

Immunization of Persons with HIV Infection and other Secondary Immunodeficiencies

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Patients with secondary immunodeficiencies are at a high risk of infection. Currently some of these infections are preventable through specific immunization. Prevention of these diseases can diminish morbidity and mortality amongst these patients. In this review we describe the use of vaccines in persons with secondary immunodeficiencies.

Key words: immunization - vaccines - HIV infection - secondary immunodeficiencies

The number of patients with secondary immunodeficiencies has increased rapidly in the last three decades. This is secondary to the improvement in cancer treatment, the use of immunosuppressive drugs in autoimmune diseases and transplants, and mainly due to HIV infection (CDC 1991, Ljungman 1995).

Immunocompromised patients are at a high risk of infection and some of these are preventable through specific immunization. Prevention of these diseases can diminish morbidity and mortality amongst these patients. Therefore, a full understanding of their disease, knowledge when to immunize them and the right use of these vaccines are mandatory to any physician following such patients.

In this review we describe the use of vaccines in persons with secondary immunodeficiencies.

VACCINES

Usually immunization is indicated to protect individuals or populations against serious infections, diminish the number of infected people and, as the main goal, eradicate the disease.

The World Health Organization (WHO) has recommended some vaccines that are used worldwide and some governments adopt other vaccines depending on the prevalence of such diseases in their countries (Table).

Vaccines can be divided into two groups (Table): killed, inactivated or subunit and live vaccines (WHO/EPI 1995).

TABLE

Vaccines used worldwide

Live vaccines	Killed, inactivated and subunit vaccines
BCG ^a	Cholera
Measles ^b	Diphtheria ^b
Mumps	Haemophilus influenza
Oral poliomyelitis (Sabin) ^b	Hepatitis A
Rubella	Hepatitis B ^b
Yellow fever ^a	Inactivated polio (Salk) ^b
	Influenza
	Japanese B encephalitis
	Meningococcus
	Pertussis ^b
	Pig Bel
	Pneumococcus
	Rabies
	Tetanus ^b
	Typhoid

a: recommended in endemic countries (EPI - WHO);

b: vaccines used in the EPI (WHO).

TYPES OF ACQUIRED IMMUNOSUPPRESSION

Secondary immunodeficiencies can be divided into three different groups: (1) Non HIV severe immunodeficiency; (2) Common variable immunodeficiency (limited immune deficits) and (3) HIV infection.

NON HIV SEVERE SECONDARY IMMUNODEFICIENCY

Non HIV severe secondary immunodeficiency can be due to a variety of conditions such as leukaemia, lymphoma, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids (CDC 1993).

Killed or inactivated vaccines do not represent a danger to immunocompromised persons and should be administered as recommended for

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healthy persons. In contrast live-virus vaccines and live-bacteria vaccines such as *Mycobacterium bovis* BCG are contraindicated for persons that are severely immunocompromised. Oral polio vaccine is contraindicated to any person that is in contact (health care providers and household contacts) with a severely immunodepressed patient (CDC 1993, WHO EPI 1995).

Administration of live-virus vaccine in patients on treatment with steroids is not contraindicated when steroid therapy is: (1) short term (less than two weeks); (2) low to moderate dose; (3) long-term alternate day treatment with short acting preparations; (4) replacement therapy; (5) administered topically. A dose equivalent to either 2 mg/kg of body weight or a total of 20 mg/day of prednisone is sufficiently immunosuppressive to raise concern about safety of immunization with live-virus vaccines (CDC 1993).

COMMON VARIABLE IMMUNODEFICIENCY

Common variable immunodeficiency is secondary to diseases that cause limited deficits and may require use of special vaccines or higher doses of vaccines but that do not contraindicate use of any particular vaccine. Some of these immunocompromised patients lose protective immunity to infections such as tetanus, poliovirus (Ljungman et al. 1990, 1991) and others become susceptible to infections such as haemophilus and pneumococcus (Ljungman 1995). Patients with limited immunocompromising conditions (e.g., asplenia, diabetes, alcoholic cirrhosis) may be at higher risk for certain diseases, and additional vaccines, particularly bacterial polysaccharide vaccines (*Haemophilus influenza* type b - Hib, pneumococcal and meningococcal), are recommended for them. Hepatitis B is indicated for patients with renal failure. Higher doses or more frequent boosters of these vaccines may be required as the immune response of these immunocompromised subjects may be suboptimal.

HIV INFECTION

HIV-infected subjects are likely to present a more severe outcome of infections targeted by immunizations than seronegative individuals. For example, measles tends to occur earlier in life (Embree et al. 1992) and has a high mortality rate in HIV-infected children as compared to seronegative ones (Kaplan et al. 1992). Other diseases like tuberculosis, whose incidence has increased dramatically worldwide due to the HIV epidemic, is more likely to be associated with progressive AIDS than in seronegative persons (Schulzer et al. 1992). The antimycobacterial therapy is less effective and the mortality rate is higher in these in-

dividuals (Nunn 1990). The severity of these illnesses is the basis for the recommendation of basic immunization in HIV-infected individuals.

A major concern regards the effectiveness of vaccines in seropositive persons and their ability to respond to immunogens. Indeed, HIV-infected children are capable of mounting cellular and humoral immune responses to common vaccines in the first two years of life, but these responses decline during the following years and the seroconversion rates decrease with progression to AIDS (Borkowsky et al. 1992). The antibody levels tend to be lower and to decrease more rapidly over time in HIV-infected individuals than in non-infected persons (Ryder et al. 1993). The suboptimal antibody responses occur particularly after immunization with CD4-lymphocyte-dependent antigens such as the polysaccharide-based pneumococcal and *H. influenzae* vaccines (Ljungman 1995).

Another major concern is the safety of immunization, particularly with live-attenuated vaccines. Since HIV infection results in progressive deterioration of the immune system, the use of live immunogens could cause severe vaccine-associated diseases. Prospective studies comparing BCG immunization in HIV-infected and non infected children have failed to show any difference in the risk of regional complications (Ryder et al. 1993). However, there have been isolated reports of disseminated BCG disease in HIV-infected adults and children (Blanche et al. 1986, Houde & Dery 1988, Smith et al. 1992). In HIV-infected adults, disseminated BCG disease can be a late complication and has been reported 30 years after immunization (Reynes et al. 1989). Studies of measles, mumps and rubella and oral polio vaccination among asymptomatic and symptomatic HIV-infected subjects have not documented serious or unusual adverse effects. However, administration of oral polio vaccine to children with congenital immunodeficiencies, particularly agammaglobulinemia, has resulted in severe progressive neurologic disorders (Davies et al. 1977).

Another important aspect to be considered in the immunization of HIV-infected individuals is the enhancement of viral replication following immune stimulation. The stimulation of CD4 lymphocytes is an important factor for HIV replication (Fauci 1996). It has been demonstrated *in vitro* that cell-cell interaction during antigen presentation, through the engagement of adhesion molecules LFA-1 and ICAM-1, is a potent inducer of HIV transcription (Shattock et al. 1996). *In vivo* increased plasma viral load has been reported following parenteral (Staprans et al. 1995, Stanley et al. 1996) as well as oral (Ortigão-de-Sampaio et

al. 1997) immunization. However, the increase in viral load in these reports was transient, returning to base levels 15 to 21 days post-immunization, and without any clinical adverse reactions.

Currently, WHO/UNICEF recommends that the immunization schedule for HIV-infected individuals should follow the national standards for each country. All live vaccines should be avoided, particularly in adults. Nevertheless, BCG vaccine is recommended for asymptomatic HIV-infected children living in high risk conditions of tuberculosis. Due to the risk of early and severe measles infection, these infants should receive two doses of measles vaccine at six and nine months of age. Although oral live-attenuated polio vaccine has not been harmful when administered to asymptomatic HIV-infected children, killed virus vaccine should be preferred when available. Pneumococcal vaccine should be given to all HIV-infected persons with two or more years of age. Children older than two years should receive Hib vaccine according to routine schedule. Other vaccines such as hepatitis B are recommended to HIV adults and children, although more studies concerning its effectiveness are still to be done.

In conclusion the use of the right vaccines in immunocompromised subjects is fundamental to increase the quality of life of these patients and the prevention of such infectious diseases is less expensive for governments than the not always well succeeded treatment of these life threatening infections.

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