REVIEW ARTICLE

HIV in the Developing World - Meeting the Challenge of the Growing Dichotomy

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> A pestilence isn't a thing made to man's measure; therefore, we tell ourselves that pestilence is a mere bogy of the mind, a bad dream that will pass away. But it doesn't always pass away, and from one bad dream, it is men who pass away …. Because they haven't taken their precautions.
>
> Albert Camus (1)

When Acquired Immune Deficiency Syndrome (AIDS) was first recognised in 1981, few would have predicted that an outbreak of immunodeficiency in young North American homosexuals would lead to one of the most important global public health challenges of recent times. It had seemed that although epidemics came and went, pandemics were a problem of the past and sexually transmitted diseases posed little threat. AIDS has now risen to become our modern day plague. Although it is a high profile issue in the West, the consequences of the disease have fallen most heavily and least visibly upon developing countries, especially Sub-Saharan Africa, where the only containment of the epidemic has been by saturation of the most susceptible portion of the population.

It is the developing world, where 800 million people lack access to health services, which bears more than 90% of the global burden of Human Immunodeficiency Virus (HIV) infection (2). The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that there are more than 30 million individuals with the HIV worldwide, with 5.6 million newly infected in 1999 at a rate of more than 15,000 new seroconversions each day (Table 1) (3). Sub-Saharan Africa, although only 10% of the world's population, makes up approximately two-thirds of this total, with over 23 million infected. A paper published in 1994 reported that in rural Uganda, more than 80% of deaths in men and women 25 – 44 years old were due to HIV-related diseases (4). India with 4 million HIV-positive people is now considered the country with the largest number of victims in the world, and with a population of almost 1 billion, the effects of the epidemic explosion are only just beginning to be recognised (5). Equally worrying is the fact that the reported risk of perinatal transmission of HIV is higher in developing countries, ranging from 30 to 45% as compared to 7 to 30% in European and American studies (6,7), which is compounded by the increasing prevalence of HIV/AIDS amongst women, particularly in Sub-Saharan Africa (3). UNAIDS estimates that while children <15 years old represent 3.5% of the total population living with HIV/AIDS in 1999, children account for greater than 10% of people newly infected in 1999 (3).

However, it is vital to recognise that the emerging theme is one of regional variation. The global pandemic is composed of different regional and local epidemics, each with their own characteristics with respect to numbers, risks, transmission categories and virus type (see Table 1). Quarraisha Abdool at the 12th World AIDS Conference 1998, presented the following broad classification in terms of the time of HIV introduction, the size of the population at risk as well as social, biological and political influences (8): *explosive* (e.g. Sub-Saharan and South Africa) – characterised by rapid growth, fuelled by a high incidence in young people especially young women, with major risk factors being population mobility and sexually transmitted diseases; *masked* (e.g. Rwanda and US inner cities) –

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Table 1. Regional HIV/AIDS statistics, December 1999[a]

Region	Adults and children living with HIV/AIDS	Adults and children newly infected with HIV/AIDS	Adult prevalence (%)	Proportion of HIV+ adults who are women (%)	Main mode(s) of transmission for adults
Sub-Saharan Africa	23,300,000	3,800,000	8.0	55	Hetero
North Africa and Middle East	220,000	19,000	0.13	20	IDU, Hetero
South and South-East Asia	6,000,000	1,300,000	0.69	30	Hetero
East Asia and Pacific	530,000	120,000	0.068	15	IDU, Hetero, MSM
Latin America	1,300,000	150,000	0.57	20	MSM, IDU, Hetero
Caribbean	360,000	57,000	1.96	35	Hetero, MSM
Eastern Europe and Central Asia	360,000	95,000	0.14	20	IDU, MSM
Western Europe	520,000	30,000	0.25	20	MSM, IDU
North America	920,000	44,000	0.56	20	MSM, IDU, Hetero
Australia and New Zealand	12,000	500	0.1	10	MSM, IDU
Total	33,600,000	5,600,000	1.1	46	

[a] Modified from reference 3

Hetero: heterosexual transmission; **IDU**: transmission by injecting drug use; **MSM**: transmission by men having sex with men.

characterised by stable overall HIV prevalence but high incidence, which is masked by high mortality and poor monitoring of certain sub-groups with high incidence, especially complicated by wars and other conflicts; *emerging* (e.g. India, Ukraine, and Russia) – characterised by low overall prevalence but increasing incidence amongst small sub-groups and regions, and with the potential for rapid spread and bridging into the general population, hence suggesting the milieu for a major epidemic.

Such diversity, coupled with the fact that general mortality data are scarce and unreliable, makes it difficult to make long-term predictions for the future of HIV in developing countries. For instance, reports of AIDS cases in Africa generally lag by an average of one year and are incomplete for numerous reasons, including lack of, or limited access to, facilities for diagnosing AIDS, differences in the clinical definition of AIDS and confusion with associated infections, e.g. tuberculosis (9). It is estimated that fewer than 10% of all AIDS cases in Africa are reported to the relevant Ministry of Health.

SOCIO-ECONOMIC FACTORS AND THE HIV EPIDEMIC

> There is no cholera, no yellow fever, no small pox, more contagious than debt. If one habitually lives among embarrassed men, one catches it to a certainty.
>
> Anthony Trollope (10)

The symbolic equation between poverty and infectious disease drawn by Trollope in 1914 is as much a reality now as ever before (see preceding paper, 11). One of the more persistent messages of AIDS prevention campaigns is the slogan "everybody is at risk". On an individual level this is undoubtedly true. However the risks to countries or societies experiencing serious AIDS epidemics are clearly not equal; for example, more than 15% of adults in Uganda are infected with HIV as compared to 0.15% in Denmark (12). As evident in Table 1, differences in adult prevalence between regions span almost two orders of magnitude and incidence data (i.e. number of new cases) show even greater disparity (3). Differences in sexual behaviour patterns alone are unlikely to account for a hundred-fold difference in rate of infection. The only way to explain the dichotomy is by invoking several powerful cofactors, associated with the developing world, which can be classified as *biological*, e.g. high prevalence of untreated genital tract infections; *cultural*, e.g. female education and large age differences in sexual partnership formation; and *structural*, e.g. population movement through labour migration and refugees (9).

These factors not only influence heterogeneity in HIV prevalence but they also confer differences in the severity of disease. The transition interval from seroconversion to AIDS is 4.4 years in the tropics as compared to >10 years in North America (13). Also in the tropics, the natural history of AIDS involves more virulent pathogens such as *Mycobacterium tuberculosis*, pneumococcus and non-typhi Salmonellae, which occur early in HIV infection despite high CD4 counts and are fatal if untreated (14). The role of women in many developing world communities and their vulnerability through social and cultural factors contributes to the preponderance of heterosexual transmission of HIV in these countries. This obviously has consequences for vertical transmission and the traditional practices associated with childbirth in many such countries (7).

Thus the prevalence of HIV may be considered an indicator of uneven and dysfunctional social development, with the highest prevalence found in poor societies, societies in turmoil, among the displaced, the powerless and the marginalised (12).

IMPACT OF HIV ON DEVELOPMENT IN THE DEVELOPING WORLD

AIDS in the developing world is more than just a medical problem. The impact on development is alarming and far-reaching with substantial effects at macro and individual/community levels. AIDS will double or triple adult mortality rates in Sub-Saharan Africa from levels already eight times those in the West (15,16). AIDS most commonly kills people in the most productive years of life, which coincides with when they are responsible for the care and support of others. It is estimated that by the year 2000 there will be 5 – 10 million orphaned children under 10 years old (17,18). Life expectancy, which had been rising, is now on the decline and by 2010 will be 30 years lower than that expected without the advent of AIDS (13). The true cost of these effects is incalculable and self-perpetuating.

Put in different terms, the relationship between HIV and the economy is circular. Infection leads to higher mortality and morbidity amongst young adults, which in turn results in a reduction in the quantity and quality of labour available to produce output or gross national product (GNP) (13). The decline in GNP translates into a destabilising effect on social factors such as future income and access to education and healthcare, as well as structural changes within households brought about by dissolution of families and children being orphaned.

The healthcare sector in many developing countries is facing a crisis, not only having to deal with unprecedented change in the burden of disease, but also coping with HIV-related sickness and death in its own workforce. As the demand for healthcare increases, the ability to supply it is declining. For terminal patients, hospital care is essential due to the lack of any structure for home-based care and stigmatisation within the community. There is also the issue of dealing with the extra volume of patients without neglecting diseases unrelated to HIV. Although the HIV epidemic threatens to disrupt the health sector and society in a way that no other contemporary disease can match, it is important to remember that the burden of non-HIV disease has not decreased. Malaria, tuberculosis, pneumonia and diarrhoeal diseases are all still major concerns that would be counterproductive to ignore (13; see following paper, 19). A secondary tuberculosis epidemic, in particular, is accompanying the rise in HIV-infected persons, making it the most common HIV-associated disease in developing countries. The WHO estimates that worldwide, 5 million people are infected with both HIV and tuberculosis, of whom two-thirds live in Africa (20). Prevention of tuberculosis amongst HIV-positive patients is an essential public health goal, given that such persons are at high risk of co-infection, which in turn is associated with an increased likelihood of death (20). Thus HIV infection has put additional strain on already overstretched healthcare systems. For example, the average annual per capita expenditure on health in Sub-Saharan Africa is $11, and in some cases less than $4 (20). Many areas lack essential drugs, and medical supplies including antibiotics, antiseptics and gloves. More than 50% of adults admitted to hospital in Uganda are HIV-positive, many are unable to pay for their care and since most are amongst the economically active age groups, the patients' families suffer tremendously as a result of the frequent illness and eventual death of those infected (20).

A microeconomic analysis by Barrett and Blaikie (21) showed that death or illness of a family member from AIDS led to a deterioration in the producer/consumer ratio in almost all the households involved. A study on the impact of HIV on rural Ugandan families described, in more tangible terms, the same result, specifically, that HIV caused a marked increase in poor households headed by poor women (22). Women bear an enormous burden of HIV morbidity and mortality, both directly and indirectly. Women account for 55% of all adult HIV/AIDS cases in Sub-Saharan Africa, which is markedly higher than other regions of the world (Table 1) (3). The impact of HIV is even more acute when one considers not only the suffering of individual women but also how this affects their crucial productive, reproductive, caregiving, and community management roles. Effects on the youngest members of society include the trauma of children forced to leave school to care for a sick family member and the devastating emotional and financial consequences of becoming an orphan (9).

At the macrolevel, the AIDS epidemic exacerbates poverty and inequality, at a time when redistributive programmes such as social welfare, healthcare and economic regeneration are already under strain. The feminisation of poverty and the maldistribution of wealth are some of the most detrimental developmental consequences of HIV, changing the face of families, community and society with potentially profound long-term effects.

AFFORDABILITY OF TREATMENT

The nature of the AIDS dichotomy has never been so tragically clear as now in the advent of treatment breakthroughs that represent for some a dawning of great hope and for many others a bitter irony: the

difference between nations able to offer effective therapy to their patients and those only able to offer merely, if at all, support and sympathy. As powerful new drug combinations have slowed the progression of HIV infection to the development of AIDS in the US for the first time in 15 years, an estimated 15,000 – 16,000 people become infected each day in countries where most will never be able to afford such treatments (23,24). The gap between what is available and what is affordable is widening into a yawning gulf, cleaving the world into the therapeutic haves and have-nots.

At present, the cost of antiretroviral therapy (ART) or highly active antiretroviral therapy (HAART) (i.e. ART plus protease inhibitors) is completely prohibitive to the extent that, despite its technically impressive performance, it will most likely be available to only one out of ten infected individuals worldwide (25). The cost of supplying HAART to 11 countries in Sub-Saharan Africa (excluding South Africa) was calculated to be more than 28% of the GNPs, where the average per capita expenditure on health is $10 (26). Given that two-thirds of all infection is in this area, this represents a financial, medical and social crisis. In South Africa, the Department of Health estimates that there are 3 million HIV-positive individuals and the cost of treating all patients for a year with HAART would be $30 billion, not including the cost of medical infrastructure needed to implement the measures or the associated monitoring required. The annual AIDS budget in South Africa is approximately $50 million, which if directed to patient care would support 5000 patients for one year on HAART, i.e. less than 0.2% of the total infected (26).

Even if ART were widely available, certain basic infrastructural requirements would need to be fulfilled, including access to HIV screening and counselling, efficient monitoring of treatment, side effects and compliance and a service able to treat other disorders such as opportunistic infections. At the most fundamental level, clean water is required to take the 20-30 tablets a day and refrigeration is required for medicines (27). Further complications of the system are evident for example, in Madras, India, where antiretroviral drugs are available in the private sector but have to be procured through black market sources since the government is reluctant to allow general use to all 4 million infected. In many countries, such as Sierra Leone, the use of drugs that have past their expiry date is also common practice. Such use of multi-drug cocktails of dubious quality will likely result in multi-drug resistant strains and further exacerbate the problem currently faced (28). It is therefore a question of ethics, morals and future risks as well as financial issues. Whilst 90% of the technical resources are in developed countries and 90% of all infected individuals are in developing countries (23), it is a fantasy to think the developing world will ever be able to afford the latest therapeutic advances. The developing world will have to find other means to confront the crisis.

STEPS FORWARD – PREVENTION AND MANAGEMENT

It is disturbing to consider that in the absence of a dramatic turn of events, such as a universal vaccine or a scheme for global access to antiretroviral therapy, almost all of the 30 million infected today will go untreated and die in the next 5 to 10 years. Equally disturbing is that of the 5.6 million new infections estimated by UNAIDS to have occurred in 1999, most do not know they are carrying the virus. Hence we are likely to see further exponential increases in the numbers infected and the annual death rate from AIDS will continue to rise. The most urgent need in these vulnerable countries is for fast and effective education and prevention programmes to help reduce the size of the next wave of potential victims (25).

The main priorities in preventing and controlling HIV infection in the developing world are: 1) prevention through health promotion and mass awareness campaigns to the general population; 2) targeted interventions to high risk groups involving (i) strategies for reduction of sexual transmission of HIV, (ii) effective treatment of sexually transmitted diseases (STDs), and (iii) strategies for reduction of vertical transmission of HIV; 3) availability of treatment for opportunistic infections, especially tuberculosis, and palliative care (27).

General population measures such as national mass awareness campaigns have been implemented in most countries worldwide, with varying degrees of commitment, but few studies have been properly planned or evaluated as to their impact. In many cases these campaigns were designed as an immediate measure to halt the spread of the epidemic rather than being formulated with specific long-term goals (29). However, lack of awareness about HIV and its transmission is common and, further, is associated with poverty and illiteracy (30). There is some evidence that some education campaigns have increased public knowledge, e.g. in Tanzania and the Central African Republic, but there is little hard evidence of behavioural change (29,31).

The use of targeted interventions at high risk groups and special circumstances focus on the prevention of infection before it reaches the general population. The great majority of HIV infection in developing countries is heterosexually transmitted (see Table 1 for comparison between regions), and the major risk factor for sexual transmission is the concurrent presence of

STDs. The burden of STDs in developing countries is enormous with a WHO estimate of 333 million new cases in 1995 of syphilis, gonorrhoea, chlamydia and trichomoniasis worldwide (32). Therefore the three pronged attack on heterosexual transmission involves promotion of condom use, encouraging reduction in the number of sexual partners, and controlling and treating STDs (29). A number of preliminary studies have shown several strategies to be effective at individual, community and national levels (33).

Grosskurth *et al*. performed a randomised controlled trial in rural Tanzania and showed a 42% reduction in HIV incidence as a result of improved management of patients with STDs (34). The intervention was economical and replicable, and involved training healthcare workers at primary health centres in the treatment of STDs, ensuring supply of antibiotics and promoting healthcare-seeking behaviour. In Thailand, a government sponsored programme was started in the early 1990s to promote safer sexual practices in commercial sex workers, and led to a 50% reduction in HIV seroprevalence in young Thai men, accompanied by a considerable increase in reported condom use (35). This "100% Condom Program" involved the distribution of condoms to brothels, media campaigns to promote condom use and an enforcement programme to monitor and encourage the use of condoms in brothels. This programme is estimated to have prevented approximately 2 million HIV infections (36). Other important strategies include the provision of voluntary counselling and testing services, youth interventions and education for girls, and provision of services at point of need, e.g. at travel rest-houses for long distance lorry drivers, in brothels and special women's groups.

As women are increasingly vulnerable to HIV infection, the issue of mother-to-child transmission becomes an important point for prevention strategies. The accepted standard of the ACTG076 trial (37) advocating maternal AZT treatment from the second trimester of pregnancy, intrapartum therapy and therapy to the infant for six weeks postpartum, is completely untenable in developing countries (7), and hence research is ongoing into alternative regimes and methods. A recent Thai study (38) showed that 4 weeks of AZT therapy antenatally produces a 51% reduction in relative risk of vertical transmission, suggesting that short-term antenatal AZT therapy may be a viable option. Other measures investigated include Caesarean section, dietary supplementation, vaginal microbiocides during labour and avoidance of breastfeeding, although the cost of formula feeding and need for clean water makes the latter an unrealistic strategy (7).

Although most public health strategies have focussed on prevention of HIV transmission, the actual burden of AIDS-related disease must not be ignored. Management of such disease in resource-poor settings is made difficult by the lack of laboratory facilities, without which precise diagnosis is often impossible, and by the prohibitive cost of treatment of many opportunistic infections. It is essential to develop clinical algorithms for diagnosis and management of the infections most prevalent in a particular region and to implement essential drugs lists. A further step would be to evaluate prophylactic regimes aimed at preventing the most common opportunistic infections such as tuberculosis, and calculate the cost-effectiveness of such measures (33).

CONCLUSION

The HIV pandemic has presented the world with major health, social and economic dilemmas associated with mortality and morbidity of tragic proportions. Its effects on the developing world make it an important factor in current issues of international development. It is the result of inadequacies in the development of social and health services, it is an indicator of uneven or dysfunctional social development and it is the cause for delayed developmental progress. Complacency, denial and ignorance have fuelled the flames of its impact upon individuals, communities and society as a whole, further plunging resource-poor countries into a vicious spiral of cause and effect. Thus, whilst the HIV patients in Europe and North America look forward to a new period of hope for quality of life and survival, patients in developing countries suffer without any prospect of treatment or effective and adequate care. It is now of utmost importance that we confront these issues and channel our energies into sustainable strategies of prevention and education before the so-called "therapeutic gap" becomes an unbridgeable gulf.

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