

GLOBAL PROGRAMME ON AIDS

**Fourth Meeting of the WHO-IFPMA Working Group
on the Development, Testing, Utilization
and Supply of Drugs and Vaccines for HIV Infection
and HIV-related disease**

Geneva, 1-2 February 1993

**Potential vaccination strategies using
HIV vaccines in developing countries:
an update (information only)**

INTRODUCTION

Although a number of scientific problems related to human immunodeficiency virus (HIV) vaccine development remain to be solved, the research community is hopeful that a safe and effective vaccine against HIV may be developed within the next ten years. The major challenge will then be to identify rational strategies for the utilization of an HIV vaccine for public health purposes.

This working paper makes an assessment of populations which could initially be targeted for HIV vaccination; such an assessment will be revised as characteristics of the vaccine, such as its immunogenicity, heat stability and cost are known.

CRITERIA FOR IDENTIFICATION OF POTENTIAL TARGET POPULATIONS FOR VACCINATION

Potential target populations for an HIV vaccine may be identified by the following criteria:

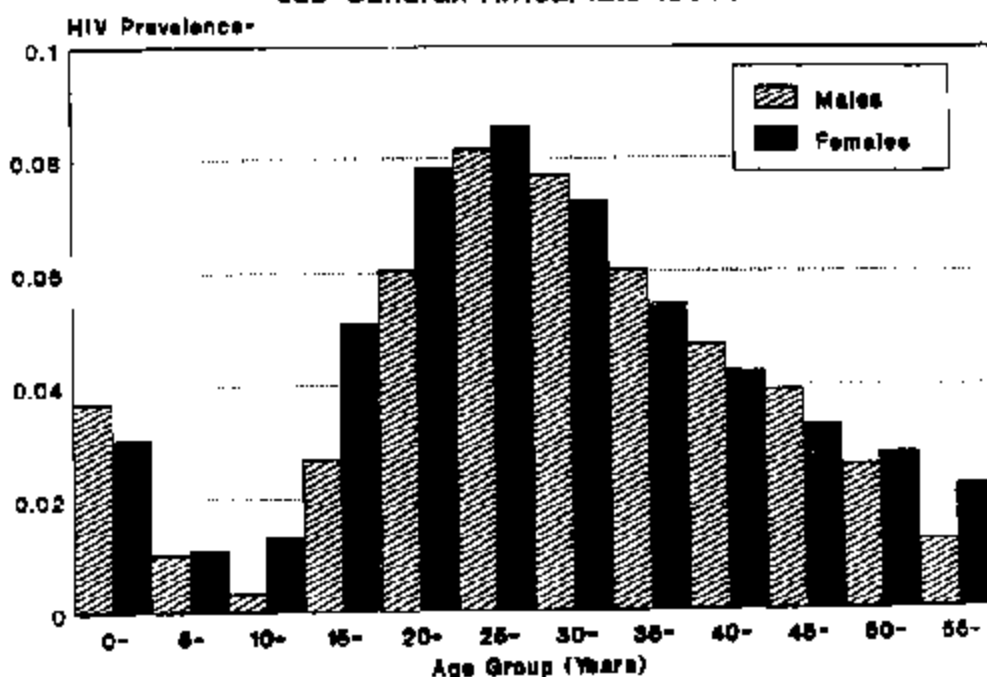
- The epidemiology of HIV-associated risk behaviours and practices;
- The current and projected future risk of HIV infection in different geographic areas; and
- The accessibility of the health care system.

Epidemiology of HIV-associated risk behaviours and practices

HIV infection is epidemiologically associated with certain behaviours or practices, which are, in general, not uniformly distributed throughout the population. They include unprotected sexual intercourse, administration of blood unscreened for HIV, and sharing of blood-contaminated needles and syringes. HIV infection is also epidemiologically associated with pregnancy and the postnatal period.

The greatest proportion of persons with HIV-associated risk behaviours or practices are infected in adolescence and young adulthood. Consistent with this fact is the typical age distribution of HIV seroprevalence, such as seen in sub-Saharan Africa, where the majority of HIV infections occurs in the 15-45 year age group. (Figure 1).

Figure 1: Typical Age-Sex Distribution of HIV Infections, sub-Saharan Africa, late 1980s



- Distributed such that M/F=0.48/0.52
(M/F Ratio 1:1)

SFI/RES/GPA/WHO

The continued epidemic transmission of any infection requires a certain "critical density" of infected and susceptible persons, hence, HIV generally spreads more rapidly in urban than in rural areas.

Table 1 shows the worldwide population estimates for the year 2000, by continent or region, in the 10-19 and 20-49 age groups, those groups at greatest risk of HIV infection.

Table 1

Demographic characteristics of potential priority age groups for HIV immunization

Area	% Urban	Urban population (millions) ¹		School enrolment (%) ¹
		10-19	20-49	
<u>High HIV prevalence</u>				
Sub-Saharan Africa	37	61	100	40
<u>Intermediate HIV prevalence</u>				
South and South-East Asia	34	151	291	47
Latin America and Caribbean	76	83	179	72
North America (USA/Canada)	83	34	110	98
<u>Low HIV prevalence</u>				
Europe	77	87	280	84
Oceania	85	4	11	76
East Asia	47	132	389	47 ²
North Africa/Middle East	59	24	43	52
GLOBAL TOTALS	576			

¹ School enrolment rates for 12-17 age group, adapted from UNESCO

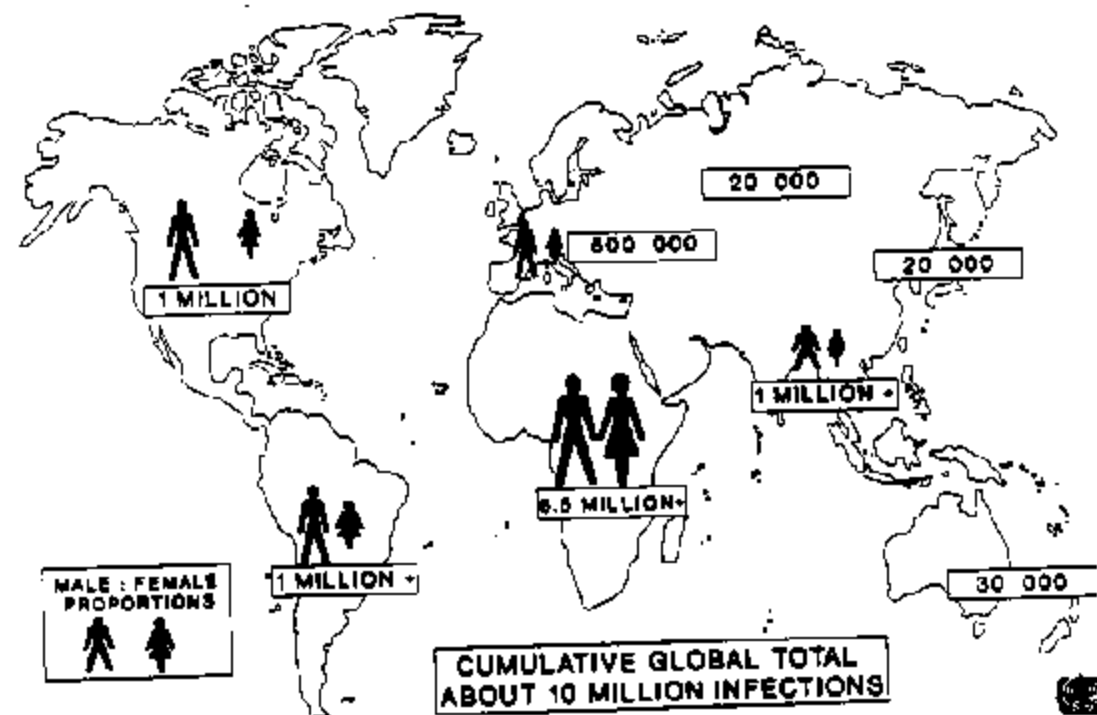
² Figures available from UNESCO do not provide separate figures for South/South-East Asia and East Asia; therefore published figure for all Asia were used for both

Current and projected future risk of HIV infection in different geographic areas

As of early 1992, the distribution of estimated cumulative HIV infections varies considerably between different continents or regions of the world, with the majority (over 80%) in developing countries. (Figure 2)

FIGURE 2

ESTIMATED GLOBAL DISTRIBUTION OF ADULT HIV INFECTIONS, EARLY 1992



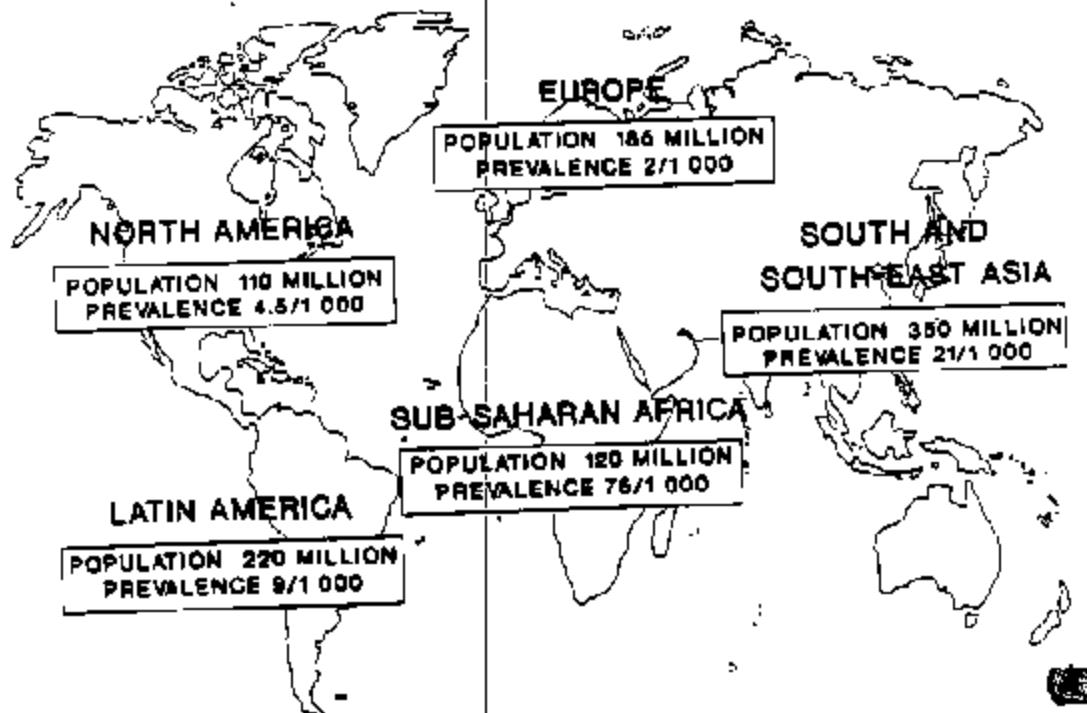
WHO/GPA/REB/SFI

Approximately two-thirds of all HIV infections worldwide are thought to have occurred in sub-Saharan Africa. The majority of the remaining HIV infections in developing countries appear to be distributed more or less equally between South and South-East Asia, Latin America and the Caribbean. (Figure 3)

Conservative projections from WHO estimate that by the year 2000 a cumulative total of 20-30 million adults and 10 million children will have been infected with HIV, over 90% in developing countries. For the foreseeable future, the highest infection risk areas will remain sub-Saharan Africa, South and South-East Asia, Latin America, and the Caribbean.

FIGURE 3

**PROJECTED ADULT HIV PREVALENCE RATES
AND URBAN 15-49 POPULATION BY THE YEAR 2000**



WHO/GPA/RES/371

Accessibility of a targeted population to the health care system.

Experience with the hepatitis B virus (HBV) vaccine delivery, as well as experience accumulated by the WHO Expanded Programme on Immunization (EPI) on the delivery of selected vaccines to infants and children in the developing world, provides important lessons which can be applied to HIV vaccine delivery. Lessons learned are that the effectiveness of any immunization strategy will always depend on the ability to reliably and consistently access the populations targeted for vaccination and the ability to reliably and consistently provide potent vaccine to such populations.

POTENTIAL TARGET POPULATIONS FOR HIV VACCINATION

The three criteria discussed above allow the identification of potential target populations for HIV vaccination. Four such potential populations are considered in detail below:

- Persons with high-risk practices;
- Adolescents attending school;
- Women of childbearing age, or women attending antenatal clinics; and
- Infants and children.

The advantages and disadvantages of each potential target population are summarized in Table 2. Because HIV immunization coverage rates would increase progressively over time from zero, an effect on HIV incidence is not likely to be immediate, no matter which population is targeted for HIV vaccination.

Table 2

Comparison of potential target populations for HIV immunization

Factor	Target population			
	"High-risk" individuals	Adolescents in school	Pregnant women	Infants children
Population access	Poor	Unknown	Good	Good
Expected effect on HIV incidence	Minimal	Slightly Delayed	Slightly Delayed	Greatly Delayed
Requirement for booster doses	Possible	Possible	Possible	Highly Possible

Adapted from: Strategies for hepatitis B vaccination (MIM/CDS/WHO).

Vaccination of persons with high-risk practices

Vaccination of persons with high-risk practice should always be pursued. By definition, these persons are at high risk of being infected, and therefore they stand to benefit greatly from HIV vaccination. A disadvantage of vaccination of these persons is, however, that a high percentage may already be infected, causing high vaccine wastage. HIV vaccination should also be provided for persons who perceive themselves to be at risk, such as health care workers.

Based on the HBV vaccine experience, however, such a strategy is unlikely to significantly alter the overall incidence of HIV infection in the general population. In the United States the initial HBV vaccination strategy emphasized the immunization of persons practising high-risk behaviour, in particular male homosexuals and injecting drug users. This strategy failed to have a significant impact on HBV incidence because of major difficulties in reliably and consistently accessing such high-risk populations. In acknowledgment of this fact, the United States has recently recommended a change to universal infant immunization as the major thrust of its HBV immunization strategy. The problems of identifying target populations and developing vaccination strategies for HIV will be similar.

Vaccination of adolescents attending school

Vaccination of adolescents attending school may have a relatively rapid effect on reducing HIV incidence, although it will depend on rates of school attendance by adolescents. School enrolment ratios have increased considerably, and today over 50% of children aged 12-17 worldwide attend school (Table 1). A major problem is that no infrastructure for providing immunization to adolescents in school exists in most countries.

Vaccination of women of childbearing age or women attending antenatal clinics

Vaccination of women of childbearing age (15-49 years) may provide a means of accessing at least a significant part of the sexually active adult population. Such women are already targeted for tetanus toxoid immunization by EPI. The realistic target for HIV vaccine coverage in this population may be deduced from current EPI tetanus toxoid coverage levels (30-60%) in pregnant women.

When compared with a strategy of targeting school adolescents, a lesser overall effect on HIV incidence may be expected, because these "non-adolescent" women may have already been infected with HIV by the time they are immunized. The safety of any HIV vaccine for use in HIV-infected persons, or for use in pregnant women, would require confirmation beforehand.

Vaccination of infants and children

The obvious and considerable advantage of a strategy to vaccinate infants and children is the opportunity it provides to potentially incorporate HIV vaccination into EPI. In conjunction with many international, multilateral, and bilateral aid agencies, EPI has over the past 15 years developed a global infrastructure for childhood immunization, and has now attained overall global coverage of childhood immunization of between 83% and 85%, although coverage by continent or region can be as low as 57%. The problems of HIV vaccine delivery

would be greatly reduced were it were possible to simply "piggy-back" HIV vaccine delivery on EPI.

The great disadvantage of this strategy is that universal immunization of infants and children would require vaccines which induce long lasting immunity, and that any possible effect on HIV incidence would require decades. The strategy would thus have to be combined, at least for several years, with another vaccination strategy capable of influencing HIV incidence more rapidly, such as targeting one or more of the other populations discussed. Furthermore, HIV-immunized infants and children are the most likely group to require booster doses of HIV vaccine in adolescence if long lasting immunity cannot be induced with the initial vaccination series. Finally, immunization of infants and children will require previous demonstration of safety and immunogenicity of the vaccine in adults, then in infants and children.

HIV VACCINATION STRATEGIES

Points for consideration

In formulating an HIV vaccination strategy the following observations should be taken into consideration:

- The objective of an HIV prevention strategy through HIV vaccination is HIV/AIDS prevention and control, not vaccination *per se*. Therefore, it is vital that other HIV prevention interventions be maintained, even as HIV vaccine delivery to populations is implemented;
- The goal must be to protect susceptible individuals by vaccination before, or very soon after, they become at risk of HIV infection;
- For successful implementation of any vaccination strategy in developing countries, accessibility of the target population is essential;
- The physical and biological specifications of the vaccine product for delivery in the field are as important as its immunogenicity; and
- Price is a major consideration for vaccine utilization. The lower the price, the larger the population which may realistically be vaccinated.

Global HIV vaccination strategy: developing countries

A global HIV vaccination strategy should initially place primary emphasis on populations in which vaccination will result in as rapid a reduction as possible in HIV incidence. Since the majority of HIV infections will continue to be in developing countries, a major HIV vaccination effort in selected target populations in the developing world will be required.

HIV vaccine should be used from the outset in both industrialized and developing countries. This could impose a restriction to HIV vaccine access due to limitations in HIV vaccine production capacity, unless an adequate capacity is planned in advance. Such capacity may well depend, among other factors, on the suitability of a vaccine for mass production, as well as on the estimated vaccine requirement.

Vaccine requirement projections depend on estimates of full immunization courses that will be needed, which in turn depend on the proposed vaccination strategy.

To provide preliminary estimates of full immunization courses required, the elements of an HIV vaccination strategy, globally-based but targeted primarily at developing countries, are suggested in Table 3.

Table 3

Elements of an initial phase global HIV vaccination strategy

-
- Targeted populations:
 - Urban adolescents attending school;
 - Women of childbearing age (15-49 years) in urban areas accessed by EPI.

 - Targeted areas, ordered by level of HIV infection risk:
 - Sub-Saharan Africa;
 - South and South-East Asia;
 - Latin America and the Caribbean;
 - Rest of Asia, North America, Middle East, Oceania.

 - Initiate plans for future extension of vaccination to rural areas.

 - Initiate safety and immunogenicity studies in children and infants, for possible future integration into EPI.

 - Phase out urban adolescents and women of childbearing age, 10-15 years after universal HIV immunization of infants and children, with boosters to accessible adolescent groups if required.
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In this strategy the, initial priority may be to immunize urban adolescents and young adults (10-19 year olds) attending school, who reside in high and intermediate HIV prevalence regions of the world.

Since an immunization infrastructure does not exist for this population, immunization coverage, and hence vaccine supply requirements, would be expected to build up slowly. Assuming a progressive rise in coverage from 0% to 25% over the first five years of the programme, 8 million full HIV vaccination courses would be required in sub-Saharan Africa over this period. Inclusion of urban adolescents attending school in South and South-East Asia, Latin America and the Caribbean would necessitate the provision of an additional

48 million full vaccination courses during the same period, for a total of 56 million courses among adolescents attending school in high prevalence areas (Table 4).

Of equal priority may be HIV vaccination of childbearing age women in urban areas who receive tetanus toxoid through EPI in the same high and intermediate HIV prevalence areas. Assuming a progressive increase in HIV vaccination coverage from an initial 0% to 40% (present average coverage of tetanus toxoid) over the first five years of the programme, at least 168 million full immunization courses would be required for sub-Saharan Africa, South and South-East Asia and Latin America and the Caribbean (Table 4).

Table 4

Expected full HIV vaccination courses which may be required in the first 5 years of an HIV vaccination programme in developing countries, by target population (in millions)

Expected Full Immunizations

	Urban school adolescents	Urban women aged 15-49 ¹	Total full HIV immunizations series required ²
<u>Higher priority areas</u>			
Sub-Saharan Africa	8	30	38
South and South-East Asia	26	84	110
Latin America and Caribbean	22	54	76
SUB-TOTALS	56	168	224
<u>Lower priority areas</u>			
East Asia and the Pacific	23	64	87
North Africa and Middle East	5	10	15
SUB-TOTALS	28	74	102
TOTAL Developing Countries	84	242	326

¹ Women of childbearing age

² Estimates assume 25% HIV vaccine coverage achieved over 5 years, for adolescents in school. For women 15-49, it was assumed that HIV could achieve 40% coverage over 5 years.

Lower priority may be the lower HIV prevalence regions. Inclusion of such areas would add an additional 102 million full immunizations, for a grand total of 326 million full immunizations in developing countries in the first 5 years of the programme.

The HIV vaccination programme would also require extension to rural areas. It is likely that without such universal immunization strategies, the longer-term control of the HIV epidemic may be not be possible.

Prior to, or concurrently with, the initial phase of the suggested HIV vaccination programme, studies of the safety and immunogenicity of the HIV vaccine in infants and children should be pursued, with the longer-term objective of introducing universal HIV immunization of infants and children, probably through EPI.

What appears certain is that when an HIV vaccine becomes available for public health use, a large demand for the vaccine in developing countries would be built up rapidly. GPA will continue evaluating potential strategies and their possible impact on HIV incidence.