

HIV/AIDS prevention in the context of new therapies



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HIV/AIDS prevention in the context of new therapies

Report of a meeting
organized by UNAIDS

and

the AIDS Research Institute
of the University of California
at San Francisco

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Background

The past few years have witnessed the advent of new and more effective therapies for the treatment of HIV disease. Highly Active Antiretroviral Therapy, or HAART as it is more commonly known, involves the simultaneous administration of several drugs to bring about dramatic reductions in the amount of virus circulating in the body. There is evidence from recent clinical trials that decreases in viral load may be associated with fewer opportunistic infections and longer life expectancy. Treatment advances may lead in time to HIV disease becoming a more manageable condition, as with certain other chronic diseases. However, HAART is extremely costly. As a result, only a few countries can afford to make it available to all who would benefit, and only very few individuals can afford to purchase the drugs themselves. This poses major challenges for governments and nongovernmental agencies, as well as for bilateral and multilateral systems of support.

In some countries, antiretroviral therapy has been made available to health-care workers who experience occupational exposure to HIV. There is evidence to suggest that if commenced early and taken consistently, antiretroviral therapy may be effective in preventing some infections incurred through accidental exposure to blood. Much less is known, however, about the effectiveness of this kind of intervention following exposure through unprotected sexual intercourse. Nevertheless, a few countries have begun to make antiretroviral therapy available to HIV-negative individuals who have recently had unprotected sex with an HIV-positive person. There is much debate, however, about the criteria that should be used when making such forms of treatment available.

Indeed, communication between patients and health care/service providers assumes a new dimension with the advent of antiretrovirals, bringing into greater prominence such issues as adherence to complex treatment drugs, infectiousness during treatment and expectations of cure.

New and increasingly sensitive tests for HIV RNA enable an assessment of the amount of virus circulating in blood plasma and other body fluids. It is commonly assumed that a high level of virus in plasma and semen, as well as in cervical and vaginal secretions, provides evidence of high infectiveness, and that a lower "viral load" signifies lower infectiveness. HAART can significantly reduce viral load. It has been suggested that this may have a major impact on transmission, and therefore on the evolution of the epidemic. However, among people with undetectable viral load, HIV may still be present in genital secretions. The potential for transmission, therefore, remains, even when levels of circulating virus in plasma and other body fluids are low.

HIV treatment and prevention are increasingly linked, and earlier distinctions between primary, secondary and tertiary prevention are beginning to break down. It has recently been suggested that primary prevention should now be conceptualized as having two components: preventing exposure by means of changes in behaviour to take account of the risk, and preventing infection by means of post-exposure antiretroviral therapy or prophylaxis. Moreover, a key component of secondary prevention with antiretroviral therapy may also have a role to play in primary prevention by reducing infectiveness. This has implications for planning and

execution of programmes, as well as for the allocation of resources.

Alongside advance in the prevention of infection and the treatment of HIV disease have been changes in public perceptions of the seriousness of the epidemic. After the XIth International Conference on HIV/AIDS, held in Vancouver, Canada, in 1996, there were numerous media reports that a cure for AIDS was close. Information about HAART and its potential spread all over the world, thanks to improved global reach of the mass media, but this also entailed a great deal of misinformation and unrealistic expectations. Given the power of the popular press to influence understandings of the epidemic, it should come as no surprise to discover that perceptions of the gravity of HIV and AIDS have declined, and that some individuals feel less need to protect themselves and their partners against

infection. Changing perceptions of the epidemic may therefore have important consequences for sexual and drug-related risk-taking. A challenge to communication, which has always been a major tool for behavioural modification or change, is how to reflect correctly the strength, limitation and potential of antiretroviral treatments to enable the public, policy-makers and others to make the right decisions.

It is also vitally important to stress the need for high levels of funding to support HIV prevention work. The development of more effective but more expensive forms of treatment may put particular stress on HIV-related budgets. It is essential to maintain a sensible balance between investment in prevention and care. Every infection prevented has a significant economic benefit, not only for the individual but for society as a whole.

Aims and objectives

It was against this background that a meeting, organized jointly by UNAIDS and the AIDS Research Institute of the University of California at San Francisco, took place. Its principal aim was to examine the changing relationship between treatment and prevention in developed and developing countries, and to identify the implications of this for policy, research, prevention, communication and funding. A linked goal was to prepare an outline statement on HIV prevention in the context of therapeutic advance.

Among the issues examined were:

- How best can we understand the changing relationship between prevention, treatment and care?
- What are the implications of advances in antiretroviral treatment (including HAART) for primary prevention?
- What role should post-exposure prophylaxis (PEP) play in HIV prevention?
- What has been the impact, and what might be the likely future impact, of therapeutic advance on perceptions, beliefs and behaviours, including the perceptions, beliefs and behaviour of those at heightened risk?

- What are the implications of treatment advance for the design, planning and implementation of prevention, care and support programmes?
- What are the implications of treatment advance for voluntary counselling and testing (VCT) programmes and their role in prevention?
- What is the likely impact of HAART on infectiveness, and what special issues arise in relation to virology, adherence to treatment, and risk perception?
- What is the implication of HAART for communication between patient and care providers, especially in relation to adherence to treatment, infectiveness during treatment, and expectations of cure?

Conclusions and recommendations of the meeting

Four working groups were established to develop recommendations relating to:

a) how best to organize the principles for the integration of prevention and care in relation to treatment and care; b) opportunities across the continuum of prevention, diagnosis, treatment and care; c) an infrastructure for integrating treatments into the prevention and care continuum; d) the key messages that should underpin future prevention efforts; and e) research priorities relevant to prevention in the context of new therapies.

a) How best to organize the principles for the integration of prevention and care in relation to treatment and care

In light of the presentations (see appendix A) and discussion, a series of principles for the integration of prevention and care were identified and then ordered:

Preamble

1. News of recent improvements in treatment effectiveness is reaching

countries all around the world, raising expectations and influencing perception of risk or vulnerability. However, major disparities in access to these treatments exist within and between countries, and these need to be addressed.

Health promotion throughout the continuum of HIV/AIDS

2. Opportunities for primary prevention exist from the time HIV is present locally, through individual exposure, to the moment of advanced HIV disease. Communication is important and relevant at all stages. Current communication approaches should evolve as the epidemic evolves.

3. HIV prevention and care are strongly interrelated. Both form a health-promotion continuum for HIV disease. Both HIV-positive and HIV-negative people have an important role to play in HIV-related health promotion.

4. Opportunities to involve persons living with HIV in prevention are often missed.

5. Guidance and support on how to disclose one's HIV status to partners should be considered an integral part of counselling and care.

6. HIV-related health promotion works best when carefully planned. Countries should be encouraged to set up a multidisciplinary council to conduct HIV-related health-promotion planning.

Antiretroviral drugs and prevention

7. It is believed that even the best treatments available at the present time do not prevent infection taking place; they merely reduce its likelihood.

8. Poor and inconsistent access to treatment drugs may facilitate the development of viral resistance. Health-care workers and patients need education on the importance of adherence.

9. Much has been learned about the determinants of adherence. Knowledge and understanding are vital, but motivation and convenient regimens also matter.

10. Post-exposure prophylaxis (PEP) should be considered as part of the overall health-promotion approach.

The role of voluntary counselling and testing

11. Confidential voluntary counselling and testing (VCT) offers the best way for people to learn about their HIV status. VCT needs to be made available in a context where broader efforts are made to prevent stigmatization and to provide good quality care and support, including access to treatment drugs.

12. Early VCT has an important role to play in prevention.

13. Knowledge of HIV infection does not in itself lead to partner notification and disclosure.

14. Partner counselling plays an important role in HIV prevention. It should be provided in a form that optimizes its benefits and avoids causing harm.

Research issues

15. Prevention messages and approaches need to be based on evidence, not speculation (e.g. the impact of HAART on rates of transmission is still poorly understood).

16. Individual and community responses to new treatments vary. Some but not all recent changes in behaviour may be attributable to treatment advance. We need a better understanding of this situation.

17. It may be useful to undertake HIV-related health-promotion research within the broader context of research to promote sexual health.

18. More needs to be learned about the impact of new treatments on risk perception and risk behaviour in developing countries.

19. Too little is known about the factors that lead to government and community commitment to HIV-related health promotion.

20. The role of communication throughout all stages of the continuum of care needs to be better understood, especially communication between care providers and the recipients of treatment drugs.

21. Communication approaches must evolve with the epidemic. A better grasp of how to redirect communication is necessary.

22. Much remains to be learned about the levels of adherence necessary for therapeutic benefit, the avoidance of viral resistance, and reduced infectiveness.

The importance of reducing stigmatization of people living with HIV/AIDS

23. Stigmatization creates barriers to health and the pursuit of care, and can interfere with the taking of medications. Conversely, reducing stigma can encourage people to seek care and support, and can encourage communities to be more supportive.

24. The absence of discrimination and stigmatization is essential for successful prevention efforts.

25. Efforts should be made to ensure that persons living with HIV are not stigmatized and discriminated against. This will facilitate greater involvement of people living with HIV in prevention work and, in turn, enhance understanding of HIV and AIDS by others.

Funding issues

26. The means of preventing HIV infection are known. Yet funding to support information, education, communication, condom promotion, needle and syringe exchange, detection and treatment of sexually-transmitted diseases (STDs) and PEP, remains woefully inadequate.

27. Funding for treatment should not deplete prevention funds. Resources are needed for both.

28. Overall donor investment in the response to HIV is declining. Many factors have contributed to this decline, including prevention and treatment success and, in some places, a declining death rate.

29. The availability of new treatments can be used to support HIV-related fund-raising. Both the public and private sectors, as well as voluntary organizations, have a potential role to play here.

Better information and communication

30. There is a pressing and continued need to emphasize the importance of primary prevention, but clearer prevention messages need to be conveyed.

31. The most effective forms of education involve multiple channels of communication.

32. Health-promotion messages need to be offered across the continuum of primary prevention, care and support.

33. Health professionals need adequate preparation for their role as providers of information.

34. Social marketing is important in encouraging the adoption and use of prevention technologies, including condoms.

35. Messages about treatment effectiveness can be used to encourage participation in VCT programmes.

36. Prevention messages should not encourage false hopes or the feeling that a cure exists and that the epidemic is "over". Media stories highlighting treatment advance need to be balanced by realistic prevention messages.

37. Efforts need to be made to resolve the conflict between messages suggesting that AIDS is a "terrible disease" and those that promote unrealistic "hope for the future".

38. Care should be taken to avoid giving misleading impressions through the use of terms such as "viral eradication" (which may encourage people to believe there is a cure for HIV disease), "partner notification" (which may make people unwilling to discover their HIV status), and "targeting" (which may lead people to feel uninvolved or stigmatized).

b) Opportunities across the continuum of prevention, diagnosis, treatment and care

Although there are major disparities of wealth between and within countries, news of treatment effectiveness has reached all parts of the world. This offers an impetus for the renewal of prevention efforts on a scale and in a form not hitherto achieved. The continuum of prevention, diagnosis, treatment and care offers a wide range of opportunities for intervention. But prevention efforts will fail unless steps are taken to reduce stigmatization and discrimination against people living with HIV and AIDS, and unless national authorities and nongovernmental organizations can promote an open and supportive climate.

Life-saving prevention strategies exist, but funding to support their implemen-

tation is often inadequate. Treatment and prevention should not be pitted against each other. Rather, opportunities for prevention linked to early detection, treatment and care should be more vigorously exploited. Treatment advance may encourage more people to seek voluntary counselling and testing, but services need to be provided in a confidential and supportive way. Partner counselling may be useful in helping individuals disclose their HIV status.

Prevention messages need to be realistic and accessible, and may need to challenge some of the unrealistic expectations created by media hype about treatment effectiveness. A range of approaches needs to be used in order to address the needs of different groups, and different interventions may be necessary at various points along the continuum between prevention, detection, treatment and care. Communication does not decrease during treatment and should include messages on prevention, treatment, care and support.

Figure 1 highlights some of the key moments for intervention, as well as the prevention options available at each of these moments.

Figure 1. Options for the prevention in the light of recent therapeutic advances

Persuasion and enablement		Voluntary counselling and testing (VCT)	HAART Opportunistic infection prophylaxis
Behavioural interventions for prevention	Post-exposure prevention (PEP)	Prevention counselling	Prevention counselling
Prevention of HIV transmission	Prevention of HIV infection	Early HIV infection	Established HIV infection

c) An infrastructure for integrating treatments into the prevention and care continuum

To be effective, treatment programmes and interventions require a sound infrastructure of support. Meeting participants felt that the establishment of "country councils" to monitor treatments could play an important role in achieving this. Such councils would have a broader remit than many national AIDS control programmes, being sensitive to the changing terrain upon which prevention initiatives are planned, and the increasingly close linkages between prevention and care.

The responsibilities of a country council might include developing appropriate information, education and communication (IEC) strategies and messages for the population as a whole, as well as for especially vulnerable groups; setting guidelines for the treatment and care of people with HIV disease; coordinating the importation and distribution of drugs, equipment and resources; arranging for the training of health-care and health-promotion workers; and identifying key research questions and issues.

Opinion differs concerning the structure and accountability of such councils. On the one hand, there was support for the idea that they might operate as a sub-committee of existing bodies with accountability to a key ministry working in the field of HIV. On the other hand, advantages could be gained through interdepartmental collaboration, and accountability to higher-level bodies such as the president's or prime minister's office. Arrangements for the setting up and functioning of such bodies might therefore vary between countries.

Membership should be as broad-based as possible, including but not restricted to, representatives of the national AIDS

control programme, representatives of medical and drug regulatory bodies; representatives of pharmaceutical, paramedical and nursing associations; representatives of nongovernmental and community-based organizations; representatives of legal and ethical commissions and councils (including, where possible, those working in the field of human rights); representatives of relevant research institutions; experts in health promotion and IEC; and representatives of people living with HIV. To these might be added key donor agencies and others with special expertise in the field of HIV prevention.

d) Key messages

1. It is important to significantly reduce levels of HIV-related stigmatization and discrimination.

HIV-related discrimination and stigmatization interfere with the transmission of prevention messages; discourage the adoption of VCT and thus access to early care; make individual and social denial appear legitimate; and make it difficult for people with HIV to be involved in prevention activity and for people not infected to talk about HIV and adopt safer practices. Governments and national authorities have a key role to play in establishing an appropriately supportive climate for prevention efforts and in fostering the kinds of social solidarity that lead to the positive involvement of all sections of the community.

2. Prevention of HIV infection remains essential in the light of new therapies.

HIV-related health promotion should continue to emphasize the importance, effectiveness and affordability of prevention programmes based on the avoidance of unprotected sexual intercourse, the use of condoms, early STD diagnosis and treatment, and the avoidance of

needle and syringe sharing. VCT has an important role to play in enabling people to know their HIV status. It has been shown to be an effective risk-reduction intervention in itself. Its success, however, depends upon a supportive social climate and respect for the confidentiality of test results. Partner counselling may have an important role to play in enabling HIV-positive individuals to reduce the likelihood of infecting their regular partners and others.

3. Comprehensive HIV-related health promotion for people living with HIV encompasses care, support, treatment and efforts to prevent HIV transmission to others.

A truly comprehensive approach to HIV-related health promotion goes well beyond primary prevention to encompass care, treatment and support for people living with HIV. The advent of new and potentially more effective therapies has led to a blurring of earlier distinctions between prevention and care, and creates new opportunities to involve all sections of the community in prevention efforts. It also encourages the greater involvement of people living with HIV. While HAART may be available in only a few countries at present, it is widely known about. Before its more general availability, enormous strides can be made in the quality of care afforded to people living with HIV and AIDS in resource-poor environments. This may be achieved through the more widespread availability of relatively cheap prophylaxis for opportunistic infections, and the greater involvement of people living with HIV in prevention work.

e) Research priorities

Several researchable issues can be identified. With respect to policy formulation and development, a priority must be

research on how best to secure and maintain government commitment to the response to the HIV epidemic. Lack of such commitment is perhaps the major barrier to the development of programmes for prevention and care. Yet relatively little is known about the factors that lead some governments to act and others to deny that there is an issue or problem. Beyond this, research is needed to identify and promote the most appropriate and cost-effective prevention strategies locally. National policy guidelines are also needed for the provision of voluntary counselling and testing (including partner counselling) and post-exposure prophylaxis.

In the field of basic and clinical science, key researchable issues include studies of the relationship between viral load and infectiveness, resistance to therapy, and adherence to treatment. In some countries, research on the role of complementary, traditional and herbal therapy may be valuable, as might be enquiry into the forms of counselling and support most likely to suit local needs.

In relation to HIV-related health promotion, research priorities include identifying the range of prevention opportunities that arise across the continuum of care. Studies need to be undertaken on changes in risk behaviour, intermediate steps leading to change, motivations and their determinants, as well as the kinds of communication approaches which are most effective in achieving and maintaining risk reduction in the context of new therapies. Work to reposition AIDS within the context of broader efforts to promote sexual and reproductive health may also be valuable.

Conclusions

The advent of new and more effective treatments for HIV creates important new challenges for HIV prevention. While some of these are linked to changing perceptions about the gravity of the epidemic, others are linked to opportunities for preventing infection through PEP and related interventions. While little is known as yet about the ability of combination therapy to reduce the sexual transmission of HIV, a reduced viral load may decrease levels of infectiousness. Among the key issues to be resolved by those involved in HIV-related health promotion are (i) how best to maintain public-health commitment to primary prevention; (ii) how best to provide an infrastructure for the integration of treatment drugs across the prevention and care continuum; (iii) how best to reduce levels of discrimination and stigmatization toward people living with HIV and their families, so as to promote the adoption of VCT; and (iv) how best to ensure that increasingly complex prevention messages can be simply and clearly conveyed. Applied social research has a critical role to play in providing answers to these questions and in enabling international agencies and other bodies to respond creatively and constructively to the opportunities and challenges that now face us.

Appendix A: Summaries of presentations

Treatment and prevention: a continuum

Tom Coates, University of California, San Francisco, USA

Professor Coates began by highlighting how new and potentially more effective therapies and post-exposure prophylaxis provide opportunities for rethinking the relationship between prevention, treatment and care. It is perhaps now more useful to speak of health preservation and promotion rather than prevention and care. The emphasis should be on supporting individuals and communities to avoid infection and, if infected, to maintain their health by managing disease and limiting the further transmission of HIV.

HIV disease is now best conceptualized as a continuum extending from (i) community exposure through (ii) personal or individual exposure through (iii) initial or primary infection to (iv) long-term or established HIV disease (Figure 2). Each of these

four stages has implications for health preservation and health promotion.

Community exposure calls for community-based prevention strategies. These may include broad-based prevention campaigns, strategies for the early diagnosis of HIV infection, and specific interventions to motivate infected individuals not to infect others.

For those who have been recently exposed to HIV through sexual or parenteral contact, two prevention strategies are warranted: PEP, and intensive counselling to reduce the risk of future infections taking place.

The period of infection has two stages. During a relatively short primary phase

Figure 2. A model for the continuum of HIV prevention and treatment

Key messages and activities	Community exposure	Individual exposure	Initial infection of antibodies	Later infection: appearance
Community prevention activities to assist individuals to avoid exposure	+	-	-	-
Intensive prevention counselling PEP (including partner notification) Post-exposure supportive counselling	+	+ Dx*	-	-
Intensive prevention counselling Commence antiretroviral therapy Supportive counselling	+	+	+/- Dx	-
Counselling for prevention Antiretroviral therapy Prophylaxis for opportunistic infections Supportive counselling	+	+	+	+ Dx

* Dx: Diagnosis

(lasting about six weeks), and before the development of antibodies, the person may be very infectious. Prevention strategies here include supportive counselling, intensive risk-reduction counselling, and treatment, including antiretroviral therapy.

A second, longer phase lasts several years. During this period, infectiveness may be lower. Subsequent to the diagnosis of AIDS, infectiveness may begin to rise again. Supportive counselling, intensive behavioural counselling, antiretroviral therapy, and prophylaxis for opportunistic infections are required for health preservation and health promotion during this phase of the disease.

In discussion, the following issues were raised:

- The extent to which the model might be generalized to other contexts: the model is largely descriptive, having been designed to help target resources, emphasize the importance of counselling infected individuals, and integrate the contribution of the social and biomedical sciences to prevention. For example, the availability of counselling and testing services varies from country to country. Opinion is also divided among physi-

cians as to the advisability of early intervention with antiretroviral drugs.

- The extent to which the model offers a realistic framework for prevention and care in developing countries; here, resources for counselling and testing may be less extensive, antiretroviral drugs may not be available, and PEP may not be provided even for occupational exposure to HIV, let alone for sexual exposure.

Useful interventions suggested by the model include the importance of early detection, and preventive activities in the period immediately after infection. Encouraging individuals to be more sensitive to the symptoms of early infection is important, as is VCT. Partner counselling and supportive counselling may have an important role to play in reducing infections in relationships in which one partner is infected and the other is not.

- The changing nature of VCT in relation to treatment advance: VCT offers important opportunities for referral to treatment and care, but is also significant for preventing transmission. Counselling may, for example, provide support to HIV-negative individuals, enabling them to avoid infection. It may also provide HIV-positive people

Impact of therapies (including PEP) on primary prevention

Impact on behaviour among men who have sex with men

Anne Laporte, Réseau national de Santé publique, France

with the means and motivation to avoid infecting others.

Four recent studies (Dilley *et al.* 1997; Adam 1998; Kravcik 1998; Kalichman *et al.*, in press) have assessed the impact of treatment advances on the sexual behaviour of gay and other homosexually active men. Three of these studies

have been conducted in the USA and one in France. In each study, a significant minority (11% to 26%) of men indicated that they were less concerned about infection as a result of the new therapies. Between 13% and 19% of men surveyed (depending on the study) indicated a reduced need for safer sex, and 8-15%

reported that they had modified their levels of protection accordingly.

Although the majority of respondents in each survey maintained their previous attitudes and behaviour, the perceptions, attitudes and safer-sex behaviour of a small subset of men in each study appears to be changing.

However, it is hard to draw firm conclusions from the above data, which are based on findings from clinic samples, men recruited at "gay pride" festivals, and men contacted via the gay press. Treatment advances may also have caused some men to justify risk-taking behaviour post hoc by reference to the new therapies. Present study designs are insufficiently strong to rule out this and other alternative explanations for the accounts given.

In discussion the following issues were raised:

Other studies have been conducted in Australia and in the United Kingdom. In Australia, research at the National Centre in HIV Social Research has shown a recent increase in unprotected anal sex with casual partners among gay and

homosexually active men (Van de Ven *et al.* 1998). The reasons for this increase are at present unclear, but may relate to changing perceptions and beliefs. There has been no parallel increase, however, in seroconversions among gay and other homosexually active men in Australia, a country with excellent surveillance data (National Centre in HIV Epidemiology and Clinical Research 1998). In the UK a recent survey by Sigma Research found no significant changes in reported patterns of sexual behaviour among gay and other homosexually active men recruited during the 1997 Gay Pride festival (Hickson 1998).

Meeting participants reported that recent data on the sexual behaviour of gay men in San Francisco suggests there has been an increase in high-risk behaviour, mostly in young men and those recruiting partners in public sex environments. Some younger men may find the prevention messages developed by and targeted at older groups less relevant. Others may not have had access to prevention messages. Still others may have changed their behaviour in response to news of therapeutic advances and the increasing availability of PEP. Without fur-

Impact of therapies on perceptions of HIV and AIDS: Asia

Anchalee Leesavan, Chulalongkorn University, Thailand

ther research it is impossible to identify which of these possible determinants is the most important.

Throughout South-East Asia, it is increasingly believed that new therapies can significantly improve the life of people living with HIV. However, the vast majority of people with HIV in Asia are unable to access these treatments, which are extremely expensive, difficult to adhere to, and require efficient health and social services.

Concrete studies of changes in perceptions are few. A small-scale survey of perceptions of HIV and AIDS conducted in Thailand between January and February 1998 suggested that most people believe that HIV will continue to spread rapidly, and that prevention programmes should give more attention to previously low-risk populations such as women, young people and children. In Thailand, it has been estimated that 20 000 pregnant women are infected yearly; 6 000 babies will be infected if interventions to pre-

vent mother-to-child transmission are not accessible.

A greater emphasis on social communication is needed, particularly involving young people and provided at community level through health-care providers.

Impact of therapies on perceptions of HIV and AIDS: Caribbean *Suzette Moses, CRN, St Maarten*

Educational messages must be simple and clear because the language of medical science often poses a barrier to understanding.

The impact of HIV on islands and countries in the Caribbean region was described. The first AIDS case in this region was reported in Jamaica in 1982. Recent UNAIDS estimates suggest that there are now at least 310 000 cases in a region of 36 million people. This is the second highest incidence in the world, after sub-Saharan Africa. Some 65% of all cases reported are the result of heterosexual transmission, and 35% of the adult cases are in women. Governments within the region have been slow to respond to the epidemic. Many seem unwilling to invest money in HIV education because of fear of affecting tourism.

New antiretroviral therapies are not widely available in the majority of Caribbean countries. Nevertheless, news of increased treatment effectiveness has been interpreted by some people as a

licence to "let loose". When well known figures announce on television that their viral load is now undetectable, many people interpret this as a cure. While the behavioural consequences of hearing such news are not known, it is not implausible to suggest that some people may take fewer precautions than before.

At present, the only drug widely available to those who can afford it is zidovudine. Only a few countries have access to new therapies, whose cost is prohibitive for most infected people. Moreover, doctors fear that, although newer drugs can occasionally be accessed, there is not a consistent and steady supply. Therefore, physicians in the region are reluctant to prescribe these drugs.

In the Caribbean, an HIV-positive diagnosis is usually seen as a death sentence. Infected people and their families need to know that there are options for living available to them. People who are suspected of being HIV-positive are

Impact of therapies on perceptions of HIV and AIDS: Africa *Godfrey Sikipa, Family Health International, Kenya*

scorned, persecuted, cast out and even killed. The wider community needs more education in order to combat this stigmatization and discrimination.

Because of cost, antiretroviral drugs are not yet widely accessible in sub-Saharan African countries. However, a few individuals have had access to zidovudine over the past several years, often through private arrangements with health providers in developed countries. AIDS is perceived by the vast majority of

Africans as incurable. This understanding has shaped most behavioural-change interventions.

Knowledge and information about the success of new therapies is reaching the public from several sources, including international meetings and through the mass media. But incorrect information is also being widely disseminated. In order to avoid fostering incorrect perceptions, accurate information about the effects

and costs of new therapies needs to be made available.

In the past few years, it has become clear that VCT, and the care and support of people with HIV, constitutes an integral part of efforts to prevent further transmission. Once available, new therapies may bring about a further reduction in infection by preventing mother-to-child transmission, reducing transmission through occupational exposure, reducing transmission in the victims of rape, and perhaps reducing transmission during primary infection.

Self help has been under-utilized in some countries in Africa. With assistance from churches, businesses and traditional and political leaders, it may be possible to persuade 2% of the population to contribute US\$ 100 each per year towards HIV-related health care. In Africa alone, more than US\$ 1 000 million dollars could be raised this way, which is several times the amount required to make antiretrovi-

ral drugs available to every pregnant woman in need.

In the short term, programmes to promote and consolidate behavioural change, and to encourage the detection and early treatment of STDs, seem likely to remain the cornerstone of HIV prevention in most countries in Africa. In the medium to longer term, new therapies may have a greater role to play in reducing new infections.

In discussion, the following issues were raised:

- The goals of VCT programmes are several. It was agreed that the "gold standard" should be genuinely voluntary testing alongside high-quality counselling to encourage those who are HIV-negative not to become infected and to support those who are infected to avoid infecting others.

Post-exposure prophylaxis and early treatment

Overview

Anne Laporte, Réseau national de Santé publique, France

- The avoidance of stigmatization is important, especially in communities that have been inadequately prepared for the introduction of VCT programmes.

Post-exposure prophylaxis (PEP) was reviewed in relation to the occupational and non-occupational risk of infection. PEP uses antiretroviral drugs to reduce the likelihood that an individual will become infected after exposure to HIV. The rationale for the use of PEP derives from three main sources of information: findings from animal trials that suggest that antiretroviral treatment may be effective in preventing infection if administered

in the few hours after exposure; evidence that zidovudine given to HIV-positive mothers and their newborn children can prevent mother-to-child transmission; and evidence that zidovudine can be effective in preventing HIV infection among health-care workers accidentally exposed to infected blood. Additionally, both toxicity and the risk of developing resistance in the context of PEP are low.

Situations in which PEP can be used are those where the quantification of risk after exposure is significant. These may include accidental exposure to blood and other body fluids in health-care settings

and the workplace, exposure through the sharing of injection equipment among injecting drug users, and exposure as a result of unprotected sexual intercourse (Laporte and Bouvet 1998). PEP is available after occupational exposure to HIV in a substantial number of countries, including Australia, most European countries, New Zealand and the USA. Its use should be considered wherever there are established protocols for the prevention of accidental occupational exposure, where there is good and rapid access to antiretroviral drugs, and where exposure is of a serious nature. While local resources must be a consideration, efforts should be made to identify sources of antiretroviral drugs for the purpose of preventing infection through accidental occupational exposure wherever possible.

Debate about the provision of PEP for non-occupational exposure is fairly new. The situation is complicated by the absence of reliable information about the ability of antiretroviral drugs to prevent the sexual transmission of HIV. Important points to consider when making PEP

available include a proper and rapid assessment of risk, the presence of clear therapeutic protocols, the existence of an infrastructure allowing emergency treatment, patient support, evaluation of the efficiency of the programme and its impact on preventive behaviour, communication with the public, and the cost to the health-care system.

While the provision of PEP for accidental occupational exposure to HIV may be taken for granted in high-income countries, the same is not true for non-occupational exposure. Some high-income countries are currently debating the advantages and disadvantages of setting up this type of programme. Arguments often advanced for the non-provision of PEP after sexual exposure include poor expectations of efficacy, high costs, and possible adverse effects on other forms of prevention. There is at present no international consensus as to whether non-occupational exposure prophylaxis programmes should be set up. However, a wide range of scientific and other arguments exists in favour of treating selected non-occupational exposures. In the

Post-exposure prophylaxis and early treatments: the view of the CDC *Robert Janssen, Centers for Disease Control and Prevention (CDC), USA*

context of occupational exposure, PEP should be viewed as a complement to, and not a substitute for, programmes aiming at preventing exposure to HIV (primary prevention).

Dr Janssen began by suggesting that, since counselling is an essential component of the intervention, terms such as post-exposure prevention and post-exposure-initiated prevention should be substituted for what is presently called post-exposure prophylaxis and post-exposure treatment. The CDC's current position on PEP is that the use of antiretroviral drugs for non-occupational exposure to HIV should be considered a

clinical intervention of unproven efficacy. Only after careful consideration of the potential risks and benefits, and with full awareness of the many gaps in our current knowledge, should therapy be administered. Given the relatively low risk of infection through sexual exposure, PEP for non-occupational exposure (i.e. the treatment component without the counselling component) is judged unlikely to have a significant impact on the course of the epidemic. It has, moreover, low cost-effectiveness since a considerable amount of resources is needed to prevent one infection taking place. These same resources would be used

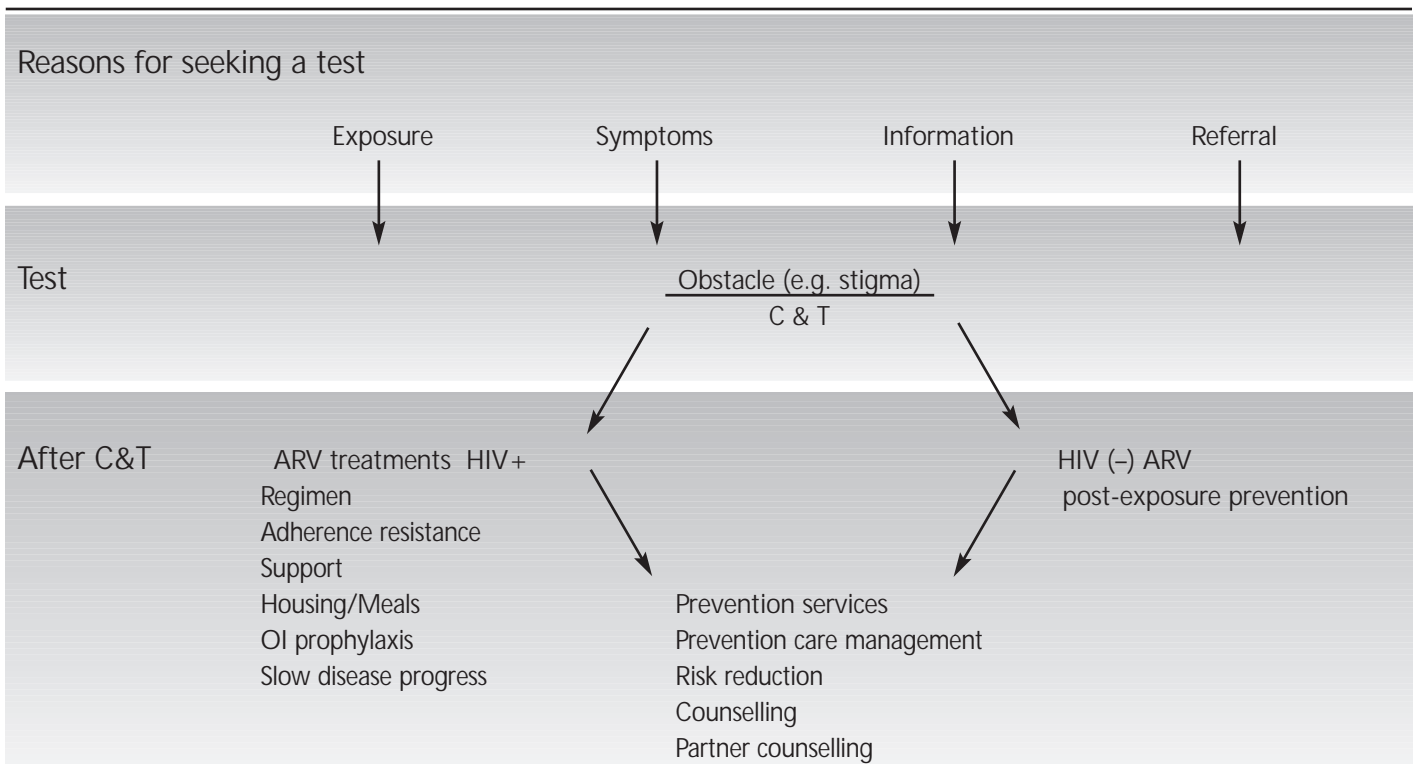
more efficiently in conventional forms of prevention as well as for the treatment of people with HIV, leading to a decrease in infectiveness, and a decrease in the incidence of HIV.

In discussion, the following issues were raised:

There are major difficulties in making PEP for non-occupational exposure

widely available. These include, but are not restricted to, efficacy as a prevention measure and cost-effectiveness. Even in resource-rich countries, there may be a lack of professional resources (e.g. doctors, trained counsellors, etc.) needed to implement programmes. Further work is needed to help people understand that PEP is a complex medical therapy often with serious side effects, not a "morning-

This model is focused on counselling and testing centres (C&T)



Voluntary counselling and testing

The Brazilian experience
Pedro Chequer, Ministry of Health, Brazil
 after" pill. There exists as yet no consensus on whether partner notification should accompany PEP for non-occupational exposure, nor on the circumstances in which couples rather than individuals should be offered testing. Centres for voluntary and confidential counselling and testing were established

in Brazil in 1988. By 1998, 104 of these centres were functioning. The overall estimated number of HIV-infected individuals is between 350 000 and 450 000, and the estimated proportion of people who know that they are HIV-positive is between 20% and 40%, depending on the region. The prevalence of HIV infec-

tion reported from VCT centres declined from 11.5% in 1990 to 5.6% in 1997, most probably because people at heightened risk were among those tested in the first years of implementation. Additionally, since November 1996, zidovudine therapy (following protocol ACTG 076) has been available to HIV-infected pregnant women.

In November 1996 a presidential decree provided universal access to antiretroviral therapy with criteria established by a national advisory committee. By late 1997 about 50 000 people were receiving anti-

retroviral therapy (about half of whom were receiving triple combination therapy). It is estimated that 85 000 people will receive antiretroviral therapy in 1998. There is a laboratory network to provide CD4+ lymphocyte and viral-load testing free of charge. Increased access to antiretroviral treatment has resulted in an estimated 50% decrease in the incidence of tuberculosis, and a substantial decrease in inpatient visits.

The Brazilian strategy for decreasing viral load among HIV-infected persons and improving the provision of testing and

Findings from recent clinical trials

Tom Coates, University of California, San Francisco, USA

counselling is expected to have an important impact on the epidemic. Policies currently exist for PEP after occupational exposure, and policies concerning non-occupational exposure will be discussed later in the year.

Professor Coates presented findings from two recent studies demonstrating that VCT may be a useful strategy for reducing HIV transmission in couples in which one person is infected with HIV and the other is not (Coates Sangiwa *et al.* 1998; Coates, Coates, *et al.* 1998). The first study described a randomized, controlled trial of the impact of VCT on sexual behaviour in three developing countries (Kenya, Tanzania and Trinidad). Participants received either VCT (pre and post-test counselling) or a standardized health-information intervention (HI). At six-month follow-up, both VCT and HI were shown to reduce sexual risk behaviour among study participants. Compared to HI, however, VCT produced a greater reduction in the prevalence of unprotected intercourse with non-primary partners, and was marginally more effective in reducing the prevalence of unprotected intercourse with paid sexual partners.

The second study explored the impact of VCT on the sexual behaviour (with primary and secondary partners) of members of couples who share the same HIV status as well as those who do not share

Impact of new therapies on infectiveness

Virological considerations

Christine Rouzioux, Hôpital Necker, France

the same HIV status. In the same three countries as above, couples were randomized to receive VCT or HI and were followed up for six months. Compared to couples in which both the man and the woman were HIV-negative, sex with the primary partner decreased significantly within couples in which both the man and woman were HIV-positive. Trends for couples containing an infected man and an uninfected woman—as well as those in which the man was HIV-positive and the woman HIV-negative—were not significant. Compared to couples in which both the man and the woman were uninfected, levels of unprotected sexual intercourse with a primary partner decreased significantly for the other three groups. Unprotected sex with non-enrolment partners was unchanged. Couples counselling and testing has been shown to reduce unprotected intercourse between spouses, especially among couples in which members have differing HIV statuses and those in which

both members are HIV-positive. VCT may therefore be a useful strategy to prevent HIV transmission in couples whose members have differing HIV statuses.

Adherence to treatment

Margaret Chesney, University of California San Francisco, USA

Viral culture from plasma or cells allows a direct measurement of infectiveness. With such techniques, positive results can be obtained from semen in about 30% of cases, and from vaginal secretions in 20–40% of cases. An indirect indication of infectiveness can be obtained by measuring viral load. This can be done in two different ways. HIV RNA in seminal plasma or in the supernatant fraction of vaginal fluid can be measured with PCR technology to estimate the quantity of free viral particles. Alternatively, HIV DNA can be identified

in non-spermatozoal cells or in cells taken from vaginal and cervical secretions. This allows identification of infection in cells, be it latent or productive. Typically, positive results are obtained in 80% of cases for semen, and in 80% or more cases for vaginal secretions taken from an infected person.

While antiretroviral therapy can reduce viral load in the blood plasma and genital tract to undetectable levels, it is important to remember that HIV may remain dormant in infected cells for a

long period of time, and that such cells constitute a reservoir of infectiveness.

Studies of the prevalence of multi-drug resistance to antiretroviral drugs have recently been carried out. It has been estimated that up to 10% of patients in the USA, 13% in Spain, 14% in Italy and 12% in France may have multi-resistant strains of HIV. The prevalence of resistance is constantly changing with therapeutic advance. It is now known that the complete cessation of all antiretroviral therapy induces a lower risk of resistance, whereas inconsistent therapy or numerous changes in therapy induce a higher risk of resistance. While HAART may help decrease the risk of transmission and the overall quantity of virus transmitted, there is a risk that transmitted virus will be multi-resistant mutants.

The clinical management of people with HIV disease has one common objective: to lower viral load levels to those that cannot be detected by existing assays. Potential reasons for failure to achieve this reduction include host factors (e.g. interference with the absorption of drugs), prior resistance and non-adherence. Non-adherence can lead to "viral breakthrough" if the individual does not take sufficient quantities of the drug to achieve clinical effects, or if he or she misses doses, which can lead to the development of resistance. Studies of adherence in relation to HIV disease suggest that, typically, 50% of patients take at least 80% of their doses. Current therapeutic regimens for the multi-drug treatment of HIV are among the most complicated ever devised, matched only by some of those required for liver transplantation.

Appendix B: References

In a recent study of adherence among patients visiting the outpatient AIDS Clinic at San Francisco General Hospital individuals were invited to complete self-report questionnaires indicating how many medications had been missed or skipped. Of 134 patients receiving a protease inhibitor drug, 12% reported missing at least one dose "yesterday", 11% reported at least one missed dose the "day before yesterday" and 13% reported at least one missed dose the "day before that". In all, 30% had missed at least one dose in the past three days. Among the reasons given for non-adherence were forgetting, being involved in other activities or too busy to take medications, side effects and feeling ill, and having a depressed mood and related negative affect.

In conclusion, health-care providers must take more time to educate patients about the nature of the drug regimen they are receiving. Developing individualized plans for integrating the regimen into daily activities may be useful, as may be efforts to enhance self-monitoring of adherence. Enhanced communication with treatment staff is valuable, and extra support may need to be provided in the context of problem-solving around reported episodes of non-adherence. In the medium to longer term, less complex drug regimens are necessary.

In discussion, the following issues were raised:

Many factors influence adherence to complex treatment regimens. From the available evidence, there appear to be no consistent sociocultural or economic predictors of adherence. Rather, the issue appears to be one of the complexity of regimens. A busy lifestyle, whatever its

causes, appears to interfere most with the capacity to take treatment drugs. Health-care workers need advice on how to encourage greater adherence among clients, a situation made more complex by the fact that we currently do not know just how much adherence is sufficient to achieve treatment goals.

Appendix C: List of participants

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The Joint United Nations Programme on HIV/AIDS (UNAIDS) is the leading advocate for global action on HIV/AIDS. It brings together seven UN agencies in a common effort to fight the epidemic: the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA), the United Nations Educational, Scientific and Cultural Organization (UNESCO), United Nations International Drug Control Programme (UNDCP), the World Health Organization (WHO) and the World Bank.

UNAIDS both mobilizes the responses to the epidemic of its seven cosponsoring organizations and supplements these efforts with special initiatives. Its purpose is to lead and assist an expansion of the international response to HIV on all fronts: medical, public health, social, economic, cultural, political and human rights. UNAIDS works with a broad range of partners – governmental and NGO, business, scientific and lay – to share knowledge, skills and best practice across boundaries.



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