Johns Hopkins University
Center for AIDS Research

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Executive Summary

The HIV epidemic in the developing world has three interrelated components that must be addressed simultaneously: one is the epidemic of new HIV infections, the second is the needs of the large number of HIV infected persons in latent stages of infection, the third is care for HIV-associated complications and AIDS in persons with immunodeficiency. These require medical, social, and economic interventions. Although control of the epidemic is the primary goal amelioration of the impact of HIV disease in those already infected must also be a priority.

Provision of Antiretroviral Therapy (ART)

Antiretroviral treatment has not been widely available due to high cost and deficiencies in infrastructure. The Consultation strongly supports access to antiretroviral therapy based on established medical benefit (improving survival and decreasing HIV-associated complications, hospitalizations, and perinatal transmission), anticipated socioeconomic benefit (reducing orphanhood, maintaining the work force, and minimizing the loss of skilled manpower), and public health benefits (decreasing TB rates, improving health care infrastructure, and improving skills of health care professionals). HIV treatment and prevention are complementary and should be addressed simultaneously. Specifically, ART can provide an incentive for voluntary counseling and testing (VCT), and reduction in viral load may reduce HIV transmission (60% reduction in incidence per 1.0 decrease in $\log_{10}$viral load). The cost-benefit of antiretroviral therapy (ART) has been demonstrated in resource rich countries, but data for developing countries are not available except for Brazil, which has shown a cost benefit. Recommendations for implementation should utilize guidelines currently being developed by WHO for persons with evidence of immunodeficiency. While the criteria for initiation of ART in resource-poor settings have yet to be established, it is likely that initially therapy will be reserved for individuals with advanced disease. The continuum of clinical services to reduce suffering will require use of palliative care programs and pain management protocols. Given the imprecision of clinical case definitions it is critical to develop simple and cost-effective CD4 counts. Affordable viral load assays are highly desirable for monitoring response to ART.

Infrastructure requirements for delivering ART include the availability of voluntary testing and counseling (VCT), including rapid testing, drug management and compliance monitoring (e.g., DOTS), lab facilities for CD4 counts or viral load assays to determine eligibility for therapy and monitoring of efficacy, HIV clinical expertise (training), and programs to promote HIV prevention in order to avoid behavioral disinhibition (as has been observed among gay men in Europe and the U.S.). Operations research is needed to develop appropriate strategies, to monitor programs, to monitor resistance, to document benefit, and estimate coverage. Simulation models suggest that ART may diminish HIV incidence, but would be insufficient to control the epidemic.

Prevention of Mother-to-Child Transmission (PMTCT)

Pediatric HIV-1 infection can be diminished in the developing world with available antiretroviral drugs. Randomized controlled clinical trials have proven the efficacy of various regimens employing ZDV,ZDVT/3TC, or nevirapine (1-8). These regimens provide protection by prophylaxis of the infant during and after exposure to virus and /or decrease of viral replication in the mother. Prevention of infection is a potential life long health benefit and cost analyses support the benefits of PMTCT. In addition, PMTCT programs provide an entry point for primary prevention, care and support of women, children and household members. Thus, they should not be considered solely as a means of preventing HIV infection among infants.

Global use of simplified regimens such as the 2-dose nevirapine regimen is feasible, but implementation will be dependent upon the availability of new resources. Even with such intervention strategies, postpartum transmission via breast milk continues to occur. WHO recommends that where replacement feeding is feasible, safe and sustainable it is the feeding method of choice. Additional resources are required to make replacement feeding available, as well as to evaluate the safety of such feeding. Where breast-feeding continues to be the only feasible, safe, and sustainable feeding method of choice, exclusive breast feeding and early weaning is recommended.

Programs preventing MTCT should be initiated as quickly as possible. Such programs should encourage the provision of a "package" of antenatal and postnatal care for all mothers (iron / folate, vitamins, malaria chemoprophylaxis, tetanus, syphilis testing and treatment, condoms). The postnatal "package" should include family planning, prevention of sexually transmitted infections and linkage to continued care. Programs preventing MTCT should enhance availability of improved maternal and child care.

Four potential approaches to PMTCT should be considered:

1) VCT and ARV intervention to HIV+ women, with opt-out testing. Disadvantages include costs of VCT, the potential for women at higher risk to selectively refuse testing and thus be excluded.
2) VCT and ARV intervention to HIV+ women and women who refuse testing: In this case, all HIV infected women could have access to the ARV intervention.
3) Counseling to all patients in ANC and nevirapine offered universally to all women: Advantages are improved coverage and savings on VCT costs, disadvantages include treatment of HIV-women.
4) Universal offering of ARV to all pregnant women.

Prevention of MTCT will intersect with administration of ART to pregnant women. Consideration should be given to reserving nevirapine for PMTCT, to avoid resistance occurring during therapy, which might hinder one of the most cost-effective and feasible PMTCT intervention strategies. However, the benefit of decreasing MTCT with nevirapine drug prophylaxis outweighs concerns of drug resistance (WHO 2000).

TB, Opportunistic Infections and Palliative Care

Comprehensive clinical care for HIV disease is an urgent clinical, public health and humanitarian need. The provision of care will relieve suffering, prevent deaths, and may reduce stigma and facilitate VCT. The most effective prophylaxis for opportunistic infections (OIs) is ART. However, in the absence of ART, or in populations covered by ART, OI prophylaxis remains a priority.

Specific recommendations for therapy to treat or prevent OIs and TB are based on data documenting the burden of disease in populations of HIV-infected people, and on clinical trials establishing efficacy. Diagnosis of TB by microbiologic means is essential, and better methods for evaluating smear-negative patients are urgently required. Treatment of TB should be based on the DOTS strategy. TB preventive therapy is recommended for HIV-infected people with known or suspected latent

TB. Since this treatment is highly effective, the probability of active TB in HIV-infected people is 10- to 100-fold higher and TB is a major public health problem. Cotrimoxazole prophylaxis is known to reduce the number of HIV-related illnesses, and is recommended for HIV-infected people with TB, other OIs, or advanced HIV disease, including low CD4 counts. Unresolved issues include the impact of antibiotic resistance on effectiveness and the emergence of resistant bacteria and malaria with widespread cotrimoxazole use. Prevention of systemic mycoses with azole antifungals is efficacious, though no impact on survival has been documented

Behavioral Interventions and Voluntary Testing and Counseling (VCT)

Behavioral interventions including voluntary counseling and testing (VCT) have been shown to be effective in preventing HIV. Moreover, persons who learn they are HIV infected can access therapeutic and preventive services such as opportunistic infections prophylaxis, PMTCT or ART.

Behaviors known to reduce risk of HIV infection include delay in sexual debut, abstinence, partner reduction, consistent use of condoms, avoidance of contaminated blood (clean needles, screening of blood for transfusion), and use of VCT. Interventions known to be effective in promoting these behaviors include availability of low-cost or free condoms, counseling (individual, couple, group), communication programs, community and workplace interventions, harm reduction strategies (clean needles, drug substitution programs), and sexually transmitted infections screening and treatment.

VCT can be offered in free-standing centers, community sites, and mobile services, or integrated into existing health structures. VCT has been shown to be effective in risk reduction (risky behavior and STI/HIV incidence). There is evidence that couple counseling and targeted services (e.g. youth friendly) can enhance the effectiveness of VCT. Voluntary programs have been shown to be more effective than mandatory testing, and should include options for confidential or anonymous testing. The goal of counseling is to provide client-centered risk reduction and support. Simple, rapid testing with same-hour results is recommended, accompanied by quality assurance methods. Along with counseling and testing, additional behavioral services should include long term support such as post-test clubs and on-going prevention counseling.

Additional medical services may enhance the acceptance of VCT, and VCT can facilitate adherence and continuity of health care. VCT can be integrated with other services including antenatal care, STD/RTI and family planning services, TB screening, treatment and prophylaxis, OI treatment and prevention, HAART, nutritional support and post-exposure prophylaxis for rape and occupational exposure

Obstacles to scaling up access to and utilization of VCT include shortage of qualified counselors, sites, and test kits, stigma, discrimination and breach of confidentiality, low return rates for results, which can be prevented with same-hour results, lack of access to convenient locations and hours of services, poor quality and service delays, and fees for services which discourage utilization.

Increasing access to VCT and expansion of VCT services should be a high priority for the GFATM.

HIV, Malaria and TB Vaccines

Our most optimistic estimates for the availability of promising (i.e., Phase III supported) vaccine candidates for HIV, Malaria, and TB are 3-5 years. However, even in the absence of efficacious candidate it has become clear that vaccines remain the best hope for cost-effective control of the epidemic, and progress in vaccine development, clinical testing and deployment, is dependent upon optimizing other aspects of public health infrastructure. Initial effective HIV vaccines may not provide sterilizing

immunity and therefore secondary endpoints such as viremia, CD4, and clinical outcome among infected vaccines may be important.

Barriers to the conduct and interpretation of vaccine trials and deployment programs include lack of ensured access to future vaccines, technical and human rights challenges, interactions between HIV, Malaria, TB, and limited community awareness and misinformation about vaccines. Recommended responses to these obstacles include, the need to subsidize the cost of producing and obtaining licensed vaccines, and strengthening vaccine delivery infrastructure. Improve surveillance programs to characterize populations with respect to biological and behavioral risk. **E**nhance community participation and make it more resistant to unfounded rumors and misinformation, via education and outreach. In addition, "rapid response teams" are needed to counter.

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Appendix 1- Obstacles to PMTCT interventions

- Health Services
  - Access and utilization of ANC/delivery services
  - Lack of rapid HIV testing and laboratory support
  - Lack of knowledge/interest among health care providers and educators
  - Failure to link ANC-postpartum care to HIV care
  - Lack of integrated strategies across HIV, FP, nutrition and safe motherhood programs

- Linked to the Intervention
  - Costs / Lack of resources
  - Drug delivery to mother and baby (hospital/clinic-based, rural, etc)
  - Absence of IEC materials: consistent and sustained messages that are culturally appropriate
  - Training of counselors/educators

- Consumer/Society
  - Non-disclosure/stigma
  - Community awareness
  - Lack of male involvement
  - Political will