HIV and Immunosuppression

Program Management

(SAGE) identified the need for appropriate immunization strategies in areas where infection with the human immunodeficiency virus (HIV) among children, adolescents or adults is high.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 9-11 November 2005

Schedule

The cell culture-based, live attenuated (JE) vaccine appears to require fewer doses for longterm protection, is in most cases less expensive, and seems to represent an attractive alternative to the mouse brain-derived vaccine. However, more needs to be known on its safety and efficacy when used in immunodeficient people, as well as on the impact of co-administrating this vaccine with other vaccines (page 332.)

The live attenuated vaccine induces protection for several years after 1 or 2 doses, whereas durable protection by the mouse brain-derived vaccine may require 2-3 initial doses followed by boosters at intervals of approximately 3 years. As the price per dose of the mouse brain-derived vaccine in most countries is higher than that of the live attenuated vaccine, the need for repeated doses renders the former vaccine unaffordable in many JE-endemic countries (page 339)
Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for vaccination (against influenza) in order to reduce the incidence of severe illness and premature death.

1. Residents of long-term care facilities for elderly people and the disabled.
2. Elderly non-institutionalized individuals with chronic conditions such as pulmonary and cardiovascular illness, metabolic diseases including diabetes mellitus and renal dysfunction, and various types of immunosuppression, including people with acquired immunodeficiency syndrome (AIDS) and transplant recipients.
3. All adults and children aged >6 months with any of the conditions mentioned above.
4. Elderly individuals who are above a nationally defined age limit, irrespective of other risk factors. Although the appropriate age for general vaccination may be considerably lower in countries with poor living conditions, most countries define the age limit to be >65 years.
5. Other groups defined on the basis of national data and capacities, such as contacts of high-risk people, pregnant women, health-care workers and others with key functions in society, as well as children 6-23 months of age.

Influenza vaccines (WHO position paper)

All infants, including HIV-positive individuals, should be immunized against pertussis.

Pertussis vaccines (WHO position paper)

Note: an infant with known or suspected HIV infection and/or signs and symptoms of AIDS should receive measles vaccine at six months and then again at nine months

Immunization in practice: a practical resource guide for Health workers – 2004 update Module 2: The vaccines

Since severe adverse effects of BCG vaccination are extremely rare even in asymptomatic, HIV-positive infants, all healthy neonates should be BCG-vaccinated, even in areas endemic for HIV. However, where resources permit, long-term follow-up of BCG-vaccinated infants of known HIV-positive mothers is desirable for early treatment, should disseminated BCG disease occur in children with rapid development of immunodeficiency.

BCG vaccine (WHO position paper)
**HIV and Immunosuppression**

BCG vaccination is indicated
– for all infants living in areas where TB is highly endemic (concerning HIV, see below);
– for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
– for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated
– for persons with impaired immunity (symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
– for patients under immunosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
– in pregnancy.

*BCG vaccine (WHO position paper)*

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Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.

*BCG vaccine (WHO position paper)*

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Immunocompromised children and adults can also benefit from vaccination (with hepatitis B vaccine.) However, the immune response may be reduced and additional injections of the vaccine may be required. Where possible, the anti-HBs antibody titres should be followed up after immunization of immunocompromised individuals.

*Hepatitis B vaccines (WHO position paper)*
HIV and Immunosuppression

Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.

Measles vaccines (WHO position paper)

The recommended age for measles vaccination depends on the local measles epidemiology as well as on programmatic considerations. In most developing countries, high attack rates and serious disease among infants necessitate early vaccination, usually at 9 months of age, despite the relatively low (80-85%) seroconversion rates following vaccination in this age group. Unless severely immunocompromised, HIV-infected infants should receive measles vaccine at 6 months of age, followed by an additional dose at 9 months.

Measles vaccines (WHO position paper)

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.

Global Advisory Committee on Vaccine Safety, 3–4 December 2003

HIV and Immunosuppression

The duration of protection following immunization with the 23-valent polysaccharide vaccine is estimated at 5 years, or more, in healthy adults. However, the duration may be considerably shorter in some high-risk groups for pneumococcal disease. Revaccination using the polysaccharide vaccine is not routinely recommended.

(Page 116) Revaccination using the polysaccharide vaccine is not routinely recommended, but immunocompromised children who have received polysaccharide vaccine may be revaccinated after 3 years. The safety of three or more doses of the polysaccharide vaccine is not known.

Vaccine Administration

The cell culture-based, live attenuated (JE) vaccine appears to require fewer doses for longterm protection, is in most cases less expensive, and seems to represent an attractive alternative to the mouse brain-derived vaccine. However, more needs to be known on its safety and efficacy when used in immunodeficient people, as well as on the impact of co-administrating this vaccine with other vaccines (page 332.)

The live attenuated vaccine induces protection for several years after 1 or 2 doses, whereas durable protection by the mouse brain-derived vaccine may require 2-3 initial doses followed by boosters at intervals of approximately 3 years. As the price per dose of the mouse brain-derived vaccine in most countries is higher than that of the live attenuated vaccine, the need for repeated doses renders the former vaccine unaffordable in many JE-endemic countries (page 339)
HIV and Immunosuppression

Testing to determine antibody responses is not necessary after routine vaccination (with hepatitis B vaccine.) However, when feasible, knowledge of response to vaccination is important in the following groups:
(i) persons at risk of occupationally acquired infection; (ii) infants born to HBsAg-positive mothers; (iii) immunocompromised persons; and (iv) sexual partners of HBsAg-positive persons.

Testing for anti-HBs should be performed by a method that allows determination of whether the anti-HBs concentration is protective (>10 mIU per ml). Adults should be tested 1-2 months after completion of the vaccination series. In settings where resources are available, infants born to HBsAg-positive mothers should be tested at 8-15 months of age, after completion of the vaccination series. Persons found to be antibody-negative after the primary series should be referred for appropriate follow-up.


If post-exposure (rabies) treatment must be given to immunocompromised individuals, HIV-positive persons, people under malaria chemoprophylaxis or people under anaesthesia, intramuscular vaccine and rabies immune globulin are mandatory and their antibody responses should be monitored serologically.


Contraindications

(Immunodeficiency including HIV infection is not a contraindication to (the use of TT or dT.)


Yellow fever vaccine is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation WHO/IVB/05.18 Page 46
Following nasal administration, transmission of the (influenza) vaccine virus to exposed non-immune people appears to be very rare. However, as a precaution the vaccine should not be given to highly immunosuppressed individuals or their close contacts.

Contraindications for use (of CAIV-T influenza vaccine) include anaphylactic reactions to eggs, a history of Guillain-Barré syndrome, patients aged <18 years on long-term aspirin therapy, pregnancy during the first trimester, and various states of immunosuppression.

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant that exhibits the signs and symptoms of AIDS.
The following are not contraindications. Infants with these conditions should be immunized:
• allergy or asthma (except if there is a known allergy to a specific component of the vaccine mentioned above);
• any minor illness, such as respiratory tract infections or diarrhea with temperature below 38.5°C;
• family history of adverse events following immunization;
• family history of convulsions, seizures, or fits;
• treatment with antibiotics;
• known or suspected HIV infection with no signs and symptoms of AIDS;
• signs and symptoms of AIDS, except as noted above (see 2.20);
• child being breastfed;
• chronic illnesses such as chronic diseases of the heart, lung, kidney, or liver
• stable neurological conditions, such as cerebral palsy or Down’s Syndrome;
• premature or low-birthweight (vaccination should not be postponed);
• recent or imminent surgery;
• malnutrition; and
• history of jaundice at birth.

Infants and children with symptomatic human immunodeficiency virus (HIV) or those known to have other immunodeficiency states should not be BCG vaccinated.
**HIV and Immunosuppression**

BCG vaccination is indicated
– for all infants living in areas where TB is highly endemic (concerning HIV, see below);
– for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
– for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated
– for persons with impaired immunity (symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
– for patients under immnosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
– in pregnancy.

*BCG vaccine (WHO position paper)*


Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.

*BCG vaccine (WHO position paper)*


Persons with a history of an anaphylactic reaction to neomycin, gelatin or other components the vaccine should not be vaccinated (with measles vaccine.) Furthermore, measles vaccine is contraindicated in persons who are severely immunocompromised as a result of congenital disease, HIV infection, advanced leukaemia or lymphoma, serious malignant disease, or treatment with high-dose steroids, alkylating agents or antimetabolites, or in persons who are receiving immunosuppressive therapeutic radiation.

*Measles vaccines (WHO position paper)*

HIV and Immunosuppression

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.

Global Advisory Committee on Vaccine Safety, 3–4 December 2003

A critical and unresolved issue is the safety and efficacy of yellow fever vaccine in human subjects infected with immunodeficiency virus (HIV). It remains to be determined whether HIV-positive status materially affects seroconversion, the risk of invasion of the nervous system and of encephalopathy, the stage of HIV disease at which yellow fever vaccination should be contraindicated, and whether there are differences in the incidence of minor and major adverse effects in HIV-positive subjects.

Global Advisory Committee on Vaccine Safety, 3–4 December 2003

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.

27 June 2008
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Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm3 who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking highdose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.

A child with a history of a severe allergic reaction (e.g. generalized urticaria, difficulty in breathing, swelling of the mouth and throat, hypertension, shock) to a previous dose of hepatitis B vaccine should not receive another dose.

The following are NOT contraindications:
- minor illness, such as respiratory tract infection or diarrhoea with temperature below 38.5°C;
- allergy or asthma;
- family history of convulsions;
- treatment with antibiotics;
- infection with HIV;
- breastfeeding;
- history of seizures (convulsions, fits);
- chronic illnesses such as chronic diseases of the heart, lung, kidney or liver;
- stable neurological conditions such as cerebral palsy and Down syndrome;
- prematurity or low birth weight;
- history of jaundice at birth.
There are few contraindications to mumps vaccination. As with all live attenuated vaccines, mumps vaccine should not be administered to individuals with advanced immune deficiency or immunosuppression. Fetal damage has not been documented when mumps vaccines have been given to pregnant women. Allergy to vaccine components such as neomycin and gelatin is a contraindication to administration of the vaccine.


It is not known whether this live attenuated vaccine (Ty21a typhoid vaccine) can cause fetal harm when administered to pregnant women. Ty21a can be administered to HIV-positive, asymptomatic individuals without risk as long as the T-cell count (CD4) is above 200/mm3.


There are no contraindications (to the Vi polysaccharide typhoid vaccine) other than prior severe reaction to vaccine components. Although the vaccine is safe for HIV-infected persons, the induction of protective antibodies is directly correlated to the levels of CD4 positive T-cells.


In immunocompromised persons, including patients with advanced HIV infection, varicella vaccination is currently contraindicated for fear of disseminated vaccine induced disease.

**HIV and Immunosuppression**

## Adverse Event

PCV-7 has been tested in trials in different parts of the world and has been proven to be safe and well tolerated even among children infected with HIV.

However, slight swelling and tenderness at the injection site may occur and transient fever of $\geq 39^\circ C$ has been reported in up to 4.7%. The incidence and severity of adverse reactions have not been reported to increase with subsequent doses.

As with the introduction of any new vaccine, however, continued surveillance for possible unexpected effects is important.

(Page 103) The safety and efficacy of PCV-7, as well as of other formulations of pneumococcal conjugate vaccines, have been well established in numerous settings both in industrialized and developing countries, and among infants with HIV infection.

*Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)*


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*Japanese encephalitis vaccines (WHO position paper)*

Occasionally (with mouse brain-derived JE vaccine,) hypersensitivity reactions, in some cases serious generalized urticaria, facial angio-oedema or respiratory distress, have been reported, principally in vaccine recipients from non-endemic areas. The reported rates of such reactions in prospective and retrospective studies are usually in the range of 18-64 per 10 000 vaccinated subjects. A complicating factor is that such reactions may occur as late as 12-72 hours following immunization. Sensitization to gelatine, a vaccine stabilizer, has been suspected in some cases in Japan, but the underlying cause remains uncertain.

The only contraindication to the use of this vaccine is a history of hypersensitivity reactions to a previous dose. However, pregnant women should be vaccinated only when at high risk of exposure to the infection. Mouse brain-derived vaccine has been given safely in various states of immunodeficiency, including HIV infection.

Outbreak Control

Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.
The burden of pneumococcal disease is substantially higher among individuals infected with HIV. Since pneumococcal conjugate vaccines have been shown to be safe and efficacious in HIV-infected children, SAGE recommends introducing PCV-7 in countries where HIV is a significant cause of mortality and it encourages evaluation of the impact of vaccination among the HIV-infected population.

Populations with a high prevalence of other underlying conditions that increase the risk of pneumococcal disease, such as sickle-cell disease, should also be targeted for vaccination.

Countries are encouraged to conduct appropriate surveillance for pneumococcal disease in order to establish a baseline measurement of disease and to monitor the impact of vaccination. This is particularly important in those developing countries that will be among the first to introduce the vaccine and in countries with a high prevalence of HIV infection or other conditions known to increase the risk of pneumococcal disease.

Countries are encouraged to conduct appropriate surveillance for invasive pneumococcal disease to establish a baseline measure and to monitor the impact of vaccination, including the occurrence and magnitude of replacement disease. This is particularly important in those developing countries that are among the first to introduce the vaccine into their national programmes; and in countries where there is a high prevalence of HIV infection or where other conditions known to increase the risk of pneumococcal disease exist.
SAGE recommends that while influenza vaccine research has considerable momentum, investigation into the development of vaccines against subtypes with pandemic potential other than H5N1 should continue (for example, H7).

So far, mainly healthy adults have been enrolled in clinical trials with H5N1 candidate vaccines. SAGE stresses the importance of evaluating their safety and immunogenicity in children and immunosuppressed individuals.

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.
**HIV and Immunosuppression**

### Introduction of Vaccines

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*Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006*  

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