How human immunodeficiency virus voluntary testing can contribute to tuberculosis control

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Abstract Human immunodeficiency virus (HIV) is fuelling the tuberculosis (TB) epidemic, particularly in sub-Saharan Africa. However, despite their close epidemiological links, the public health responses have largely been separate. WHO has set out a strategy to decrease the burden of HIV-related TB, comprising interventions against both TB and HIV. Voluntary counselling and testing (VCT) for HIV can link TB and HIV programme activities. The benefits of VCT for HIV to TB patients include referral for appropriate clinical care and support for those testing HIV-positive. Likewise, people attending a centre for VCT can benefit from TB screening: those found to be both HIV-positive and with active TB need referral for TB treatment; those without active TB should be offered TB preventive treatment with isoniazid.

To explore how VCT for HIV can contribute to a more coherent response to TB, WHO is coordinating the ProTEST Initiative. The name ''ProTEST'' is derived from the **Pr**omotion of voluntary **test**ing as an entry point for access to the core interventions of intensified TB case-finding and isoniazid preventive treatment. 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 centres for VCT for HIV and TB prevention and care. This will pave the way for large-scale operationalization of the comprehensive range of interventions needed to control TB in settings with high HIV prevalence.

Keywords Tuberculosis, Pulmonary/prevention and control/epidemiology/diagnosis; AIDS serodiagnosis; Counseling; Volition; AIDS-related opportunistic infections/prevention and control; HIV seroprevalence; Delivery of health care, Integrated; Cost of illness; Pilot projects; Africa South of the Sahara (*source: MeSH, NLM*).

Mots clés Tuberculose pulmonaire/prévention et contrôle/épidémiologie/diagnostic; Sérologie HIV; Conseil; Volition; Infections opportunistes liées SIDA/prévention et contrôle; HIV séroprévalence; Distribution intégrée soins; Coût maladie; Projet pilote; Afrique subsaharienne (*source: MeSH, INSERM*).

Palabras clave Tuberculosis pulmonar/prevención y control/epidemiología/diagnóstico; Serodiagnóstico del SIDA; Consejo; Volición; Infecciones oportunistas relacionadas con el SIDA/prevención y control; Seroprevalencia de VIH; Entrega integrada de atención de salud; Costo de la enfermedad; Proyectos piloto; África del Sur del Sahara (*fuente: DeCS, BIREME*).

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Voir page 943 le résumé en français. En la página 944 figura un resumen en español.

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 programmes 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 programmes 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 programmes (*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 counselling for decreased sexual risk behaviour, 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 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 programmes and general health services.

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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, 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 co-infected with *Mycobacterium tuberculosis*, and 8.4 million (70%) 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. Fig. 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 case-loads 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 programme 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 preventive (*12*) and therapeutic approaches (*13*), and more vigorous application of specific measures to prevent and interrupt transmission in prisons (*14*), healthcare institutions (*15*) and other congregate settings.

Fig. 1. **The trend of cases of tuberculosis (TB) 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[a] is based on the temporal relation between the two epidemics and their known biological and epidemiological links

[a]HIV = human immunodeficiency virus.
[b]TB = tuberculosis.

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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 counselling 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 centres 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 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 neighbours (*17*).

Epidemiological impact

Consideration of the basics of TB epidemiology and control (*18*) is necessary to understand the impact of HIV. In the poorer regions of the world, annual risks of infection by *M. tuberculosis* are typically 1–3%, leading to prevalence rates of *M. tuberculosis* infection among young adults of 30–70% (*19*). Fig. 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%.

In the absence of HIV, only about 10% 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 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 (i.e. the case reproduction number is one), as shown in panel A of Fig. 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.

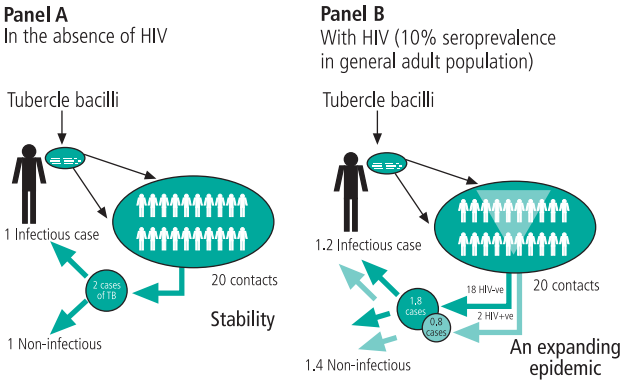
In the presence of HIV infection (the single strongest risk factor for progression from infection to active disease (*21*), about 40% of people infected with *M. tuberculosis* will develop active TB in their lifetime (*22*). Panel B of Fig. 2 shows what happens to 20 people with *M. tuberculosis* infection when the HIV seroprevalence in the population is 10%. There will thus be 18 HIV-negative and 2 HIV-positive people with *M. tuberculosis* infection. With a 10% risk of developing active TB, the 18 HIV-negative people will generate 1.8 cases of TB. With a 40% risk of developing active TB, the 2 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 (i.e. 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 programmes 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, e.g. by reducing diagnostic and treatment delays.

Since the mid-1980s, in many African countries, including those with well-organized programmes (*24, 25*), annual TB case notification rates have risen up to fourfold, reaching peaks of more than 400 cases/100 000 population (Fig. 3). The annual risk of infection may also have risen in some of those countries most severely affected (*26*). Increased funding of TB programmes has generally not kept pace with this increasing case-load (*27*), and many programmes 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 seroprevalence (*29*) (Fig. 4). The burden of TB is so closely linked to the HIV epidemic that prevention of HIV must become a priority for TB programmes, just as TB care and prevention should be a major concern of HIV/AIDS programmes.

Fig. 2. **Schematic representation of the impact of human immunodeficiency virus (HIV) the absence of HIV (Panel A) and where the HIV seroprevalence in the general adult population is 10% (Panel B).**



Note: see text for full explanation.

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

Interventions to prevent HIV infection include behavioural factors (e.g. counselling to decrease sexual risk behaviour), biological ones (e.g. 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 programmes, 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%, only 6.5% of adults had previously had an HIV test (*31*). VCT is sometimes available in special groups, such as TB patients at outpatient treatment centres 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 counsellors 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 behaviour 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, the Republic of Tanzania and Trinidad and Tobago estimated that the cost of preventing a new HIV infection (assuming that the reported behaviour 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 health care as

Fig. 3. **Tuberculosis case notifications rates, 1980–98 in selected African countries**

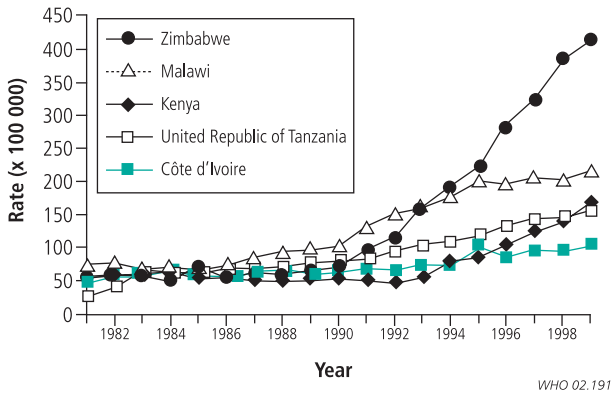
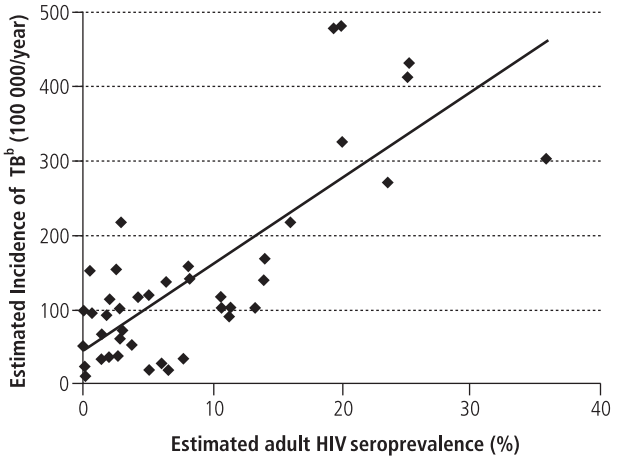


Fig. 4. **Estimated adult HIV[a] seroprevalence and tuberculosis incidence in African countries**



[a] TB = tuberculosis.

[b] HIV = human immunodeficiency virus.

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 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 counselling can help to translate this motivation into behaviour change (*40*). Counselling 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, counselling aims to prevent transmission of HIV infection as well as to offer psychosocial support. Up to 50% 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*). Counsellors 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 centres 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. Fig. 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.

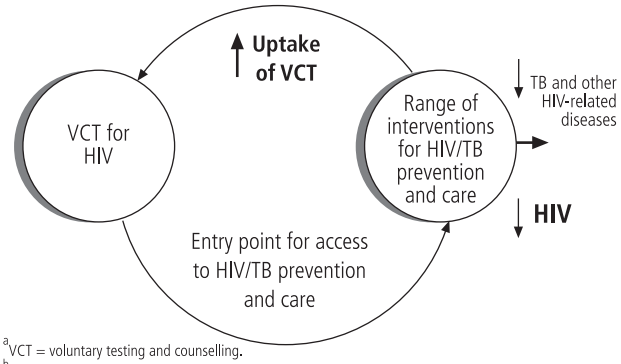
By identifying and linking the government and non-governmental organizations currently offering support and care for PLWH and by involving the community, the ProTEST Initiative aims to facilitate referral and to provide the opportunity for improving the quality of services. These include provision of 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 diarrhoea 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 programmes to deliver antiretroviral drugs to reduce transmission of HIV from mothers to their children (*51*). By linking

Fig. 5. **Schematic representation of the proposed virtuous circle linking VCT[a] to HIV[b] and TB[c] 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



[a]VCT = voluntary testing and counselling.
[b]HIV = human immunodeficiency virus.
[c]TB = tuberculosis.

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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 centre in Uganda reports an increasing proportion of their 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 centres after the introduction of health care 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 under way 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 modelling 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 programme 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 programmes to collaborate in carrying out these activities as widely as possible. The ProTEST Initiative can greatly help to build alliances between TB and HIV programmes and to scale up the full range of interventions to decrease the burden of HIV-related TB. ■

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Résumé

Comment le dépistage volontaire du VIH peut contribuer à la lutte antituberculeuse

Le VIH intensifie l'épidémie de tuberculose, particulièrement en Afrique subsaharienne. Cependant, malgré leur relation épidémiologique étroite, ces deux infections donnent lieu à une réponse très différente de la part des services de santé publique. L'OMS a élaboré une stratégie visant à réduire la charge de la tuberculose liée au VIH et comprenant des interventions dirigées à la fois contre la tuberculose et contre le VIH. Le conseil et dépistage volontaire pour le VIH (VCT) permet de relier les activités des

programmes de lutte contre le VIH et contre la tuberculose. L'intérêt du conseil et du dépistage du VIH chez les patients atteints de tuberculose réside dans la possibilité d'adresser les sujets VIH-positifs à un service spécialisé en vue d'un traitement et d'un soutien appropriés. De même, les patients qui viennent en consultation pour un VCT peuvent bénéficier d'un dépistage de la tuberculose. Les sujets à la fois VIH-positifs et atteints de tuberculose active doivent être orientés en vue d'un traitement antituberculeux ; ceux qui ne présentent pas de tuberculose active se verront proposer un traitement antituberculeux préventif par l'isoniazide.

Afin de rechercher de quelle façon le conseil et dépistage volontaire pour le VIH peut contribuer à l'adoption d'une réponse plus cohérente face à la tuberculose, l'OMS assure la coordination de l'initiative ProTEST. Le nom de cette initiative renvoie à la promotion du dépistage volontaire comme point de départ pour l'accès aux interventions de base que sont la recherche intensifiée des cas de tuberculose et le traitement préventif par l'isoniazide. D'autres interventions pourront être ajoutées pour parvenir à tout un éventail d'interventions de prévention et de traitement du VIH et de la tuberculose. Dans le cadre de l'initiative ProTEST, des districts pilotes établissent des liens entre les centres de VCT pour le VIH et les centres de prévention et de traitement de la tuberculose. Cela ouvrira la voie à la mise en œuvre à grande échelle de toute la gamme d'interventions requise pour combattre la tuberculose dans les régions de forte prévalence du VIH.

Resumen

Las pruebas voluntarias del VIH, una posible ayuda para combatir la tuberculosis

El VIH está atizando la epidemia de tuberculosis, sobre todo en el África subsahariana. Sin embargo, pese a su parentesco epidemiológico, las respuestas de salud pública contra las dos enfermedades han sido en gran medida independientes. Para disminuir la carga de VIH relacionada con la tuberculosis, la OMS ha formulado una estrategia que comprende intervenciones tanto contra ésta como contra el virus. El asesoramiento y las pruebas voluntarias (APV) para el VIH pueden constituir un puente entre las actividades de los programas dirigidos contra la tuberculosis y contra el VIH. Entre los beneficios del APV para los pacientes con tuberculosis cabe citar la derivación hacia servicios de atención clínica y apoyo apropiados para las personas VIH-positivas. Análogamente, las personas que acuden a un centro de APV pueden beneficiarse de las actividades de cribado de la tuberculosis: los pacientes que además de ser VIH-positivos sufren tuberculosis activa deben ser derivados para recibir tratamiento antituberculoso; y a aquellos sin tuberculosis activa se les debe administrar isoniazida como tratamiento preventivo contra la tuberculosis.

A fin de determinar cómo puede el APV para el VIH contribuir a responder de forma más coherente a la tuberculosis, la OMS está coordinando la Iniciativa ProTEST, así bautizada por cuanto pretende promover las pruebas voluntarias como punto de entrada para acceder a las intervenciones básicas e intensificadas de detección de casos y tratamiento preventivo con isoniazida. Se pueden añadir otras intervenciones para proporcionar finalmente un conjunto integral de medidas de prevención y atención contra el VIH y la tuberculosis. En el marco de la Iniciativa ProTEST, diversos distritos piloto están estableciendo vínculos entre los centros de APV para el VIH y la prevención y atención ofrecidas contra la tuberculosis. Esto sentará las bases para aplicar a gran escala el amplio conjunto de intervenciones que exige el control de la tuberculosis en los entornos con alta prevalencia de infección por el VIH.

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