients also have an allergy to egg, the vaccine should be administered under close supervision

Table 1. National Expanded Programme on Immunization (EPI SA)

Recommended age of immunization	Vaccine	Vaccine characteristic
Birth	OPV (0) Oral polio vaccine (trivalent) BCG (Bacillus Calmette-Guérin)	Live attenuated Live attenuated
6 weeks	OPV (1) DPT (Diphtheria, pertussis, tetanus) (1) HBV (Hepatitis B virus) (1) Hib (Haemophilus influenza type b) (1)	 Diphtheria & tetanus = toxoid (inactive) vaccines Pertussis = whole cell vaccine HBV = Sub-unit vaccine Hib = Sub-unit polysaccharide-protein conjugate vaccine
10 weeks	OPV (2), DPT (2), HBV (2), Hib (2)	
14 weeks	OPV (3), DPT (3), HBV (3), Hib (3)	
9 months	Measles (1)	Live attenuated
18 months	Measles (2), OPV (4), DPT (4)	
5 years	DT, OPV (5)	

Table 2. Common problems encountered with immunization schedules

Problem	Solution
Premature infant	Immunize at usual recommended chronological age with the standard vaccine dose
Child lapsed immunization Unimmunized older children	Do not restart schedule. Give remaining dose(s) at least 4 to 6 weeks apart Should receive measles vaccine and 3 primary doses of OPV, DPT (if >2 years of age, give DT), and HBV spaced 4 to 6 weeks apart. Give booster dose of OPV, DT and measles vaccines 1 year after the last primary dose. Hib vaccine: number of doses depends on child's age: 2-6 months old = 3 doses; 7-15 months = 2 doses; >15 months to 5 years = single dose. BCG: do tuberculin skin test; if negative and no clinical signs of immunosupression, BCG may be given
HIV-infected child: Asymptomatic	Immunize as per national immunization schedule
HIV-infected child: Symptomatic	BCG contraindicated. All other immunizations still recommended
Egg allergy	Not a contraindication for measles vaccine. Only a relative contraindication for measles vaccine if egg allergy manifests as anaphylaxis. Immunization should be given in a setting where anaphylaxis can be managed. No need to administer egg prior to measles vaccine.
Mild illness (e.g. cough or cold) with low-grade fever (<38.5oC), or convalescent phase of illness	Proceed with scheduled immunizations
Family history of convulsions or sudden infant death syndrome	No immunizations contraindicated
Non-progressive neurological condition (e.g., cerebral palsy, Down syndrome) or well controlled epilepsy	No immunizations contraindicated
Mild reactions to previous DPT vaccine or other vaccines e.g. soreness, redness and fever <40oC	Not a contraindication for a follow-up dose
Pregnancy	Live attenuated vaccines contraindicated 10
Pregnant woman in the same house	Not a contraindication for MMR or other live vaccines in a child
Other conditions, such as breastfeeding, mild diarrhoeal disease, malnutrition, even if severe, non-specific allergies, asthma, hay fever, dermatosis or eczema and current treatment with antibiotics	These do not constitute contraindications for immunizations

as described above. In the case of yellow fever vaccine a history of egg allergy and adverse reactions to previous yellow fever vaccines should be obtained and if the vaccine is really indicated, it should be given in small incremental dosages under close supervision of an experienced team.

Anaphylaxis due to vaccines

Anaphylaxis, although extremely rare, can occur following any vaccine. Immediate anaphylactic reaction to any vaccine is a contraindication for a follow-up immunization with that specific vaccine.

Moderate to severe illness with or without fever

Although mild illness, such as a cough or cold, with low-grade fever (<38.5°C) or a convalescent phase of illness is not a contraindication for immediate continuation of immunization, in case of moderate to severe illness with or without fever it is best to postpone immunization until the child is well.

Immunosuppression

Children with congenital immunodeficiencies, malignant disease, or those receiving cytotoxic drugs, high-dose, prolonged steroid treatment or radiation therapy should not be given live vaccines, i.e. BCG, measles, MMR and/or OPV. Defer immunizations with these vaccines for at least 3 months after cessation of immunosuppressive therapy. However, in immunosuppression because of HIV infection only measles (and BCG if not yet given at birth) is contraindicated if the child

is already severely symptomatic (CD4 percentage <15%). Immunosuppression due to kwashiorkor is not a contraindication for routine immunization.

Contraindications for pertussis vaccine

Pertussis vaccine is contraindicated if; a) a child has a progressive central nervous system disease, including progressive convulsions, b) develops encephalopathy within 7 days of a previous dose of DPT, c) had a severe reaction to a previous dose including collapse or shock-like state, convulsions within 3 days, temperature >40.5°C unexplained by another cause within 48 hours, and persistent inconsolable crying for more than 3 hours and d) develop Guillain Barré syndrome within 6 weeks of DPT.

Eradication of polio and measles:

National immunization campaigns against polio and measles are held every 4-5 years in addition to scheduled immunizations with the aim to eradicate these diseases that only have human reservoirs. To further this cause all acute flaccid paralysis and suspected measles cases are notifiable to the Department of Health as a matter of urgency and EPI case numbers will be issued for these patients.

Important vaccines not included in the EPI SA schedule

Several vaccines, protective against diseases with high morbidity, are available that are not included in the national immunization schedule. Knowledge of these vaccines and indications for their use is important for optimal patient care.

Specific indications exist for pneumococcal, influenza, hepatitis A, measles-mumps-rubella (MMR) and chickenpox vaccines. Furthermore, passive immunization is indicated after exposure to some diseases in certain circumstances. Travelers to certain areas must also be made aware of requirements concerning immunizations before entering these countries.

Individual non-EPI SA vaccines and their indications

MMR vaccine

Measles vaccine is included in the national immunization programme, but rubella and mumps vaccines are not. Congenital rubella remains an important preventable problem in South Africa. Mumps, specifically in adults, can cause severe morbidity (orchitis, infertility) whilst meningo-encephalitis and deafness can occur in childhood. MMR is safe in HIV-infected children unless severely immunosuppressed. Parents should be advised to substitute the 18-month measles immunization with MMR if financially possible. Maintenance of the cold-chain is essential and contraindications are as for measles vaccine. Epidemiological studies have not found an association between MMR vaccination and autism.[6]

Diphtheria, tetanus and acellular pertussis (DTaP) vaccine

The whole cell pertussis vaccine is currently included in the national immunization schedule. Due to the whole cell vaccine's relatively high reactogenicity, a number of acellular pertussis vaccines, which have a lower reactogenicity, have been developed and are widely in use in developed countries. A DTaP(HBV) vaccine is available in South Africa, but has only been registered for the 15-18 months booster dose, as there is some concern about reduced immunogenicity against *H. influenza* type b if acellular pertussis vaccine is administered together with Hib conjugate vaccine at 6-10-14 weeks.

Pneumococcal vaccine

A 23-valent polysaccharide pneumococcal vaccine (Pneumovax®) is currently available in South Africa, but is only immunogenic in children over 2 years of age. Current indications are: a) sickle cell disease, b) functional or anatomic asplenia, c) nephrotic syndrome or chronic renal failure and d) immunosupression (including drug therapy, but excluding acquired immunodeficiency syndrome as the risk-benefit for the latter is debatable).

A new generation 7-valent pneumococcal conjugate vaccine has recently been licensed and will be available in South Africa in 2004. A surveillance study of >200 000 patients showed a marked reduction in invasive pneumococcal disease in children less than 5 years of age with routine use.[7] It is immunogenic in children from 6 weeks of age and is indicated in HIV-infected and -uninfected children.

Influenza vaccine

Currently only a subunit influenza vaccine is available. A cold-adapted live attenuated trivalent influenza A/B intranasal vaccine is to be licensed in the near future. All children more than 6 months of age can receive the vaccine. If given for the first time in children less than 8 years of age, 2 doses 1 month apart is indicated. Thereafter and for older children a single annual dose before the start of the influenza season, usually March to April, is sufficient. Current specific indications in children are: a) asthma and other chronic pulmonary conditions, b) haemodynamically significant cardiac disease, c) immunosuppressive disorders including HIV infection, d) diabetes mellitus e) chronic renal disease f) chronic metabolic disease and g) diseases requiring long-term salicylate treatment (to prevent Reye's syndrome). A contraindication is gentamicin/neomycin allergy and in asthmatics with allergy to egg, the vaccine should be administered under close supervision.

Hepatitis A vaccine (HAV)

HAV consists of whole inactivated virus. It is administered as 2 doses 6 months apart. It is advised for all children more than 2 years of age. In case of exposure to hepatitis A disease, passive immunization with human immunoglobulin 0.02 ml/kg intramuscularly as soon as possible but no more than 2 weeks after exposure is indicated. HAV can be given concurrently at a different site.

Varicella vaccine

This is a live attenuated virus vaccine. Although chickenpox is not usually associated with severe morbidity or mortality this is higher for those more than 15 years of age, HIV-infected and other immunocompromised individuals, and in infants less than 12 months of age. Health care workers are at special risk. Outbreaks in paediatric wards are common. The vaccine is administered as a single dose in children less than 13 years of age and as 2 doses 4-8 weeks apart in children more than 13 years of age.

Current indications are: a) HIV-infected children with mild immunodeficiency (CD4 lymphocyte count >25%), b) all health care workers and medical students who are varicella antibody negative, c) effective in oncology patients with a lymphocyte count >1000 and no steroids >1 month in 90%, and d) can be given to any healthy child more than 9 months of age.

Contraindications are severe immunodeficiency, pregnancy and hypersensitivity to neomycin. If a patient is exposed during pregnancy, Varicella Zoster immunoglobulin (VZIG) can be administered. Side effects are infrequent. Rash is the most common. Encephalitis, ataxia, erythema multiforme and thrombocytopenia occur in <2/100 000 vaccinations.

Combination vaccines

Combination vaccines merge antigens that prevent different diseases (e.g. DPT, DPT-Hib, DPT-HBV) into a single product or protect against multiple strains of infectious agents causing the same disease (e.g. trivalent OPV). Licensed combination vaccines reduce the number of injections without increasing the rate of adverse events. Combination vaccines have some potential disadvantages. These include an inability to decide which component is responsible for a particular adverse event the possibility of reduced immunogenicity.

Tetravalent vaccines (DTP-Hib, DTP-HBV) are well established. Recently, a pentavalent DTP-HBV/Hib vaccine (separate DTP-HBV plus Hib vaccines mixed in one syringe) has become available in South Africa and can be used at 6, 10 and 14 weeks. Studies have shown this combination vaccine to be safe and well tolerated, with high immunogenicity against all component antigens and without an increase in reactogenicity.[8,9]

Passive immunization

Passive immunization is when a person recently exposed or about to be exposed to an infectious agent is given preformed human or animal antibody. Non-human antibodies stimulate production of anti-idiopathic antibodies that may lead to either serum sickness or arthus reaction. Passive immunization is used with exposure to the following diseases:

Measles

Give susceptible (unimmunized) children human immunoglobulin 0.25 ml/kg (for immunocompromised children give 0.5 ml/kg) with a maximum of 15 ml within 6 days of exposure.

Hepatitis A

Household or day-care centre contacts should be given human immunoglobulin 0.02 ml/kg IMI as soon as possible but no more than 2 weeks after exposure. Hepatitis A vaccine can be given concurrently at a different site, but the vaccine alone is not sufficient to prevent disease after contact. Passive immunization also works for pre-exposure prophylaxis, although only for 2-3 months.

Hepatitis B

Hepatitis B Immunoglobulin (HBIG) is for post-exposure prophylaxis if not previously immunized (EPI SA routinely includes HBV from July 1995). Newborns of mothers with acute or chronic hepatitis should be given HBIG together with first dose HBV (different site) within 12 hours of delivery as post-exposure prophylaxis.

Varicella Zoster immunoglobulin (VZIG)

This is specifically indicated for high-risk susceptible children (immunocompromised, kwashiorkor, immunosuppressive therapy) within 96 hours of contact with chickenpox and newborns of mothers who contracted chickenpox 5 days before or up to 5 days after delivery. In a hospital setup it may be used in all children who come into contact with a new case of chickenpox in the ward. It should, however, be remembered that VZIG is only protective for a period of two weeks. The dose is 0.15 ml/kg IMI with a minimum dose of 1 ml.

Vaccines for the traveling child (area dependent)

It is wise to clarify with the travel agent or the South African Society of Travel Medicine (contact telephone number: 0861-300911 or website address: www.traveldoctor.co.za) what immunizations are required for visits to specific areas or countries. Vaccines that are commonly required especially in Africa and other developing countries are hepatitis A and B, yellow fever, typhoid, meningococcus (strain types A, C, Y, W-135; in South Africa mainly strain type B – no vaccine available) and cholera.

Opportunities to immunize

Finally, it remains the responsibility of every member of the health care team to make sure that no opportunity to immunize a child is missed, even if it means opening a new multiple dose vial for a single patient. To avoid missed opportunities three components are necessary: an awareness to screen every child's Road to Health Card, a well-organized referral system within each health facility, especially now that no facility is dedicated only to prevention, and regular availability of vaccines.

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