Highly active antiretroviral therapy and tuberculosis control in Africa: synergies and potential

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Abstract HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome) and TB (tuberculosis) are two of the world's major pandemics, the brunt of which falls on sub-Saharan Africa. Efforts aimed at controlling HIV/AIDS have largely focused on prevention, little attention having been paid to care. Work on TB control has concentrated on case detection and treatment. HIV infection has complicated the control of tuberculosis. There is unlikely to be a decline in the number of cases of TB unless additional strategies are developed to control both this disease and HIV simultaneously. Such strategies would include active case-finding in situations where TB transmission is high, the provision of a package of care for HIV-related illness, and the application of highly active antiretroviral therapy. The latter is likely to have the greatest impact, but for this therapy to become more accessible in Africa the drugs would have to be made available through international support and a programme structure would have to be developed for its administration. It could be delivered by means of a structure based on the five-point strategy called DOTS, which has been adopted for TB control. However, it may be unrealistic to give TB control programmes the responsibility for running such a programme. A better approach might be to deliver highly active antiretroviral therapy within a comprehensive HIV/AIDS management strategy complementing the preventive work already being undertaken by AIDS control programmes. TB programmes could contribute towards the development and implementation of this strategy.

Keywords HIV infections/drug therapy; Acquired immunodeficiency syndrome/drug therapy; Antiretroviral therapy, Highly active; Anti-HIV agents/administration and dosage; Antitubercular agents/administration and dosage; Drug costs; Delivery of health care, Integrated; Africa South of the Sahara (*source: MeSH, NLM*).

Mots clés HIV, Infection/chimiothérapie; SIDA/chimiothérapie; Thérapie antirétrovirale hautement active; Agents anti-VIH/administration et posologie; Antituberculeux/administration et posologie; Coût médicaments; Distribution intégrée soins; Afrique subsaharienne (*source: MeSH, INSERM*).

Palabras clave Infecciones por VIH/quimioterapia; Síndrome de inmunodeficiencia adquirida/quimioterapia; Terapia antirretroviral altamente activa; Agentes anti VIH/administración y dosificación; Agentes antituberculosos/administración y dosificación; Costos en drogas; Entrega integrada de atención de salud; África del Sur del Sáhara (*fuente: DeCS, BIREME*).

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Introduction

Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) is the modern world's principal pandemic. It has claimed 22 million lives and created 13 million orphans (*1*). Sub-Saharan Africa bears the brunt of the catastrophe. In this region with less than 10% of the world's population there are 25.3 million people with HIV/AIDS, i.e. 70% of all cases globally. In 2000 there were 3.8 million new HIV infections in sub-Saharan Africa and 2.4 million people with HIV/AIDS died, representing 80% of all deaths attributable to AIDS.

AIDS kills young adults in their most productive years, depriving the region of the skills and knowledge that are essential for economic development. Because of AIDS, large numbers of children have to be brought up by their grandparents. Many orphans cannot attend school, suffer from poverty and malnutrition, and are drawn into crime, violence, and commercial sex. AIDS retards development and may create conditions conducive to political instability.

In 1999 there were estimated to be 8.4 million new cases of TB in the world (*2*). Sub-Saharan Africa is the region most severely affected by this disease (*3*). HIV fuels the tuberculosis (TB) epidemic: nearly three-quarters of people infected with both HIV and *Mycobaterium tuberculosis* live in sub-Saharan Africa (*3*). WHO predicts that by 2005 there will be 3.4 million TB cases in Africa (*2*).

Efforts to control HIV/AIDS and TB in sub-Saharan Africa

HIV/AIDS control efforts

Control efforts have largely centred on prevention. Strategies for reducing the sexual transmission of HIV have focused on condom usage, treating sexually transmitted infections, and

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reducing unsafe sexual behaviour. In hospitals, donated blood is screened for HIV, reducing but not eliminating the risk of transmitting HIV during transfusions (*4*).

Voluntary counselling and HIV testing have been advocated as a golden opportunity for educating and bringing about behavioural change. However, nearly 90% of infected people in Africa do not know their HIV serostatus (*5*). Among the many reasons for this are a general shortage of accessible voluntary counselling and HIV testing services, counselling of poor quality, poor uptake of voluntary counselling and HIV testing, and denial of the HIV/AIDS problem by both individuals and communities. Until now there has been a lack of understanding among policy-makers and health care providers that voluntary counselling and HIV testing and prevention should be linked to care. For the majority of people with HIV-related disease in Africa, only poor-quality clinical care and inadequate resources are available for treating serious opportunistic infections and tumours, e.g. Kaposi's sarcoma. There is almost no routine use of prophylaxis against opportunistic infections and virtually no access to antiretroviral drugs. Thus there is little incentive for people to ask for their HIV serostatus to be determined.

The aspect of care most likely to benefit an individual with HIV/AIDS is highly active antiretroviral therapy (HAART). Furthermore, there is evidence that lowering the viral load with HAART may reduce the likelihood of transmitting HIV to others (*6*). In industrialized countries, HAART has dramatically improved the survival of patients living with HIV/AIDS. Indeed, it has transformed AIDS from a fatal disease into a potentially treatable and chronic condition. HAART is the standard care for all patients with HIV-related disease in these countries. In contrast, only some 25 000 of Africa's 25 million HIV-positive individuals receive antiretroviral therapy of any kind. Many of these patients receive the drugs in a chaotic and unregulated manner in the private sector, with grave implications for the rapid development of drug resistance (*7*). The main reasons given for lack of availability of this therapy have been the high cost of the drugs and the perceived inability of the health infrastructure in Africa to manage the complexities of HAART.

TB control efforts

Control efforts have centred on case detection and treatment. The strategy is simple. Standardized combination chemotherapy is provided at least to all patients with smear-positive pulmonary TB. This treatment cures the disease and aims to prevent further transmission of infection. The targets for control include curing 85% of detected new smear-positive cases of pulmonary TB and detecting 70% of existing cases (*8*).

The success of this strategy depends on the implementation of a control policy known as DOTS. DOTS is a five-point package (Box 1) associated with various key operations (*9*). Despite the poor health infrastructure in Africa, 55% of the population is covered by DOTS, 60% of TB cases notified are treated under a DOTS programme, and 63% of such cases successfully complete treatment. However, the implementation of a good DOTS programme is not easy and requires adequate funding and human resources (*10*).

Negative effects of HIV on TB control efforts

HIV infection of TB patients adds to the difficulties encountered in programmes trying to implement the DOTS strategy (Box 2). The large increase in the number of cases of TB during the last 15 years has created a need for more staff, drugs, and resources. Where patients are hospitalized for the initial phase of treatment, TB wards have become overcrowded. This has forced the decentralization of treatment to peripheral health centres and the community. Decentralization, although patient-friendly, complicates the logistics of observing drug administration and maintaining the security of anti-TB drugs (especially of rifampicin, which is known by communities to be a useful drug for treating cough, diarrhoea, and sexually transmitted infections). The supervision and monitoring of TB control activities also becomes more difficult and demanding with a decentralized approach. HIV-positive TB patients experience many HIV-related illnesses during treatment. They also experience an increased frequency of adverse drug reactions leading to interruptions of treatment and occasional fatalities (*11*). Mortality rates have risen: 20–30% of HIV-positive smear-positive pulmonary TB patients die before the end of treatment (*11*). Even higher mortality rates are observed in patients with smear-negative TB (*12*). Recurrence rates of TB have increased (*11*), adding to the large number of new patients presenting annually for treatment. Health care workers also experience considerable morbidity and mortality attributable to AIDS, and this in turn compromises the quality of health care delivery.

African countries with good DOTS programmes continue to have escalating notifications of TB cases in the face of high HIV infection rates (*13*). DOTS alone may not be sufficient to control TB in areas of epidemic HIV infection: additional strategies may be needed (*14*).

Box 1. **DOTS: a five-point tuberculosis (TB) control policy package**

The package contains the following components:
1. Sustained government and political commitment.
2. Case detection through passive case-finding by ensuring access to high-quality TB sputum microscopy.
3. Administration of standardized short-course chemotherapy to all cases of TB under proper conditions of case management, including direct observation of therapy.
4. An uninterrupted supply of drugs of assured high quality, with reliable drug procurement and distribution systems.
5. A recording and reporting system permitting assessment of the outcome of each patient and of overall programme performance.

Interventions to control TB and HIV

Various additional interventions may help to control TB and HIV concomitantly (Box 3). Where TB transmission is likely to be high, e.g. in prisons, boarding schools, health care institutions and households of diagnosed TB patients, active rather than passive case-finding may be better for rapid case detection. Access to specific interventions targeted at HIV-related diseases requires knowledge of the individual's HIV serostatus. This is best achieved through voluntary counselling and HIV testing sites, which can either be free-standing and providing a service to the general population or integrated into the general health care service and providing a service to the sick. Same-day HIV testing, especially by means of rapid whole-blood finger-prick kits, facilitates voluntary counselling and HIV testing and allows quick referral to other support

Box 2. **Negative effects of human immunodeficiency virus infection on tuberculosis (TB) control**

The negative effects include:
- increased case numbers;
- the need for more staff and resources;
- overcrowding on TB wards because of increased case numbers;
- increased morbidity and adverse drug reactions;
- increased mortality;
- increased rates of recurrence of TB;
- poor delivery of health care.

Box 3. **Additional interventions to control tuberculosis (TB) and human immunodeficiency virus (HIV) infection**

- Active case-finding where high rates of TB transmission occur.
- Voluntary counselling and HIV testing.
- Comprehensive care for HIV/AIDS (acquired immunodeficiency syndrome) with two-way referral systems between health services and the community.
- Isoniazid preventive therapy (primary and secondary) for HIV-positive people.
- Adjunctive treatments to reduce morbidity and mortality: cotrimoxazole prophylaxis and antiretroviral therapy.

services. A package of care is required which includes a two-way referral system between health facilities and the community. This package involves psychosocial support, screening for sexually transmitted infections and TB, clinical care for opportunistic infections, palliative care for terminal illness, prevention of mother-to-child transmission of HIV, home-based care, preventive therapy, and the possibility of using antiretroviral drugs.

In Africa, preventive therapy for HIV-related infections in general and for HIV-related TB is currently based on cotrimoxazole and isoniazid, respectively. In Côte d'Ivoire, cotrimoxazole significantly reduced the case-fatality rate in HIV-positive TB patients (*15*) and reduced morbidity in HIV-infected patients without TB (*16*). The Joint United Nations Programme on HIV/AIDS has therefore provisionally recommended that cotrimoxazole be given to all patients in Africa living with AIDS, which, by definition, includes HIV-positive patients with TB (*17*). However, it would be prudent to gather more evidence about the efficacy of this intervention because of different patterns of disease and differing drug-resistance profiles in other parts of the region. Even if cotrimoxazole is effective, its widespread use by AIDS patients may have serious adverse consequences for the treatment of malaria in countries where sulphadoxine-pyrimethamine is used (*18*).

The efficacy of primary preventive treatment with isoniazid to reduce the incidence of TB in HIV-positive persons, at least in the short to medium term, has been demonstrated in placebo-controlled studies (*19*). Secondary isoniazid preventive therapy in HIV-positive patients who had completed rifampicin-containing anti-TB treatment significantly reduced the risk of recurrent TB in a small study in Haiti (*20*). Although there are doubts about the value of isoniazid preventive therapy as a TB control strategy, it deserves to be included as part of the package of care offered to HIV-positive individuals.

Antiretroviral therapy

The greatest improvement in the quality of life and the largest reduction in death rates among HIV-positive patients, whether or not they have TB, is likely to be achieved by HAART. If HAART is to become more available to people in Africa the drugs have to be made accessible and an infrastructure has to be created in order to ensure that they can be administered in a structured, safe and secure way.

Access to antiretroviral drugs

Pharmaceutical companies have significantly reduced the cost of antiretrovirals, and drug companies in Brazil, India, and Thailand are producing cheap generic versions (*21*). However, for very poor countries spending less than US$ 5 per capita per year on health, antiretroviral drugs are still too expensive unless there is additional assistance.

A meaningful challenge to the AIDS epidemic requires a huge increase in donor support, not only for antiretrovirals but also for basic prevention and care packages (*22*). During 1996–98, official development assistance for HIV/AIDS in sub-Saharan Africa was approximately US$ 130 million per year, a funding level totally incommensurate with the severity of the AIDS epidemic. A strong case has been made for a global annual budget of US$ 7.5 billion in the form of grants in order to support HAART and palliative treatment (*22*).

In July 2001 the Global Fund to Fight AIDS, Tuberculosis and Malaria was established in order to support research into these conditions and their prevention and treatment (*23*). The United Nations has calculated that up to US$ 10 billion are needed annually to fight AIDS alone.

Administration of antiretroviral drugs

Antiretroviral drugs must be provided within a structured framework. The structure used to deliver and monitor anti-TB treatment to TB patients throughout the developing world could be a model for delivering antiretroviral therapy (*24*). The overall objective would be to reduce mortality, morbidity, and the transmission of HIV. Standardized combination antiretroviral therapy would be used for HIV-positive patients with symptoms. Targets for antiretroviral therapy would have to be developed: they might include lifelong treatment and high drug-adherence rates to minimize the development of drug resistance. There would be an antiretroviral policy package, with five key elements (Box 4), similar to that adopted for TB control. An important aspect of proper case management is the supervised administration of tablets, i.e. directly observed therapy, in order to ensure that patients adhere to the regimen. This is vital if individual benefit is to be maximized and drug resistance is to be forestalled. In an impoverished community in rural Haiti, directly observed HAART was effective as part of a package of care for a small number of patients with AIDS (*25*). This supported the view that HAART could be delivered within the setting of a minimum health infrastructure.

Such a programme could not be implemented country-wide all at once. A phased approach would be necessary. A preparatory phase would establish the infrastructure necessary for the administration of HAART. This might include: management and coordination structures; HIV/AIDS clinics and laboratory support facilities; recording, reporting, and training materials; systems for drug procurement, distribution, and security; and plans for supervision.

Box 4. **Antiretroviral policy package**

The package would contain the following components:

1. Sustained government and political commitment:
   - nationwide coverage of the service
   - central, regional, and district units
   - full integration of the service into the health system at all levels
   - antiretroviral drugs as part of an essential packet of care for HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome) patients.
2. Case detection through passive case-finding, ensuring access to high-quality voluntary counselling and HIV testing:
   - focus should be on HIV-positive patients with symptoms who have undergone voluntary counselling and HIV testing (e.g. those fulfilling WHO's case definition for AIDS in Africa).
3. Administration of standardized antiretroviral regimens under proper conditions of case management, including direct observation of therapy:
   - Choice of drugs depends on simplicity, efficacy, cost, and safety;
   - once-a-day administration is preferable;
   - protease inhibitors are best avoided because of interactions with rifampicin;
   - first-line and second-line regimens are required in case of adverse effects and development of drug resistance.
4. An uninterrupted supply of drugs of assured high quality, with reliable drug procurement and distribution systems.
5. A recording and reporting system permitting assessment of the outcome of each patient and of overall programme performance.

In the second phase, there would be rigorous piloting of the chosen triple combination therapy. Intensive clinical and laboratory monitoring would ensure that the regimen was safe and well tolerated. The aim would be to define simple and robust clinical management algorithms for the monitoring of treatment and complications, because, in most districts of Africa, laboratory monitoring using CD4+-lymphocyte counts and the determination of viral load would not be feasible. While this phase was taking place, the third phase, involving feasibility assessment, would begin. Earmarked districts would be strengthening their infrastructure so as to provide a package of care for people living with AIDS. The introduction of HAART would be conditional on this package of care being in place and operational. Once districts were ready the feasibility of managing HIV/AIDS patients using HAART would have to be tested. If the feasibility studies were successful the programme could be expanded to become countrywide.

Should antiretroviral therapy be delivered to AIDS patients through national TB control programmes?

Arguments for

The proposed programme for delivering HAART is based on a framework similar to that for TB control. Building on an established TB control infrastructure would be cost-effective. National TB control programmes have experience of providing, monitoring, and supervising the care of patients for long periods of time and are in a position to develop and implement a structure within which HAART can be effectively and safely administered.

As HIV is the main factor responsible for the current epidemic of TB in Africa, an integrated programme has a greater chance of affecting the TB burden here than any course of action undertaken by TB control programmes alone. TB is the main opportunistic infection resulting from HIV: consequently, many patients would have both conditions. Adverse drug effects occurring when patients are on both anti-TB treatment and HAART are best managed in a single programme. Directly observed therapy in respect of anti-TB treatment and HAART can be administered by the same provider. In each country a joint approach would provide a real focus for collaboration between the national TB programme and the national AIDS programme.

Arguments against

In a country with a well-established HIV/AIDS epidemic, the demand for antiretroviral drugs would probably be enormous and the large additional number of patients would threaten to overwhelm the services of the TB programme, even if extra staff and resources were allocated. HIV-positive patients without TB might be at risk of acquiring TB when undergoing HAART if they had to join outpatient queues in which there were both TB patients and suspected cases. Anti-TB treatment continues for six to eight months, whereas HAART is lifelong. An antiretroviral programme requires more demanding logistics. Although rifampicin has a well-known street-market value for the treatment of conditions other than TB, antiretroviral drugs can be expected to have an enormous national and international street value, and rigorous systems of monitoring drug use would have to be developed in order to safeguard the drugs from theft and prevent abuse.

A compromise

One way forward is to use the DOTS model and integrate the delivery of HAART into a comprehensive HIV/AIDS management strategy to complement prevention efforts already undertaken by AIDS control programmes. The key entry point to comprehensive HIV/AIDS management would be voluntary counselling and HIV testing. HIV-positive patients without TB would receive HAART and have their treatment monitored at AIDS clinics. If adequate human resources were available, HIV-positive patients with TB could be treated by national TB programmes, which could also take responsibility for the management of antiretroviral therapy during the course of anti-TB treatment. This would obviate the need for TB patients having to visit different units in order to obtain anti-TB drugs and HAART. Because rifampicin interacts with protease inhibitors and non-nucleoside reverse transcriptase inhibitors (*26*), special attention would have to be paid to the antiretroviral regimen during anti-TB treatment. It would be necessary to train the staff on TB programmes to manage the most appropriate antiretroviral regimens for the initial and continuation phase of anti-TB treatment. Once anti-TB treatment had been completed the patient could return to the main antiretroviral drug monitoring system.

In any of these approaches there might be reluctance by donors to support what appeared to be another vertical disease programme at a time when thinking on health delivery in Africa hinges on health sector reform. It would be essential for staff on AIDS and TB control programmes to work closely with health planners in order to ensure that core activities such as regular drug supplies, supervision, monitoring, and recording were maintained and that they continued uninterruptedly.

Conclusion

Whether HAART becomes part of the package of care for HIV-positive patients in sub-Saharan Africa depends on the support and commitment of the international community, because countries with very limited resources would be unable to support an antiretroviral programme, notwithstanding large reductions in drug costs. Also critical is the success or otherwise of phased studies on effectiveness and feasibility. The challenges are considerable, but given the scale of the epidemic, the first steps should be taken as soon as possible. ■

Conflicts of interest: none declared.

Résumé

Traitement antirétroviral et lutte antituberculeuse en Afrique : synergies et potentiel

Le VIH/SIDA (virus de l'immunodéficience humaine/syndrome d'immunodéficience acquise) et la tuberculose figurent parmi les grandes pandémies qui sévissent à l'échelle mondiale, particulièrement en Afrique subsaharienne. Les efforts de lutte contre le VIH/SIDA ont été largement axés sur la prévention et ont peu porté sur les soins. Les travaux sur la lutte antituberculeuse se sont quant à eux concentrés sur la détection et le traitement des cas. L'infection par le VIH complique la lutte contre la tuberculose. Il est peu probable que l'on puisse assister à un déclin du nombre de cas de tuberculose tant qu'on n'aura pas élaboré de nouvelles stratégies pour lutter simultanément contre cette maladie et contre le VIH. Ces stratégies devront comporter un dépistage actif des cas là où la transmission de la tuberculose est intense, la fourniture d'un ensemble de soins pour les maladies associées au VIH et l'application d'un traitement antirétroviral efficace. C'est ce dernier élément qui devrait avoir le maximum d'impact, mais pour le rendre plus accessible en Afrique, il faudra mettre les médicaments à disposition par le biais d'un soutien international et mettre en place une structure programmatique en vue de leur administration. Le traitement pourrait être dispensé selon une stratégie en cinq points appelée DOTS adoptée pour la lutte antituberculeuse. Cependant, il n'est peut-être pas réaliste de charger les programmes de lutte antituberculeuse de ce surcroît de responsabilité. Une meilleure approche pourrait consister à délivrer un traitement antirétroviral efficace dans le cadre d'une stratégie globale de prise en charge du VIH/SIDA, en complément du travail de prévention déjà réalisé par les programmes de lutte contre le SIDA. Les programmes de lutte antituberculeuse pourraient contribuer au développement et à la mise en œuvre de cette stratégie.

Resumen

Terapia antirretroviral de gran potencia y lucha contra la tuberculosis en África: sinergias y posibilidades

La infección por el VIH/SIDA (virus de la inmunodeficiencia humana/síndrome de inmunodeficiencia adquirida) y la tuberculosis son dos de las pandemias más graves del mundo, y castigan en especial al África subsahariana. Los esfuerzos encaminados a combatir el VIH/SIDA se han centrado en gran parte en la prevención, habiéndose prestado poca atención a la asistencia, y las actividades de control de la tuberculosis se han centrado en la detección y el tratamiento de los casos. La infección por el VIH ha complicado el control de la tuberculosis. Es improbable que se produzca una disminución del número de casos de tuberculosis a menos que se desarrollen otras estrategias para controlar simultáneamente esta enfermedad y el VIH. Esas estrategias incluirían la búsqueda activa de casos en las situaciones de alta transmisión de la tuberculosis, el suministro de un paquete asistencial para las enfermedades relacionadas con el VIH, y la aplicación de terapia antirretroviral de gran potencia. Esto último es lo que más impacto podría tener, pero para ampliar el acceso a ese tratamiento en África los medicamentos se deberían ofrecer con ayuda internacional, y habría que desarrollar una estructura de programa para su administración. Podría establecerse una estructura basada en la estrategia en cinco puntos DOTS adoptada para combatir la tuberculosis. Sin embargo, la pretensión de delegar en los programas de control de la tuberculosis la responsabilidad de ejecutar un programa de esa naturaleza es quizá poco realista. Una alternativa preferible consistiría tal vez en el suministro de terapia antirretroviral de gran potencia en el marco de una estrategia integral de manejo de la infección por el VIH/SIDA que complementase las actividades preventivas ya emprendidas por los programas de control del SIDA. Los programas contra la tuberculosis podrían contribuir al desarrollo y aplicación de esa estrategia.

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Commentary

TB and HIV: joint problems, joint solutions?

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In their article (*1*), Harries and his colleagues turn the spotlight on one of the major problems confronting control of tuberculosis (TB) today. Despite heroic and successful efforts to establish DOTS programmes in sub-Saharan Africa, TB continues to rise in countries with significant HIV (human immunodeficiency virus) epidemics. DOTS alone is insufficient to prevent such increases. Furthermore, HIV calls into question the global targets of 85% cure of the 70% of all smear-positive cases that should present for treatment by the year 2005. These targets were set because their achievement would, in the absence of other factors, lead to a reduction in TB incidence. Many working in Africa now believe that control of TB, especially reduction in its incidence, is dependent upon mitigating the impact of HIV. What else must we do to control TB in settings of high HIV prevalence?

From an HIV perspective, it seems probable that two things are required: a reduction in the number of HIV-infected people, i.e. a decrease in the transmission of HIV; and lessening the immunosuppression caused by HIV in those already infected. In the absence of a vaccine, we are limited to education for behaviour change, condom provision to prevent transmission, treatment of sexually transmitted diseases and, in the absence of a definitive cure, antiretroviral drugs to lessen the effects of HIV. From the TB perspective, the additional possible approaches are active case-finding and prevention of TB.

Combined approaches at the district level against TB and HIV were merged in the ProTEST initiative (*2*), set up by WHO and partners in the late 1990s. On the part of clients, the interventions include discovering HIV status through counselling and testing, using condoms, and modifying sexual behaviour; on the part of providers, actively looking for cases of TB among the HIV infected and the provision of isoniazid preventive therapy to those who are HIV positive, but without active TB. The impact of all this on risk behaviour and on the burden of TB awaits the final results from the initiative, expected within the year.

But a few key national managers in high HIV-prevalence countries made it clear that the international and local response to control of TB was simply inadequate to address the enormous scale of the problem. WHO and the Global Working Group on TB/HIV then considered options additional to DOTS in high HIV-prevalence settings (*3*). A considerable expansion of the original ProTEST work has begun in eight African countries (Ethiopia, Kenya, Malawi, Mozambique, South Africa, the United Republic of Tanzania, Uganda, and Zambia) with the Centers for Disease Control and Prevention's Global AIDS Program, the Joint United Nations Programme on HIV/AIDS, and the United States Agency for International Development as the main partners. These projects aim to establish an affordable, cost-effective package

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of joint measures against HIV/AIDS and TB that will reduce the burden of both diseases more efficiently than separate approaches. The interventions included are laid out in Box 3 of the paper by Harries et al. (*1*), who focus on the thorniest of them all, namely highly active antiretroviral therapy (HAART).

They put to one side some of the key unknowns, namely, the impact HAART will have on the transmission of both HIV and TB, and the development of resistance, and turn to the key question of how HAART should be delivered. And will the HIV community learn the hard-won lessons of the TB community?

Until just recently, the cost of antiretrovirals relieved health and development workers of having to think much about them, but the major price reductions announced last year and the establishment of mechanisms to support the purchasing of these drugs (*4*), have brought the issue to the forefront. There is the very real risk that the drugs will be delivered to systems ill-prepared to receive them and ill-designed to deliver them (*5*). Harries and his group are among the first to point to a solution. In a previous paper (*6*), they clearly put forward the idea of using well-performing national TB programmes to deliver not only anti-TB treatment, but also antiretrovirals. In this issue of the *Bulletin*, they are less absolutist and point to the necessity of a comprehensive HIV/AIDS management strategy to which TB programmes could contribute. The central pillar of their thesis is Box 4 which extrapolates directly from the five-point policy framework for DOTS (*7*) to lay out the five essential elements of an antiretroviral policy package.

From experience with TB, this approach, or one very like it, would seem logically necessary for an antiretroviral delivery policy. But is it sufficient? Of course not. Full implementation of the package can only follow the strategic planning, human resource investment, and financial support required to provide and sustain the infrastructure necessary for successful delivery of HAART, and arguably would need to be the largest expansion of health services in low-income countries ever seen. Antiretroviral treatment is a lifelong undertaking. In order to assuage the doubts surrounding sustainability, HAART must be embedded in a broader developmental context such as those currently offered in the Heavily Indebted Poor Countries Initiative and the World Bank's poverty reduction strategies (*8*). ■

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