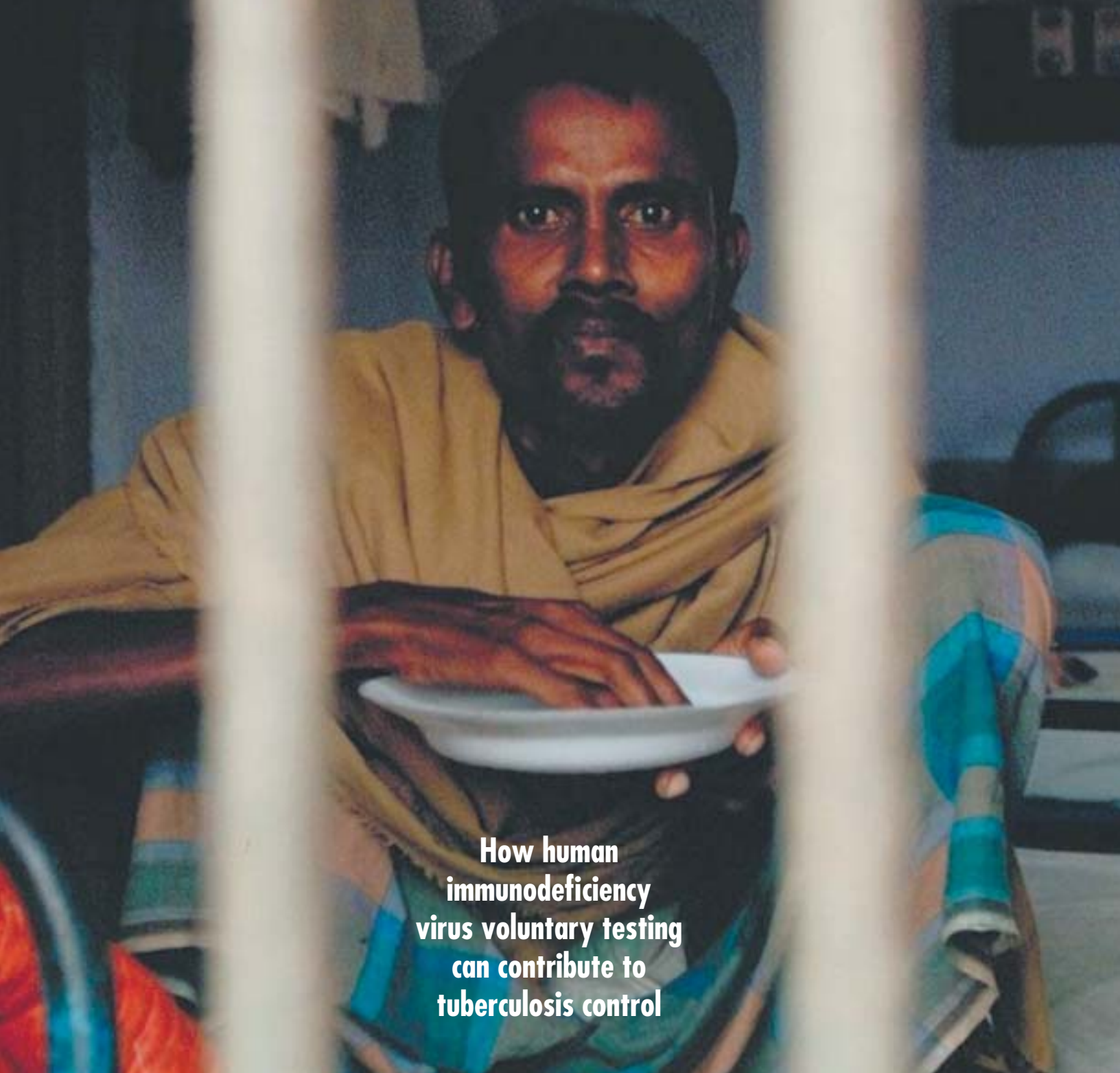


March 2003 VOL. 9, NO. 3

IAPAC

MONTHLY



**How human
immunodeficiency
virus voluntary testing
can contribute to
tuberculosis control**

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How human immunodeficiency virus voluntary testing can contribute to tuberculosis control

Peter Godfrey-Faussett, Dermot Maher, Ya Diul Mukadi, Paul Nunn, Joseph Perriens, and Mario Raviglione

HIV is the world's leading public health emergency—destroying the health of millions while impacting the economies of every country, rich and poor. HIV is also fueling the tuberculosis epidemic. The World Health Organization posits that HIV voluntary testing may contribute to tuberculosis control.



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Smallpox vaccination and the patient with HIV/AIDS

John G. Bartlett

The US Centers for Disease Control and Prevention (CDC) unveiled an operational plan for implementing large-scale smallpox vaccination in the United States. Should HIV-infected patients receive smallpox vaccination? What factors are HIV care providers to consider in the event of a smallpox outbreak?



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R E P O R T F R O M T H E P R E S I D E N T

TB can be cured

José M. Zuniga

M tuberculosis has been killing human beings for millennia. Signs of the effects of tuberculosis (TB) have been discovered in the remains of Egyptian mummies dating to almost 3,500 years ago.

Measured on this scale, the period of time during which we have had any effective medical knowledge of TB is quite short. In 1720 it was first suggested that “wonderfully minute living creatures” might be the cause of the disease. Developments in the second half of the 19th century included the first elucidation of the benefits of the fresh air sanitarium cure. And, in 1882, the bacterium was seen and identified by the aided human eye for the first time. But the most important breakthrough came in 1944 when streptomycin successfully, and very quickly, cured a critically ill patient. Scientists believed the ancient nemesis of humankind would be vanquished at last.

Alas, this was not the case. We should applaud the power of science for so advancing in less than 300 years our knowledge and treatment of a disease that has been an insidious killer for at least ten times that long. But we should be humbled, and moved to action, by the fact that nearly 60 years after a cure was discovered, TB continues to kill 2 million people every year, and remains the primary cause of death from a single infectious agent among adults in the developing world.

During the last five decades, the cure for TB has been available in theory. But rates of infection held stable or increased in impoverished regions of the world where poor living conditions remained the norm and/or the regimen of TB-treating drugs were not supplied or properly administered.

Now, with the advent of HIV, our primordial foe has returned as firmly entrenched as ever, and even more deadly. HIV and TB

work together with a grim efficiency. It is estimated that among people infected with *M. tuberculosis*, only one in ten people with healthy immune systems will develop TB over the course of their lifetimes. Among *M. tuberculosis*-infected individuals with HIV, that number changes to one in ten per year, while one in every two or three such patients whose HIV has developed into AIDS will suffer from TB each year.

In other words, there is a direct correlation between HIV prevalence and incidence of TB infection. The increased incidence of TB in turn exacerbates death rates in HIV-infected patients, among whom TB is the single most common coinfection. The highest rates of TB/HIV coinfection can be found in sub-Saharan Africa, with large and growing epidemics in Asia (already home to the highest total number of TB-infected people) and Eastern Europe.

Given the ways these two diseases work in synergy, it is imperative that we devise strategies that allow us to fight them simultaneously. The World Health Organization (WHO) encourages voluntary counseling and testing programs to screen for both HIV and TB and, thus, to link individuals to treatment or prevention of both diseases. In short, healthcare programs combating HIV should cooperate with programs combating TB.

One method of TB treatment has become a shining example of effective medical and social interventions in resource-limited settings over the past ten years. Under the auspices of the WHO’s Stop-TB Program, the Directly Observed Treatment, Short Course (DOTS) strategy has, by improving adherence, proven a means of ensuring successful therapy—where medication and infrastructure permit.

Therein, however, lies the current dilemma in redressing the plight of the TB pandemic.

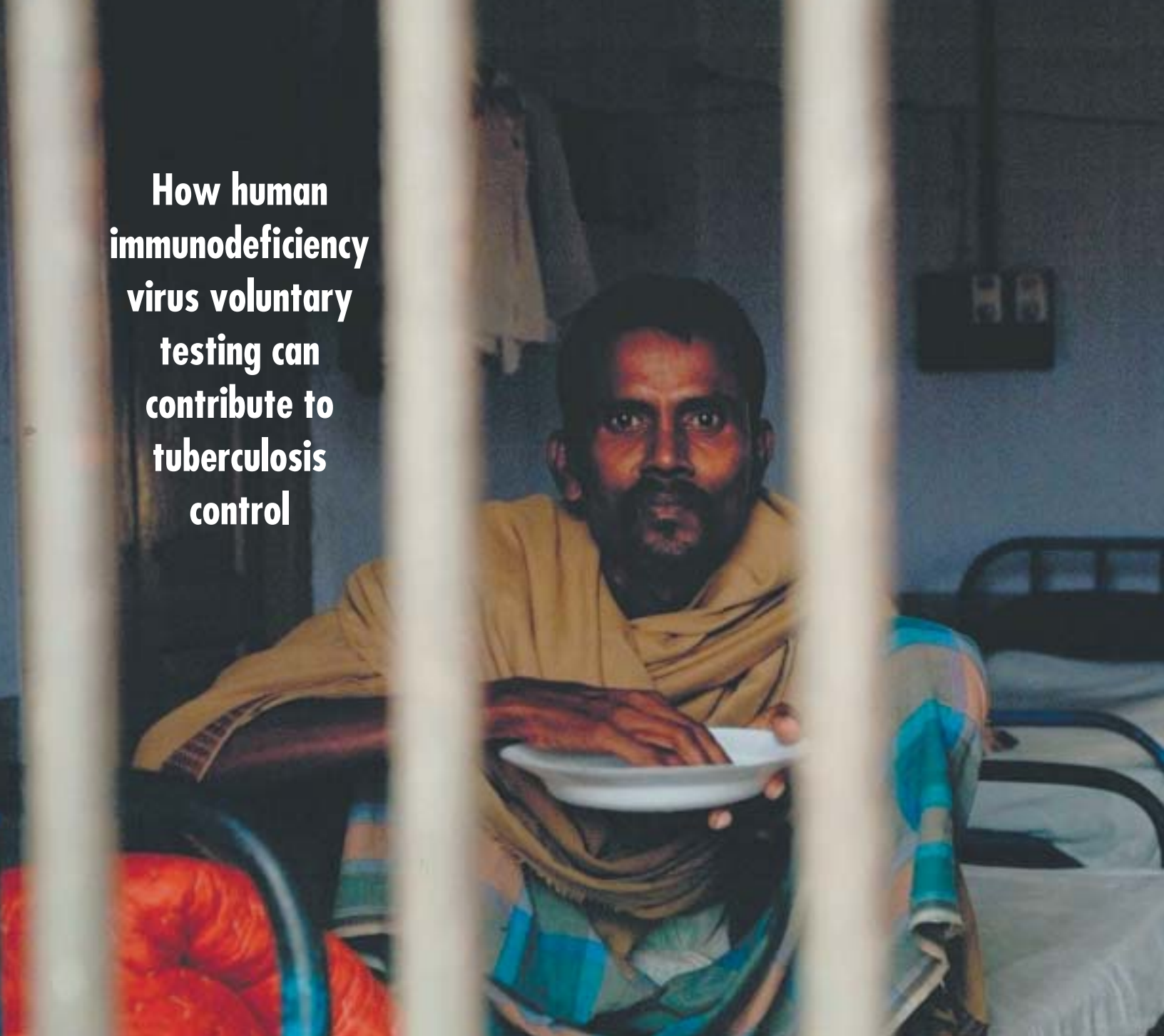
When seen from clinical and public health perspectives, there has not been the full global commitment to providing said medication and infrastructure, both of which are also critical to addressing HIV and HIV-related morbidity and mortality. And while the curability of TB should in and of itself prompt us to necessary global action, the often-intimate relation of TB treatment to reduced HIV infection and complications is all the more reason to act.

Thinking more radically, the world community could make the most difference in fighting TB, HIV, and the other so-called “diseases of poverty,” by addressing their root causes. They are endemic in nations with inadequate nutrition, underdeveloped medical infrastructure, insufficient housing, and the host of problems that both encourage the spread of these diseases and make them more lethal. Interventions addressing these problems of global development can be effective against both epidemics and improve overall quality of life.

Finally, at the individual level, members of the International Association of Physicians in AIDS Care (IAPAC), and all healthcare workers, must commit to understanding and implementing the practices by which HIV and TB can be simultaneously fought in daily interactions with their patients. Many thousands of years ago, TB began its prolonged attack on humanity with the illness of a single person. And it is at this grassroots point of contact—supported by increased global policy and regional programmatic commitment to fighting HIV, TB, and the conditions that engender their devastation—that these diseases might finally be brought to heel. ■

José M. Zuniga is President of the International Association of Physicians in AIDS Care (IAPAC), and Editor-in-Chief of the IAPAC Monthly.

How human immunodeficiency virus voluntary testing can contribute to tuberculosis control



*Peter Godfrey-Faussett,
Dermot Maher, Ya Diul Mukadi,
Paul Nunn, Joseph Perriens,
and Mario Raviglione*

Introduction

The human immunodeficiency virus (HIV) pandemic is the world's leading public health emergency, with a particularly severe impact on sub-Saharan Africa. It is destroying the health of Africans, the economies of African nations and their prospects for development. HIV infection is also

fuelling the tuberculosis (TB) epidemic, but TB programs have focused on TB case-finding and treatment, with little attention to HIV/AIDS interventions. Although TB is a leading cause of HIV-related morbidity and mortality, HIV/AIDS programs have generally paid little attention to TB. Thus, despite close epidemiological links between HIV and TB, the public health responses have largely been separate.

WHO has developed an expanded strategy to decrease the burden of HIV-related TB, requiring close collaboration between

TB and HIV programs.¹ The strategy comprises interventions against TB, including intensified case-finding, cure and preventive treatment, as well as interventions against HIV (and therefore indirectly against TB). The latter include counseling for decreased sexual risk behavior, provision of condoms, treatment of sexually transmitted infections, promotion of safety for intravenous drug users and provision of highly active antiretroviral treatment. WHO and collaborating bodies have embarked on "The ProTEST Initiative" as a starting point at district level for this



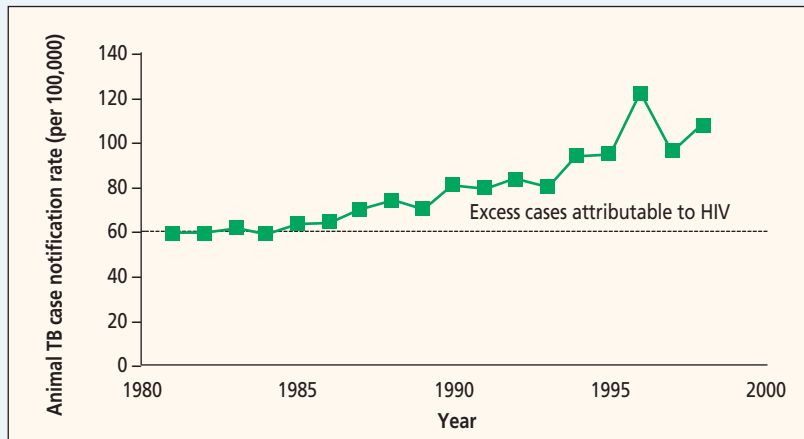
Photo: WHO/TBP/Davenport

comprehensive range of interventions aimed at decreasing the burden of HIV-related TB. The initiative promotes HIV voluntary testing as a key to a more coherent response to TB in high HIV-prevalence settings, through strengthening links between HIV and TB programs and general health services.

As part of a new approach to TB control in high HIV-prevalence settings, the rationale for the ProTEST Initiative needs public debate. This concept paper sets out the rationale for the initiative, based on an analysis of the impact of HIV on TB control,

Figure 1. The trend of cases of tuberculosis in sub-Saharan Africa (defined as the WHO region) since the mid-1980s

The assumption that the excess of tuberculosis cases since the mid-1980s is attributable to HIV is based on the temporal relation between the two epidemics and their known biological and epidemiological links.



Source: WHO 02.190

describes the elements of the ProTEST approach, reviews progress so far and sets out the future direction. The purpose is to generate discussion and ideas which will help the initiative to make a good start in establishing the comprehensive range of interventions needed to control TB in settings with high prevalence of HIV infection.

Background

TB is a leading cause of death among people living with HIV (PLWH).² About 12 million out of the 36 million HIV-infected people worldwide at the end of 2000 were coinfected with *Mycobacterium tuberculosis*, and 8.4 million (70 percent) of those co-infected live in sub-Saharan Africa.³ In countries with advanced HIV epidemics, particularly those of sub-Saharan Africa, the majority of TB patients are also infected with HIV.⁴

Largely associated with poverty and an inadequate health service response, the TB epidemic in sub-Saharan Africa remained at a relatively constant level until the onset of the impact of the HIV epidemic in the 1980s.⁵ Since then, HIV has caused a rapid increase in the TB epidemic. In HIV-infected people, HIV promotes progression to active TB in people with latent or recently acquired *M. tuberculosis* infections; increasing TB cases in HIV-infected people poses an increased risk of TB transmission to the general community,

whether or not HIV-infected. Figure 1 shows the trend of cases of TB in sub-Saharan Africa (defined as the WHO region of Africa) since the mid-1980s, with a relatively constant level of cases of TB until the onset of the impact of the HIV epidemic in the 1980s. The assumption that the rising trend since the mid-1980s is attributable to HIV is based on the temporal relation between the two epidemics and their known biological and epidemiological links.

Escalating TB caseloads in many countries in the region are outstripping the ability of health services to cope. Despite the epidemiological links, the public health responses to HIV and TB have largely been separate, and have so far had little success in interrupting the sequence of events by which HIV infection fuels the TB epidemic. Better coordination of HIV and TB program activities may lead to more effective implementation of interventions to decrease HIV transmission and the burden of TB.

There is an urgent need, particularly where HIV is increasing the prevalence of TB, to ensure that all TB patients have access to effective TB diagnosis and treatment. Failure to ensure the essential basics of case-finding and treatment in countries with severe HIV epidemics will result in an increased burden of TB over the coming decades, including increased risk of drug resistance.⁷ In turn, drug resistance (with its associated increased TB morbidity and

mortality) enormously complicates TB control and increases its costs.⁸

Because of the impact of HIV on the TB epidemic, additional measures beyond TB case-finding and treatment are necessary to control TB.¹⁻⁹ These measures should complement ongoing efforts to improve specific TB control tools such as the development of a more effective vaccine,¹⁰ better diagnostic tests,¹¹ better preventive¹² and therapeutic approaches,¹³ and more vigorous application of specific measures to prevent and interrupt transmission in prisons,¹⁴ healthcare institutions¹⁵ and other congregate settings.

WHO is coordinating the ProTEST Initiative with the aim of exploring how HIV voluntary testing can contribute to a more coherent response to TB in settings with high HIV prevalence. The core interventions offered to people attending for voluntary counseling and testing (VCT) for HIV are: intensified TB case-finding, and isoniazid preventive treatment for those without active TB. Starting with these core interventions, other interventions may be added to provide finally a comprehensive range of HIV and TB prevention and care interventions. Under the ProTEST Initiative, pilot districts are establishing links between centers for VCT for HIV and TB prevention and care. The aim is to derive mutual benefits by promoting VCT for both improved HIV prevention and care and improved TB control. This will pave the way for operationalization of the comprehensive range of interventions needed to control TB in settings with high HIV prevalence.

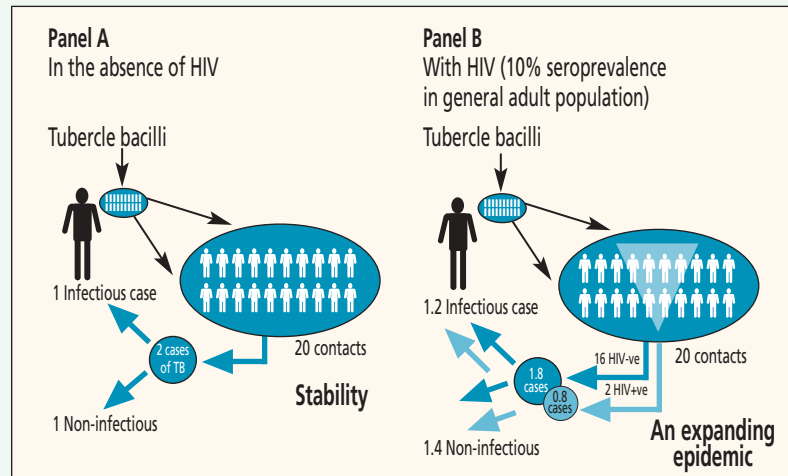
The goal of the ProTEST Initiative is to reduce the combined burden of TB and HIV through a concerted approach that will achieve the following objectives: to reduce the number of people becoming infected with HIV; to reduce the number of people transmitting both HIV and *M. tuberculosis*; and to reduce the risk of developing active TB in those infected with both HIV and *M. tuberculosis*.

Impact of HIV on TB control

Social impact

The stigma and silence surrounding HIV may extend to TB (already a stigmatized disease in many societies) in communities which have recognized the link between TB and HIV.¹⁶ Thus the stigma attached to HIV may have an adverse effect on TB

Figure 2. Schematic representation of the impact of HIV, the absence of HIV (Panel A), and where the HIV seroprevalence in the general adult population is 10 percent (Panel B)



Note: see text for full explanation.

Source: WHO 02.189

control activities. For example, people may be frightened to seek a diagnosis for a persistent cough, and try to avoid standing in a line of TB patients, identifiable by their neighbors.¹⁷

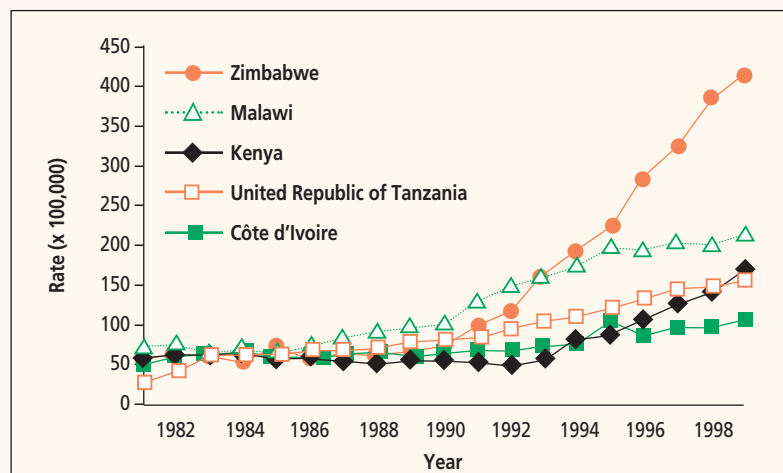
Epidemiological impact

Consideration of the basics of TB epidemiology and control¹⁸ is necessary to understand the impact of HIV. In the poorer regions of the world, annual risks of infection by *M. tuberculosis* are typically 1 to 3 percent, leading to prevalence rates of *M. tuberculosis* infection among young

adults of 30 to 70 percent.¹⁹ Figure 2 is a schematic representation of the impact of HIV on the cycle of *M. tuberculosis* transmission, showing first the situation in the absence of HIV and then the situation where the HIV seroprevalence in the general population is 10 percent.

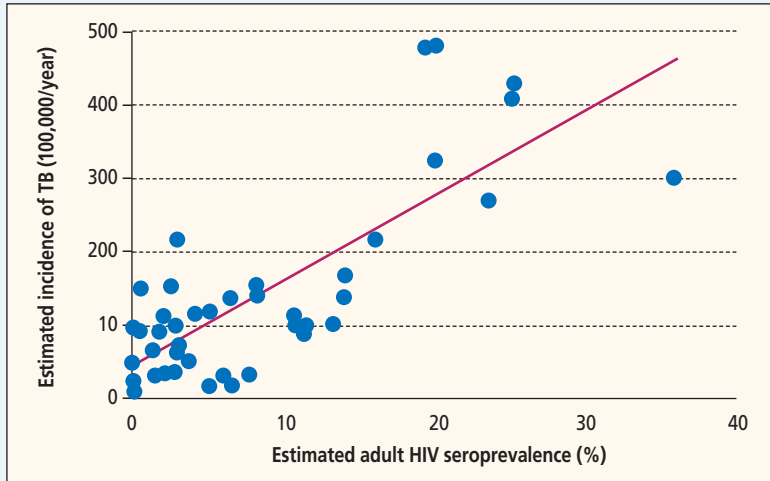
In the absence of HIV, only about 10 percent of people infected with *M. tuberculosis* will develop active TB (whether from progression of recent infection or from reactivation), of whom about one half will be infectious (usually smear-positive).²⁰ Thus, only one in 20 people

Figure 3. Tuberculosis case notification rates, 1980-1998 in selected African countries



Source: WHO 02.191

Figure 4. **Estimated adult HIV seroprevalence and tuberculosis incidence in African countries**



Source: WHO 02.192

infected with *M. tuberculosis* develops infectious TB, and each infectious case in its turn needs to infect about 20 people in order to generate one further infectious case. This is the situation of stable TB disease incidence (ie, the case reproduction number is one), as shown in Panel A of Figure 2. The primary stratagem of TB control is to reduce the average number of people infected by each infectious case so that the case reproduction number is less than one.

In the presence of HIV infection (the single strongest risk factor for progression from infection to active disease,²¹ about 40 percent of people infected with *M. tuberculosis* will develop active TB in their lifetime.²² Panel B of Figure 2 shows what happens to 20 people with *M. tuberculosis* infection when the HIV seroprevalence in the population is 10 percent. There will thus be 18 HIV-negative and two HIV-positive people with *M. tuberculosis* infection. With a 10 percent risk of developing active TB, the 18 HIV-negative people will generate 1.8 cases of TB. With a 40 percent risk of developing active TB, the two HIV-positive people will generate 0.8 cases of TB. Although each individual HIV-positive TB patient may be less infectious,²³ each infectious case now leads to 2.6 new cases, of whom more than one is infectious. This leads to an expanding epidemic (ie, the case reproduction number is more than one).

These simple calculations illustrate the implications of HIV for TB control. In order to lower the case reproduction number

in the face of the HIV-fuelled TB epidemic, TB control programs have not only to detect and cure the additional cases of HIV-related TB, but also to handle each case more effectively. This means reducing the average number of people infected by each case (eg, by reducing diagnostic and treatment delays).

Since the mid-1980s, in many African countries, including those with well-organized programs,^{24,25} annual TB case notification rates have risen up to four-fold, reaching peaks of more than 400 cases/100,000 population (Figure 3). The annual risk of infection may also have risen in some of those countries most severely affected.²⁶ Increased funding of TB programs has generally not kept pace with this increasing caseload,²⁷ and many programs are not achieving adequate case-detection and treatment outcomes.

Although it has been shown that “good” traditional TB control measures do blunt the impact of HIV on TB,²⁸ the best available estimates of the incidence of TB in all African countries show a striking correlation with estimates of adult HIV seroprevalence²⁹ (Figure 4). The burden of TB is so closely linked to the HIV epidemic that prevention of HIV must become a priority for TB programs, just as TB care and prevention should be a major concern of HIV/AIDS programs.

VCT for HIV as a link between control activities for HIV and TB

Interventions to prevent HIV infection include

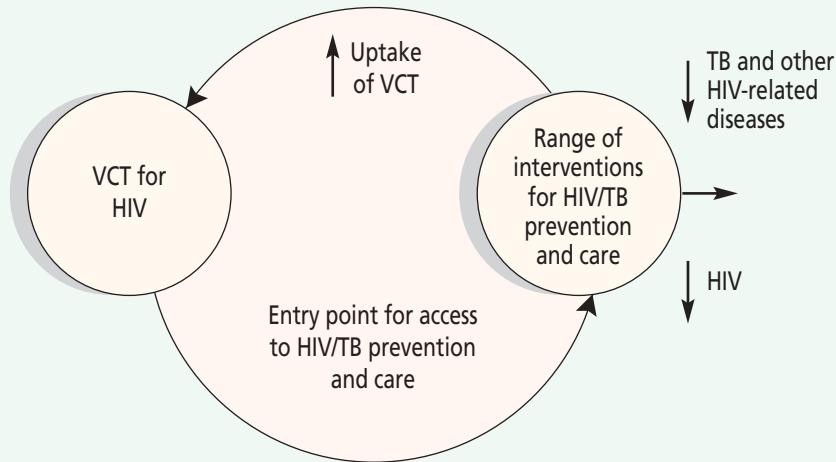
behavioral factors (eg, counseling to decrease sexual risk behavior), biological ones (eg, treatment of sexually transmitted infections) and the promotion of barrier methods (condoms).³⁰ In industrialized countries VCT has long been an established part of HIV programs, and many HIV-infected people know their HIV status. However, the vast majority of people in developing countries living with HIV infection do not know that this is the case. For instance, in a random population sample in Zambia, where at the end of 1999 the HIV seroprevalence among the general adult population was 20 percent, only 6.5 percent of adults had previously had an HIV test.³¹ VCT is sometimes available in special groups, such as TB patients at outpatient treatment centers in Abidjan, Côte d’Ivoire.³² However, in most regions of Africa routine VCT for the general population is rarely available,³³ although there are a few notable exceptions.³⁴ Reasons include, on the supply side, the high cost of VCT services, and on the demand side, the stigma of identification as HIV-positive and the widespread perception that HIV testing offers little to the individual who tests positive. “Why should I be tested? I will only die sooner if I know” is a remark counselors in developing countries frequently hear.³⁵

From an individual’s perspective, the medical and psychosocial support that can be offered to the majority of people who test positive in developing countries remains largely inadequate. However, from the public health perspective, evidence is accumulating that VCT does enable individuals, whether they test positive or negative, to change their behavior in ways that should reduce rates of HIV transmission.^{36,37} An economic evaluation of a randomized comparison of VCT versus health information alone in Kenya, Tanzania, and Trinidad and Tobago estimated that the cost of preventing a new HIV infection (assuming that the reported behavior change does translate into decreased HIV transmission) is around US\$250.³⁸ This ranks VCT alongside strengthened syndromic management of sexually transmitted infections (STIs) in primary healthcare as a cost-effective intervention to prevent HIV infection.³⁹ This is an important development for TB control.

VCT offers a direct entry point for more effective TB prevention and care for

Figure 5. **Schematic representation of the proposed virtuous circle linking VCT* to HIV and TB care**

Promotion of VCT for HIV provides an opportunity to offer interventions for tuberculosis prevention and care, which themselves provide an incentive for people to undergo VCT for HIV.



*VCT - voluntary testing and counseling.

Source: WHO 02.193

HIV seropositive and seronegative people. The majority of people infected with HIV have no symptoms and the proportion of people who choose to be tested for HIV is smallest among those who are without symptoms, irrespective of their HIV status. As symptoms of HIV-related disease develop, a few people choose to find out whether HIV is likely to be the cause. Those with more advanced HIV-related disease are more likely to be tested by the clinician as part of clinical management.

Those who discover that they are not infected with HIV have a strong motive to ensure that they remain so. Appropriate counseling can help to translate this motivation into behavior change.⁴⁰ Counseling also offers the opportunity to promote more optimistic messages that may help to destigmatize both HIV and TB.

In those who have no symptoms but are HIV seropositive, counseling aims to prevent transmission of HIV infection as well as to offer psychosocial support. Up to 50 percent of these people will subsequently develop active TB. The incidence of TB in this group can also be reduced, at least for some time, by preventive therapy with isoniazid.^{41,42} Counselors need training to offer preventive therapy safely and to ensure that their clients are diagnosed promptly if they later develop symptoms suggestive of TB.

In those who do already have symptoms

of HIV-related disease, the challenge is to detect active cases of TB early and to treat them effectively. Not only will early case detection prevent ongoing transmission of TB, it may also slow the progression of HIV infection.⁴³

Finally, among those with TB and advanced HIV disease, many of whom are housebound and unable to visit their local clinic for supervision of treatment, community-based care teams,⁴⁴⁻⁴⁶ while caring for aspects of other HIV-related diseases, can promote adherence to TB treatment and so prevent the development of chronic or drug-resistant TB.

The elements of the ProTEST Initiative

Under the initiative, the core interventions offered to people receiving VCT for HIV are intensified TB case-finding and isoniazid preventive treatment for those without active TB. Pilot districts are establishing links for centers for VCT for HIV with TB prevention and care in order to derive mutual benefits for promoting VCT for HIV and for improving TB control. Figure 5 shows schematically this link between VCT and access to interventions for HIV and TB prevention and care as a “virtuous circle”: promotion of VCT for HIV provides an opportunity to offer interventions for TB prevention and care, which themselves provide an incentive for people to undergo VCT for HIV.

By identifying and linking the government and nongovernmental organizations currently offering support and care for PLWH and by involving the community, the ProTEST Initiative aims to facilitate referral and to provide the opportunity for improving the quality of services. These include provision of the core ProTEST interventions of TB prevention and care, as well as an expanded range of interventions. For example, those with more advanced HIV disease may benefit from cotrimoxazole prophylaxis against some bacterial causes of pneumonia and diarrhea and their complications.⁴⁷ As antiretroviral drugs become much more widely affordable and available in resource-poor settings, the ProTEST Initiative may be an opportunity to increase access to highly active antiretroviral therapy, which has been shown to reduce the incidence of TB and other HIV-related infections in other settings.^{48,49}

The elements of the ProTEST Initiative are part of comprehensive care for PLWH, which includes communicable disease control (particularly for TB and STIs), symptom control and pastoral care. This requires close collaboration between community-based care services and government or private health facilities. Developing and making available the “continuum of care”⁵⁰ should encourage more people to find out their HIV status. To meet increased demand, it will be necessary to expand VCT services and ensure they are accessible and user-friendly.

Openings and opportunities

The ProTEST Initiative therefore fits well with other movements to encourage HIV testing, such as those linked to programs to deliver antiretroviral drugs to reduce transmission of HIV from mothers to their children.⁵¹ By linking with the ProTEST rationale, the benefits can be extended beyond the child to the parents and family and, by reducing transmission of HIV, TB and STIs, to the broader community.

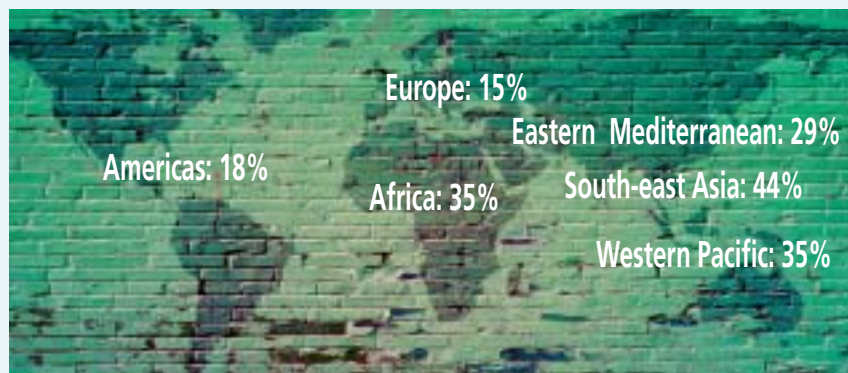
The acceptability of VCT seems to be rising for various reasons, which include increasing awareness of personal responsibility as the HIV epidemic continues to devastate families, communities and countries. The reasons for people to get tested may be shifting. For example, the AIDS information center in Uganda reports an increasing proportion of their

About Tuberculosis



Epidemiology

Each year, 1 percent of the global population is infected. From 5 to 10 percent of those infected become sick or infectious. The incidence of tuberculosis by region of the world is as follows:



Causative agent

There are three causative agents of tuberculosis infection:

- *Mycobacterium tuberculosis* is the most widespread bacterium responsible for infection.
- *M. africanum* is primarily found in Africa.
- *M. bovis* is found worldwide, but is limited by pasteurization of milk in the developed world and low milk consumption and boiling milk in developing countries.

Transmission

Tuberculosis is a contagious, airborne infection. A patient with pulmonary tuberculosis can spread bacilli when exhaling, coughing, sneezing, talking, or spitting. Infection occurs when a susceptible human inhales these bacilli.

A person infected with tuberculosis bacilli incurs a 10 percent risk of developing active tuberculosis. Though most can carry tuberculosis bacilli without becoming sick, any weakening of the immune system (eg, caused by HIV infection or malnutrition) increases the chance that the tuberculosis bacilli will become active.

On average, each infective person will infect 10 to 15 people each year. Although inhalation is the primary mode of transmission, infections can also occur through ingestion and direct inoculation.

Symptoms

The disease is caused by the body's attempt to control the bacilli. Besides causing lung disease, bacteria can infect many parts of the body.

People may be unaware that they are infected because their bodies respond effectively and control the infection. In some, bacteria remain dormant and become active when the immune system is depressed.

A tuberculosis patient will exhibit chest pain, fever, and a persistent cough, lasting for more than three weeks, and often coughing up blood. Other symptoms include localized bone pain and lymphadenopathy.

Prevention and control

Since tuberculosis is an airborne contagious disease, primary control is effected through finding and treating infectious cases and thus limiting the risk of acquiring infection.

Directly Observed Treatment, Short-Course (DOTS) is a proven system for tuberculosis treatment, based on accurate diagnosis and patients taking a full course of a cocktail of anti-tuberculosis drugs (which include isoniazid, rifampicin, pyrazinamide, streptomycin, and ethambutol). The success of DOTS hinges on government commitment, detection, treatment, uninterrupted supply of anti-tuberculosis drugs, and a monitoring and reporting system to evaluate treatment outcomes for each patient.

Source: *Special Program for Research and Training in Tropical Diseases, World Health Organization.*

HIV testing to be carried out for couples who are using the information to help them plan realistically for their future.⁵² The falling proportion of positive results among clients attending testing centers after the introduction of healthcare services linked to testing may also reflect a shift towards more proactive planning.

The silence and denial that surround HIV have been well described.⁵³ As more and more people choose to find out about their HIV status, this silence and denial should lessen, with benefits for efforts to control HIV and TB transmission. By engaging with community organizations and encouraging greater openness about TB and HIV, and specifically highlighting the positive steps that can be taken to reduce the burden of TB and HIV, the ProTEST Initiative can help to alter the community's perception of HIV and reduce the associated stigma. "Normalization" of HIV infection should facilitate other efforts aimed at HIV and TB prevention.

Current progress and future direction of the ProTEST Initiative

WHO is coordinating a network of partners involved in the ProTEST Initiative, including ministries of health of countries bearing the dual burden of HIV and TB, international development assistance agencies, nongovernmental organizations, and academic institutions. The network will facilitate the exchange of information and experience between partners and provide oversight of ProTEST projects. Implementation of the first projects is underway in Malawi, South Africa, Uganda, and Zambia.

The projects share the objective of finding out and demonstrating what can be achieved and at what cost. The approach is paving the way for scaling up of the comprehensive range of interventions needed to control TB in populations with high HIV prevalence. WHO is currently supporting the mathematical modeling of the potential impact of a range of interventions on the combined burden of TB and HIV. The projects also act as a catalyst to draw national TB and HIV program staff together in discussions about training, information, education, communication, service delivery, and information management, as well as more upstream activities such as planning and prioritization.

Recent events hold out the promise of substantially increased aid for the priority diseases of poverty—HIV/AIDS, TB, and malaria. For example, some large-scale funding is becoming available through the Global Fund to Fight AIDS, Tuberculosis and Malaria. The ProTEST Initiative represents an opportunity for financial and technical partners to collaborate with governments and civil society in the countries most badly affected by the HIV epidemic in substantially increasing concerted action against HIV and TB.

Conclusions

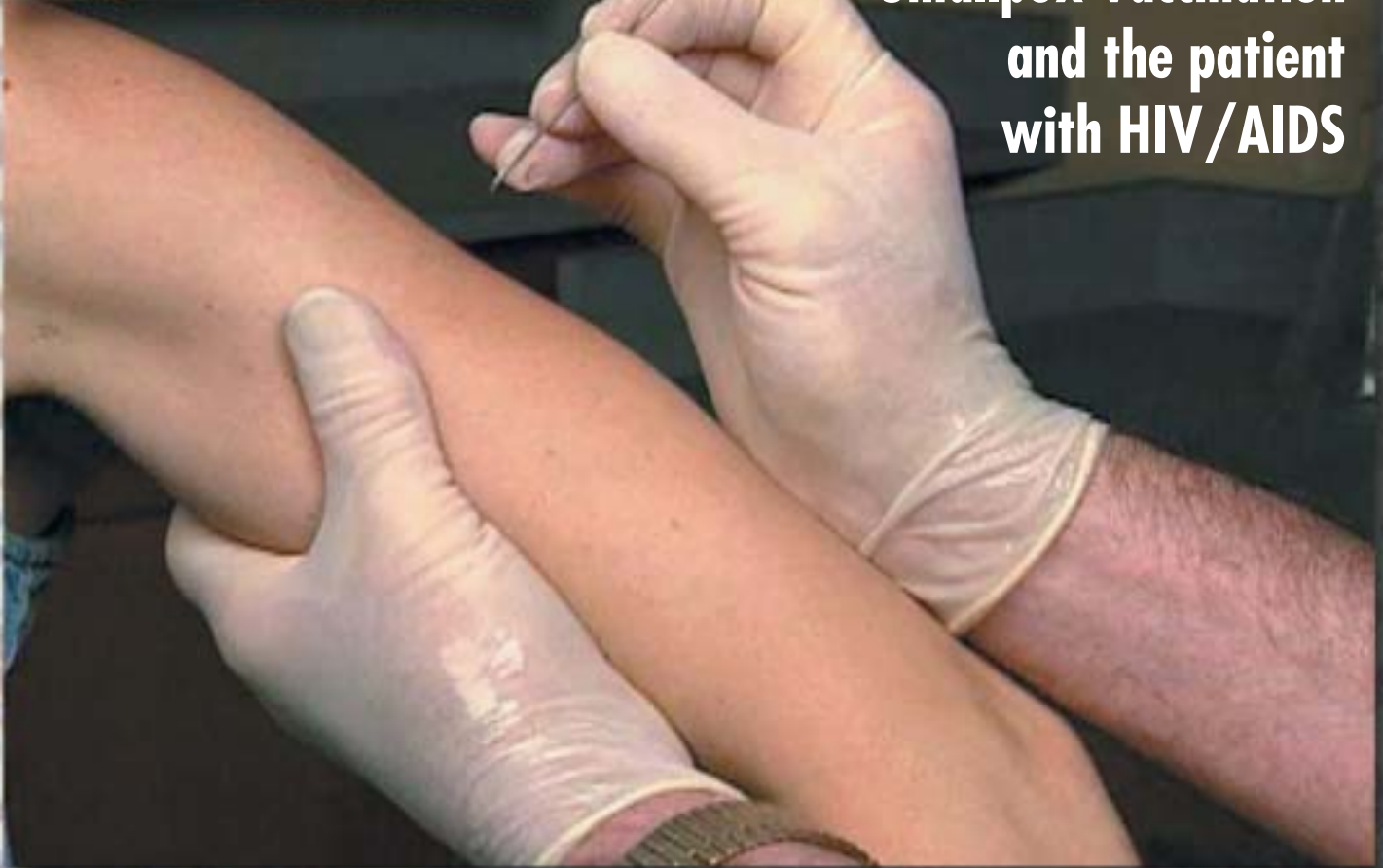
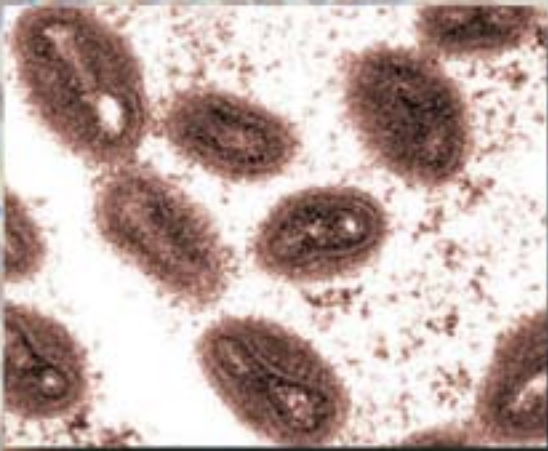
Interventions are available to decrease the burden of HIV-related TB. Therefore, the time is ripe for TB and HIV programs to collaborate in carrying out these activities as widely as possible. The ProTEST Initiative can greatly help to build alliances between TB and HIV programs and to scale up the full range of interventions to decrease the burden of HIV-related TB. ■

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Peter Godfrey-Faussett is from the Infectious and Tropical Diseases Department of the London School of Hygiene and Tropical Medicine; Dermot Maher, Paul Nunn, and Mario Raviglione are from the Stop TB Department of the World Health Organization in Geneva; Ya Diul Mukadi is from Family Health International in Arlington, Virginia, USA; and Joseph Perriens is from the Department of HIV/AIDS at the World Health Organization in Geneva.

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Smallpox vaccination and the patient with HIV/AIDS

Photo caption: US Centers for Disease Control and Prevention Image Library, 2002.

John G. Bartlett

On September 23, 2002, the US Centers for Disease Control and Prevention (CDC) presented a detailed operational plan for implementing a large-scale smallpox vaccination.¹ The purpose of this article is to review the CDC plan and the relevant issues as applied to individuals

with HIV infection and their providers. With regard to the CDC plan, the following points are emphasized:

- Smallpox vaccination will be voluntary.
- In the presence of an outbreak, everyone who has been in contact with a case of smallpox or determined to have been exposed to a biological weapon disseminating the smallpox virus is advised to get smallpox vaccine regardless of medical condition.
- In the absence of contact or other type of exposure, smallpox vaccination is not recommended for individuals with HIV infection regardless of CD4 cell count.
- Individuals with immune deficiencies, including HIV/AIDS, may develop severe complications from smallpox

vaccination with generalized vaccinia or progressive vaccinia.

- For vaccination, medical screening must be done including HIV serology if requested, and vaccination should generally not be recommended for persons with contraindications including HIV infection unless they are contacts of persons with smallpox infection. Screening should include voluntary rapid HIV testing if such tests are available and approved by the US Food and Drug Administration (FDA).
- Severe reactions to the vaccine may be treated with Vaccinia Immune Globulin (VIG) and/or cidofovir; both are considered investigational requiring informed consent.
- If the HIV-infected patient is not vaccinated and lives with someone who has been vaccinated, he/she should consider living apart to avoid contact vaccinia. The period of separation required should last until public health officials state there is no longer a risk, which is usually 14 days after vaccination or 18 days after contact with a smallpox case.

The following are relevant additional points to smallpox vaccination in patients with HIV/AIDS.

Q. What is the expected outcome of smallpox in the HIV infected person in the absence of vaccination?

- A.** The answer is unknown because smallpox was eradicated before AIDS was described. However, we do know that patients with CD4 counts <100 to 200 cells/mm³ have major defects in both cell-mediated immunity and humoral immunity as indicated by susceptibility to opportunistic pathogens and reduced antibody response to vaccine antigens.^{2,3} Both humoral and cell-mediated defense mechanisms are considered important in containing variola.⁴ Since the mortality rate in unvaccinated immunocompetent patients with naturally acquired disease is about 30 percent in the general population, it is speculated that the mortality rate would be much higher in patients with HIV and this risk would correlate inversely with CD4 count; for those with AIDS or a CD4 count <200 cells/mm³, the mortality rate is likely to be very high.

Q. Would patients with HIV infection generate an immune response to smallpox vaccine?

- A.** The experience with other vaccines is that serologic response is CD4 cell count-dependent. In general, antibody titers are nil or reduced with CD4 counts <100 to 200 cells/mm³ for nearly all vaccines in common use including tetanus, hepatitis B, influenza, *S. pneumoniae*, polio (eIPV), and measles.^{2,3,5,6} Response rates are better or normal with CD4 counts >200 cells/mm³.^{5,6} The same applies to a large extent with cell-mediated immune responses based on the experience with PPD skin tests.⁶⁻⁸

Q. Will smallpox vaccine cause progression of HIV?

- A.** Vaccines may stimulate an immune response including activation of CD4 cells that harbor HIV, thus increasing HIV viral load. The increase is generally <1,000 copies/ml and lasts two to six weeks.^{9,10} This has not been problematic even in untreated patients or those receiving highly active antiretroviral therapy (HAART) using non-live microbe vaccines. However, vaccinia is a live virus vaccine, which may result in persistence of vaccinia infection that conceivably could cause persistent CD4 activation; in this case progressive vaccinia is probably a much greater concern as discussed below.

Q. What are the risks of smallpox vaccine with HIV infection?

- A.** Progressive vaccinia (or vaccinia necrosum) is the major risk.⁴ This is one of the most dreaded complications of vaccinia and is seen primarily in patients with compromised cell-mediated immunity such as patients with AIDS, organ transplants, cancer chemotherapy, chronic corticosteroids, hematologic malignancies, and combined immunodeficiency disorders; it has also been seen in some with hypogammaglobulinemia.⁴ This reaction consists of progressive enlargement of the primary site of inoculation and viremic spread to other sites with new disseminated lesions. The lesions show minimal local inflammation, biopsies confirm minimal lymphocytic infiltrates, and cultures of these distant sites yield vaccinia.^{4,12-16} This complication may occur after primary vaccination or revaccination and is usually fatal.^{4,14,16} A possibly typical case has been described in a 19-year-old military recruit not previously known to have HIV infection who had a smallpox vaccination

in May 1984.¹⁶ This patient developed new satellite ulcers at the site of inoculation and then a widespread, disseminated pustular rash that yielded vaccinia on culture. The patient was treated with VIG and had a complicated course with both disseminated vaccinia and AIDS-related complications that culminated in death at 18 months post-vaccination. Zagury has also reported cell immunotherapy with recombinant vaccinia that resulted in "wide necrosis" at the site of subcutaneous/intramuscular injections resulting in death in three of eight AIDS patients; all three had CD4 counts <50 cells/mm³.¹⁷

A case with analogous pathophysiology was noted in a 20-year-old college freshman who received live measles vaccine despite advanced HIV infection with prior *P. carinii* pneumonia and no detectable CD4 cells.¹⁸ This patient developed progressive pulmonary infiltrates ten months later that yielded the measles vaccine strain (Moratan strain) on lung biopsy. He was treated with IVIG and ribavirin, but had progressive disease and died five months later. There have been nine reported cases of disseminated BCG with six deaths in AIDS patients following vaccination.¹⁹ These cases illustrate the hazard of disseminated disease following live microbe vaccinations in patients with late-stage HIV.

Q. Is there a treatment for progressive vaccinia?

- A.** The standard treatment is Vaccinia Immune Globulin (VIG), although the experience is limited and somewhat variable.^{4,12-16,20} The CDC controls availability of VIG. The usual dose is 0.6 mL/kg IM or about 40 ml that is usually given over 24 to 36 hours. Cidofovir has also been suggested based on *in vitro* activity versus vaccinia and activity *in vivo* in a rodent model.²¹⁻²³ Nevertheless, clinical experience is nil for cidofovir treatment of vaccinia and related poxviruses with the exception of topical use for molluscum contagiosum.²⁴ A study of immunodeficient mice challenged with cowpox showed cidofovir failed to prevent death.²⁵ Perhaps the most important therapeutic intervention would be HAART combined with these other treatments.

Q. How great is the risk of secondary spread of vaccinia from vaccines to patients with HIV infection?

A. Vaccinia causes an ulcer often with satellite lesions that shed the virus for about 10 to 14 days post-inoculation. Shedding occurs even through sealed bandages.¹¹ The frequency of contact vaccinia is rare — about 2-6/100,000 with primary vaccination based on prior reports.^{26,27} These cases required close contact and rarely occurred outside the home except for a few hospital-related contact cases.¹¹ Contact vaccinia in immunodeficient patients is a larger concern than these numbers indicate because the frequency may be substantially higher in immunodeficient patients and the consequences far greater. The implication is that vulnerable patients, including those with HIV infection, should be removed from direct contact with vaccine recipients until inoculation sites no longer shed virus.¹¹ Recommendations include separate housing or, in the case of contact with vaccinated fellow workers, it could mean furloughing. The experience with varicella vaccine is possibly analogous since this also involves live virus that can be spread to contacts from inoculation sites, but here the consequences are far less devastating.

Q. What will be the policy for HIV screening for vaccination?

A. The CDC's "Smallpox Vaccination Clinical Guide" states that HIV screening should be available if requested by the participant and that rapid tests for HIV should be considered if available and FDA approved. A potential problem with logistics of HIV testing as a contingency for smallpox vaccination is the need for informed consent for HIV serology and the delay in results using standard serologic methods. The only rapid test currently available that is FDA approved that could provide results in minutes is SUDS, but this test requires interpretation in a CLIA-certified lab. Several provider-read rapid HIV tests are under review by the FDA and these could simplify the process. Two of these tests (Oraquick and Reveal) have received "FDA-approvable" letters and FDA approval is expected soon. A major concern is the inadvertent vaccination of some of the estimated 300,000 patients with HIV infection who are unaware of their status; this includes the approximately 25,000 health

care workers who may be prioritized for vaccination as first responders.¹¹

Q. How much does the CD4 count matter?

A. The CD4 count is the barometer for susceptibility to opportunistic infections and it would appear to be critical in defining the risk for both smallpox and for progressive vaccinia following vaccination or accidental contact with a vaccinee. Nearly all complications of live vaccines in patients with HIV infection have occurred in those with CD4 counts <200 cells/mm³. The commonly accepted threshold of susceptibility has always been 200 cells/mm³ or 14 percent, which defines AIDS. Measles vaccine is considered safe in HIV-infected children with a CD4 count above 15 percent, and there is an ongoing trial of varicella vaccine in HIV-infected children also using a CD4 threshold of 15 percent to define safety. Based on these observations, many authorities would consider smallpox vaccination as clearly unsafe in those with a CD4 <200 cells/mm³ or <14 percent. The problem is assumption of safety with a CD4 count >200 cells/mm³ since there is no experience. The CDC recommendations define risk by the presence of HIV regardless of CD4 count, presumably due to the lack of supporting clinical data with vaccinia. Nevertheless, the CD4 count would appear to be a critical variable that emphasizes the potential importance of disease stage and the utility of HAART in determining risk.

Q. Does prior smallpox vaccination make a difference?

A. Most Americans aged >30 years received smallpox vaccinations. These patients do not have detectable vaccinia antibody, but there may be persistent CMI protection and/or an amnesic response with revaccination.^{28,29} Neither of these observations is regarded as likely in the face of severe immunosuppression. Patients >30 years with early-stage disease or immune reconstitution seem likely to behave like immunocompetent individuals with prior smallpox vaccination, although this is speculation. ■

Dr. John Bartlett, Professor of Medicine and Chief, Division of Infectious Diseases, Johns Hopkins University School of Medicine, Johns Hopkins Hospital; Founding Co-director, Johns Hopkins Center for Civilian Biodefense Strategies.

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I N T H E L I F E



Hoosen M. Coovadia

Vanity Fair readers have every month since 1993 enjoyed *The Proust Questionnaire*, a series of questions posed to celebrities and other famous subjects. In May 2002, *IAPAC Monthly* introduced "In the Life," through which IAPAC members are asked to bare their souls by answering 10 questions.

This month, *IAPAC Monthly* is proud to feature Hoosen M. Coovadia, Victor Daitz Professor in HIV/AIDS Research at the Centre for HIV/AIDS Networking, University of Natal-Durban, South Africa.

What proverb, colloquial expression, or quote best describes how you view the world and yourself in it?

The world in which I live has been shaped through aeons by the evolution of natural forces (air, land, water, temperature, sub-atomic particles, atoms, molecules, etc.) and recently by human agency. I see myself as a creature of circumstance (family, community, environment) and heritable traits.

What activities, avocations, or hobbies interest you? Do you have a hidden talent?

Literature, especially modern works; arts; music; tennis; discovery; political-economic-social developments. Like other foolishly ambitious individuals, I imagined I could

have written semi-historical novels on the changing landscape of South Africa's people.

If you could live anywhere in the world, where would it be?

I cannot think of anywhere other than South Africa; although the devastating crime rate, persistent racism, and an inability to achieve equity and justice, occasionally test my loyalty. I am here because I belong!

Who are your mentors or real life heroes?

Mentors in my professional life: Professor Patrick Smythe (taught me paediatrics); Professor John Soothill (introduced me to research and science). Heroes: Peter Medawar, James Watson, [Gabriel] Garcia Marquez, Salman Rushdie, Nelson Mandela.

With what historical figure do you most identify?

Peter Medawar. He was brilliant; he wrote knowledgeably on many important scientific issues; he was an immunologist (I did an early MSc in this in the United Kingdom); in short, he was near enough to a Renaissance man.

Who are your favorite authors, painters, and/or composers?

See above authors and many others. Painters: the range of nineteenth century impressionists. Music: Mozart, Beethoven, the Beatles, and many Indian composers of music and song.

If you could have chosen to live during any time period in human history, which would it be?

I am afraid the future will jettison many of the values I hold dear, and I am uncomfortable with the past, which did not have the things that make today worthwhile.

If you did not have the option of becoming a physician, what would you have likely become, given the opportunity?

A writer of great ideas and novels.

In your opinion, what are the greatest achievements and failures of humanity?

Achievements: Science, technology, and art. Failures: Failure of socialism, and the elusive search for social justice, equity, and global peace.

What is your prediction as to the future of our planet one full decade from present day?

Hopelessly self-seeking and mercenary, dangerously unstable, irredeemably inequitable and unjust, environmentally precarious, and crippled in part by AIDS. ■



[Strength in Numbers]

[IAPAC Welcomes New and Renewing Members]

In February 2003, the International Association of Physicians in AIDS Care (IAPAC) welcomed 54 new and renewing dues-paying members from four countries and one US territory. IAPAC thanks the following physicians and allied health professionals for their support of the association's mission to improve the quality of care provided to men, women, and children who are living with HIV/AIDS.

Elfaith Abter, *USA*
Joseph Baran Jr., *USA*
Paul Bellman, *USA*
Andre Bester, *South Africa*
Ellen Birenbaum, *USA*
Larry Bruni, *USA*
Jeff Collins, *USA*
Carlos Dominguez, *Puerto Rico*
Harvey Elder, *USA*
Manuel Feregrino-Goyos, *Mexico*
Neil Flynn, *USA*
Linda Frank, *USA*
Robert Gale, *USA*

Joan Goldberg, *USA*
N. Patrick Hennessey, *USA*
John Hostetler, *USA*
Richard Hudson, *USA*
Joseph Jackson, *USA*
Asim Jani, *USA*
Mahlon D. Johnson, *USA*
Stephan Knox, *USA*
Susan Kruse, *USA*
Ernesto Lamadrid, *USA*
James Lee, *USA*
J. Michael Lee, *USA*
Anthony Mangia, *USA*
W. Christopher Mathews, *USA*
Christopher McMackin, *USA*
Jane Mobley, *USA*
Joni Nickens, *USA*
Harry Nickle, *USA*
Anthony F. Ognjan, *USA*
Bruce Oran, *USA*
Victor Palmer, *USA*
Rick Pesano, *USA*
John Prichard, *USA*
Irma Rey, *USA*
Marc Rubenstein, *USA*

Shannon Schrader, *USA*
Gary Schroeder, *USA*
Steven Sotman, *USA*
Ruth Soto-Malave, *Puerto Rico*
Jonathan Stake, *USA*
Jay Sullivan, *USA*
Donna Sweet, *USA*
J. Wesley Thompson, *USA*
Divya Verma, *USA*

In addition, the following institutions renewed their institutional memberships: the AIDS Action Coalition; AIDS Research Alliance; Alamance Care; Greenwich House; New York Academy of Medicine; Positive Health Project; and Statni Zdravotni Ustav.

To learn more about professional and institutional memberships, call (312) 795-4935 or send an e-mail to member@iapac.org. For more information regarding Corporate Partner opportunities, call (312) 795-4941 or send an e-mail to partner@iapac.org.

[Recruit your colleagues to join IAPAC]

Health professionals who join the International Association of Physicians in AIDS Care (IAPAC) benefit from the research and expertise disseminated through the association's journals, Web site, care tools, and annual symposia. Greater membership in IAPAC also means more support for the association's training programs. These programs are making great strides in helping professionals learn best practice care techniques in the developing world, where the pandemic is taking its heaviest toll. Finally, as IAPAC continues to find strength in numbers, and represent more and more of the

world's health professionals, expanded membership means a more powerful voice in discussions that can lead to increased funding for medications, more effective inter-organizational cooperation, and simply better quality of life for those living with HIV disease.

These reasons should be more than enough to encourage you to recruit colleagues to join IAPAC. Nonetheless, we want to provide you with personal rewards for your recruitment efforts.

Through the end of 2002, every new recruit who lists you as the member who referred him/her to IAPAC brings you

closer to winning free travel and/or a complimentary membership extension. For each member you recruit, your name will be entered in a drawing for one roundtrip airline ticket within your continent or region of the world. If you recruit five new members before the end of the year, you will receive 12 months of dues-free membership.

Battling complacency and advancing commitment in the international struggle against HIV/AIDS requires a strong, coordinated effort. Encourage your colleagues to join that effort as members of IAPAC.



ABSTRACTS

AIDS

HIV increases the risk of malaria in women of all gravidities in Kisumu, Kenya

AM Van Eijk et al.

Objective: To study the importance of HIV infection for malaria in pregnancy in Kisumu, Kenya. **Methods:** Healthy women with an uncomplicated pregnancy of 32 weeks or more attending the prenatal clinic in the Provincial Hospital between June 1996 and March 1999 were tested for HIV and malaria after consent had been obtained. For participating women who delivered in the same hospital, a blood smear of the mother and the placenta were obtained. **Results:** In the third trimester, 5,093 women consented to testing: the prevalence of malaria and HIV was 20.1 and 24.9 percent, respectively. Among the 2,502 [HIV- and malaria-] screened women who delivered in the hospital, the prevalence of HIV, peripheral parasitaemia and placental malaria was 24.5, 15.2, and 19.0 percent, respectively. Compared with HIV-seronegative women, HIV-seropositive women were more likely to be parasitaemic, to have higher parasite densities, and to be febrile when parasitaemic. Placental infections in HIV-seropositive women were more likely to be chronic, as indicated by the presence of moderate to heavy pigment depositions. When adjusted by age, the typical gravidity-specific pattern of malaria in pregnancy disappeared in HIV-seropositive women; HIV-seropositive primigravidae had a similar risk of malaria as HIV-seropositive multigravidae. The excess malaria attributable to HIV in the third trimester increased from 34.6 percent among HIV-seropositive primigravidae, to 41.5 percent among HIV-seropositive secundigravidae, and 50.7 percent among HIV-seropositive gravidae with three or more pregnancies. **Conclusion:** HIV infection alters patterns of malaria in pregnant women; in areas with both infections, all pregnant women should use malaria prevention.

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Journal of Clinical Virology

The role of observational data in monitoring trends in antiretroviral treatment and HIV disease stage

K Petoumenos

Objective: To illustrate how human immunodeficiency virus (HIV) observational databases may be used to monitor trends in HIV treatment and HIV disease outcomes through data reported from the Australian HIV Observational Database (AHOD). **Methods:** Time trends in the use of antiretroviral treatment, and changes in treatment strategies were calculated in patients recruited to AHOD from HIV specialist clinics including hospitals, sexual health clinics and general practices. These results were then compared to trends reported from other observational cohorts. **Results:** By September 2001, 1,961 patients were recruited to AHOD. Since entering AHOD, 3 percent

of patients have been diagnosed with an AIDS defining illness, and 2 percent of patients have died, of which, 54 percent were non-HIV related deaths. The proportion of patients receiving antiretroviral therapy increased from 66 percent between January and June 1998 and 77 percent between July and September 2001. The most commonly received treatment regimen was triple therapy including a protease inhibitor (PI), ranging between 36 percent in January and June 1998 and 31 percent in July to September 2001. Triple therapy including a non-nucleoside reverse transcriptase inhibitor (NNRTI) more than doubled to 32 percent between July and September 2001. The proportion of patients receiving either stavudine (d4T)-containing or zidovudine (ZDV)-containing treatment regimens decreased from 92 percent between January and June 1998 to 76 percent between July and September 2001. Patients receiving ritonavir (RTV) in combination with another protease inhibitor increased, as did the proportion of patients interrupting therapy for more than three months. **Conclusion:** These findings suggest there have been changes in the way antiretroviral treatments have been used in Australia, and are consistent with the current literature. Furthermore, these findings demonstrate the usefulness of observational cohorts as a surveillance tool monitoring trends in treatment and disease progression.

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Cytometry

Normal values of CD4 and CD8 lymphocyte subsets in healthy Indian adults and the effects of sex, age, ethnicity, and smoking

SS Uppal, S Verma, and PS Dhot

Background: Information on lymphocyte populations (T, B, and natural killer cells) and subpopulations (CD4 and CD8) in India is generally lacking. Measurement of T-cell subsets is important in India for evaluating disease stage and progression in individuals with the human immunodeficiency virus (HIV). Hence, this study was conducted to provide normal ranges of absolute and percentage values of CD4 and CD8 T-lymphocyte subsets and the ratio of CD4 to CD8 in normal Indian adults. **Methods:** Flow cytometric analysis (EPICS-XL) was used to determine the range of T-lymphocyte subpopulations in normal Indian blood donors at Command Hospital and the Armed Forces Medical College, Pune, India. The reference population consisted of 94 healthy HIV-seronegative blood donors. T-lymphocyte subsets were analyzed with two-color immunophenotyping of peripheral blood lymphocytes with the use of a lysed whole-blood technique and enumerated. **Results:** For normal values of various blood components, we found mean values of 2,114 cells/ μ l for total lymphocytes, 865 cells/ μ l (40.2 percent) for CD4 lymphocytes, 552 cells/ μ l (31.3 percent) for CD8 lymphocytes, and 1.7 for the CD4:CD8 ratio. The 95 percent confidence intervals for the same parameters were 1,115-4,009 cells/ μ l, 430-1,740 cells/ μ l (30.75-49.60 percent), 218-1,396 cells/ μ l

(20.06-42.52 percent), and 0.39-3.02 respectively. Females had significantly higher CD4 counts ($P < 0.05$), percentage of CD4 lymphocytes ($P < 0.01$), and CD4:CD8 ratio ($P < 0.01$). Males had a significantly higher percentage of CD8 lymphocytes ($P < 0.01$). They also had higher CD8 counts that did not reach significance. Age, ethnicity (Dravidian versus Aryan), smoking, alcohol consumption, and the interval between drawing the blood sample and its analysis were factors that did not produce statistically significant differences in the T-cell subsets studied. **Conclusion:** When compared with other published series, the CD4 and CD8 values in healthy Indians were no different from those reported in the West. These observations have important clinical implications for the use of T-lymphocyte subset measurements in India, especially in the management of HIV infection.

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Revista de Neurología

AIDS by vertical transmission: Neurological disorders

NT Rotta and A Legido

Introduction: Forty million people are currently infected with HIV. Of these, 50 percent are women and children. Vertical transmission occurs in 90 percent of the cases reported in the literature and was also observed by the authors of the present study at Hospital de Clinicas de Porto Alegre, Brazil, in the follow up of 340 HIV-positive children since 1985. Transmission can occur during pregnancy (intrauterine) or during labor and delivery (intrapartum). In addition, HIV has been identified in the breast milk of infected mothers, which represents a contraindication for breastfeeding in these cases. Laboratory diagnosis is carried out using the following tests: ELISA, Western blot, and indirect immunofluorescence. **Development:** Neurological manifestations in children may be divided into primary neurological diseases and secondary complications. Primary neurological diseases include both static encephalopathy, of slow evolution, and progressive encephalopathy, which affects neuropsychomotor development. The follow up of 340 children with AIDS showed encephalopathy in 32.5 percent of cases and delayed neuropsychomotor development in 42.5 percent. Opportunistic infections occurred in 33.8 percent of cases (one infant presented meningoencephalitis). One child presented lymphomas, 2.6 percent had cerebrovascular accidents, and 5 percent had peripheral neuropathies. Currently, 54 children of those followed since birth are over 10 years of age, and of these, 31 (57 percent) present neurological symptoms, 40 percent with encephalopathy, and 30 percent with neurological complications; the remaining children present educational, behavioral, and developmental difficulties. **Conclusion:** Several factors have influenced the natural history of AIDS in childhood, such as early diagnosis, drug regimen used, social, economic, and nutritional conditions, as well as health practices aimed at this population.

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SAY ANYTHING



This is a serious issue... It means me... It means you...

Malawi Cabinet Minister Thengo Maloya discussing the AIDS epidemic in his country in a statement quoted February 18, 2003, by Agence France Presse. In calling for an end to the stigma that he feels has prevented HIV/AIDS from being given due attention within the government, Maloya disclosed that three of his own children died of AIDS-related illness. UNAIDS estimates that 11 percent of Malawi's 14 million citizens are HIV-infected. Yet the country is only now putting in place an official HIV/AIDS policy, establishing a legal and administrative basis for an official public health response.



This little virus is only 22 years old but has killed 23 million people. And in the best of all worlds, it's going to kill another 45 million. And I want the history books 30 years from now to look back and say America stood up and changed the course of history, which will affect tens of millions of people, saving their lives.

US Senate Majority Leader Bill Frist (R-Tennessee) speaking February 14, 2003, as quoted in the New York Times, on the occasion of the Republican Party's introduction of spending proposals for fiscal year 2004. The proposed spending for the international fight against HIV/AIDS equaled the amount called for by President George W. Bush in his January 26, 2003, State of the Union

address. A few days earlier, Frist withdrew support for a bipartisan bill he previously co-sponsored with US Sen. John Kerry (D-Massachusetts) that would have provided more funding in the first years of Bush's five-year international AIDS relief plan and channeled more money to the Global Fund to Fight AIDS, Tuberculosis, and Malaria. The bill championed by the Bush Administration, which Frist is now backing, also differs from the Frist/Kerry legislation in that it removes specific funding levels for AIDS programs named in the bill, eliminates congressional oversight of the way approved funding is spent, and replaces the word "shall" with "should" in referring to the activities the government will be mandated to carry out.



Newly diagnosed patients are evaluated by medical officials, and most patients are required to spend eight weeks at a sanitarium. While there, patients complete courses on how to live with the virus, how to avoid spreading the virus, the importance of follow-up treatment and safe-sex procedures, and how to handle discrimination.

From a February 10, 2003, Denver Post article describing HIV/AIDS public health procedure in Cuba. The island nation has a very low prevalence rate; according to the government, only .03 percent of the population is HIV-infected. Cuba's aggressive HIV strategy is controversial. Hundreds of thousands of Cubans, particularly those who had spent time in Africa, were subjected to mandatory testing in the early 1980s. HIV-infected patients were required to live in sanitariums from 1986 to 1993. According to the Denver Post, Cubans living with HIV/AIDS continue to face pervasive discrimination from fellow citizens.



Nobody can stand outside the need for action here and nobody can claim special interests or special privileges when people are dying unnecessarily. It's time that all recognize the responsibilities to help avoid unnecessary deaths and that means we've got to get an agreement for the trade round... A failure to act in these areas offends not only basic values, the dignity of individuals, and their right to a decent life but also... it affects national interests.

UK Chancellor of the Exchequer Gordon Brown in the February 18, 2003, issue of London's The Guardian.

Brown called for a quick settlement to World Trade Organization (WTO) negotiations, ongoing since December 2002, that were working to establish the terms by which drugs needed for public health crises could be exempted from patent restrictions in resource-limited countries. Several proposed plans were scuttled by the United States, which wishes to limit exemptions to drugs for AIDS, tuberculosis, and malaria, and only for the poorest countries. Under the rubric of increased autonomy, several leaders of developing countries deemed as unacceptable proposals that established a list of diseases for which drug patents could be overridden, or called for an official declaration of a public health emergency before allowing exemptions. Unable to traverse the impasse, the WTO ended talks a few days after Brown's comments in The Guardian.