

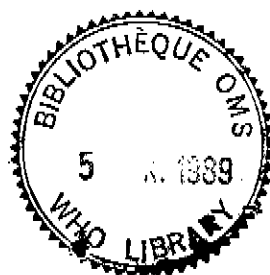
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GLOBAL  
PROGRAMME  
ON **AIDS**  
AND  
TUBERCULOSIS  
PROGRAMME

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STATEMENT ON AIDS AND TUBERCULOSIS

GENEVA  
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WORLD  
HEALTH  
ORGANIZATION

IN COLLABORATION WITH  
INTERNATIONAL UNION  
AGAINST TUBERCULOSIS  
AND LUNG DISEASES



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## **Statement on AIDS and tuberculosis\***

Tuberculosis (TB) has already been recognized as one of the most frequent opportunistic infections in persons with HIV infection in developing countries. In some HIV affected developing and industrialized countries, the number of reported cases of TB is increasing. In addition to an increasing number of new cases of TB in some areas, health programmes face new problems related to unusual clinical presentations of TB and proper management of *M. tuberculosis* and HIV-infected persons.

This statement is based upon collaboration\* between the World Health Organization's Global Programme on AIDS (GPA) and the Tuberculosis Unit (TUB) of the Division of Communicable Diseases and the International Union against Tuberculosis and Lung Diseases (IUATLD).

This joint statement is addressed to all health care personnel engaged in TB and AIDS control activities worldwide for the purpose of providing technical direction and guidance to national and local efforts for AIDS/TB control and research.

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### **Summary**

In a number of developing countries, particularly in Sub-Saharan Africa, infection with both *M. tuberculosis* and human immunodeficiency virus (HIV) is highly prevalent. HIV infection results in an impairment of the immune system and entails a substantial risk of TB in those individuals who are or become infected with the tubercle bacillus. Because persons with both infections have an increased risk of developing clinical TB and further transmitting *M. tuberculosis* infection, some of these countries are facing, or will have to face, a rapid upsurge of the TB problem.

The interaction between HIV and *M. tuberculosis* infection poses a serious health problem which will result in a major increase in disease, death and health care service needs in many countries. Immediate action at the global, national and local levels is needed to address this problem. In their national plans of action, national AIDS and TB control programmes should include coordinated activities to reduce the impact of the problem and international organizations and donor countries should be encouraged to support them technically and financially.

Control of this TB epidemic linked with HIV infection will depend largely on the availability of prompt diagnosis and adequate treatment for TB, and possibly of effective chemoprophylaxis, not just for HIV-infected persons but for other groups as well. To deal with this problem, a number of issues need to be studied urgently. In addition, a number of immediate steps can be taken by control programmes.

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### **Background**

#### **The AIDS pandemic**

WHO estimates that at least five million persons in the world are already infected with HIV-1. As of 1 February 1989, approximately 140 000 cases of AIDS had been reported to WHO by 144 countries. Owing to underdiagnosis, underreporting, and delays in notification, this represents only part of the global cumulative total which is estimated at about 400 000 cases.

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\* Joint WHO/IUATLD working group on HIV infection and tuberculosis, Geneva, 18-19 January 1988;  
WHO technical advisory meeting on research on AIDS and tuberculosis, Geneva, 2-4 August 1988.

The pandemic started in the 1970's with a period of unrecognized spread of the virus. The first cases of AIDS were recognized in 1981. During the following years the virus was identified, the modes of spread defined and laboratory methods to detect HIV antibodies developed. The infection is transmitted by sexual intercourse, by blood (transfusions, needles, organ transplants) or from mother to infant before, during or shortly after birth. The risk of transmission varies with the mode of transmission. Transfusions of infected blood have a probability of transmission of over 90%, perinatal transmission from an infected mother of 25-50%; and each needle puncture from an infected source of less than 1%. A single episode of penile-vaginal sexual intercourse with an HIV-infected individual carries an estimated transmission risk of from 1/100 to 1/1000 but this risk may be increased by the presence of genital ulcerative disease. The HIV-infected individual becomes a potential source of infection for life even in the absence of symptoms. Clinical AIDS may not appear for many years, but nearly half of infected individuals appear to develop AIDS within 10 years. Death almost invariably occurs within two years of the diagnosis of AIDS.

HIV infection is not evenly distributed around the world. In general, urban areas are more affected than rural areas. Three patterns of HIV/AIDS can be recognized depending on when HIV began to spread extensively in the population and the socio/sexual risk factors/behaviours in the community.

In pattern I areas, most cases occur in homosexual men and there are relatively few HIV-infected women and children. Transmission through blood has been virtually eliminated since HIV-antibody testing began in 1985. Transmission through needles is frequent among intravenous drug users. This pattern is seen in North America, Western Europe, Oceania and parts of Latin America and the Caribbean.

In pattern II areas transmission is mainly heterosexual, with almost equal numbers of male and female cases. Transmission via blood transfusions is not controlled or is only partially controlled; the use of unsterilized syringes and needles and other skin piercing instruments outside health services represents a potential risk and perinatal transmission is relatively common. In some countries the prevalence of infection in the sexually active population in the cities reaches 10-25% and in certain high risk groups over 50%. This pattern is seen in Sub-Saharan Africa and increasingly in parts of Latin America and especially in the Caribbean.

In pattern III areas the infection has been introduced more recently (1980s) and most of the initial cases have been infected through exposure in other countries or by international travellers. In most countries in these areas, there has not yet been sufficient indigenous spread to determine what will be the predominant forms of transmission. This pattern is presently seen in Eastern Europe, Asia, the Middle East and the Pacific.

These patterns can be seen simultaneously in a single country or areas of the same country, and there is a general trend towards pattern II (heterosexual transmission) in some pattern I areas.

No vaccine or cure is yet available for HIV infection; it is not expected that a vaccine will be available in the near future (5-10 years). The main strategies for prevention and control of HIV infection are therefore information and education to reduce the risk of sexual transmission through behavioural changes - reduction and selection of sexual partners, use of condoms; control of blood and blood products (including reduction of unnecessary transfusions); information and training to reduce the risk of transmission by syringes and other skin piercing instruments; and information and counselling to reduce the social, familial and individual impact of infection and disease. Even if these strategies are effective, they will not alter the number of AIDS cases anticipated in the next several years, because most of these will arise from existing infections.

### **The tuberculosis pandemic**

It is estimated that 30-60% of adults in developing countries are infected with *M. tuberculosis*. Approximately 8-10 million individuals develop clinical TB and 3 million die of TB each year.

Infection with *M. tuberculosis* is transmitted through droplet nuclei suspended in the air as a result of the cough of persons with pulmonary TB. About half of the close contacts of an infectious patient will become infected. Patients are infectious only after developing pulmonary disease and in proportion to the number of bacilli expectorated. An untreated smear-positive case may infect on average 10-20 individuals in two years.

The risk of acquiring infection depends on the prevalence of infective sources - smear-positive cases - in the community. Males are more commonly infected than females. Household contacts of an infectious patient are at especially high risk of infection. Infection with *M. tuberculosis* may last for life and disease may appear soon after infection or after a long time. The risk of disease among infected persons is highest in the first few years following infection. The average lifetime risk of progression to active disease is about 10%, and varies with age and immunological status. Half the cases develop infectious pulmonary disease; children usually develop non-infectious types of tuberculosis. Case fatality in the absence of treatment is over 60% in five years. With prompt diagnosis and adequate chemotherapy it may be reduced to 3% or less.

Disease control methods include case finding and chemotherapy of patients, Bacille Calmette-Guerin (BCG) vaccination for those not yet infected and preventive therapy for infected individuals at a high risk of progression of clinical TB.

The most common strategy used in developing countries is case detection through direct sputum smear examination of persons with symptoms suggestive of TB and ambulatory chemotherapy.

At present there is a reduction of the risk of infection of over 10% per year in industrialized countries, a reduction of 5% to 10% in some developing countries with good control programmes and general health service structures, and a reduction of 0-4% in other developing countries. Due to the fact that the last group comprises most of the world population and has the highest prevalence of TB as well as a population growth of 2-3% per year, the general reduction of the global TB problem in absolute numbers of cases is very small.

Overall, the world TB situation is thought to be improving very little despite the existence of effective therapy and a partially effective vaccine. This may be due in part to the need for more effective application of existing strategies as well as the need for improved technology.

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### **Association of HIV and tuberculosis**

Individuals infected with *M. tuberculosis* have a high risk of progression to TB if they are also infected with HIV. Therefore, the proportion of AIDS patients with TB will be high where *M. tuberculosis* infection is highly prevalent. In many instances these patients may present to the health service as TB patients so that the proportion of HIV seropositive cases among TB patients is also increased. Overall, the number of TB patients will also be increased where *M. tuberculosis* and HIV infection are highly prevalent.

It is possible that TB may also accelerate the evolution from HIV infection to overt disease (AIDS) in dually infected individuals.

The possibility also exists for transmission of HIV among TB patients through the use of inadequately sterilized syringes used in the treatment of TB (eg, for streptomycin injections).

Interactions of mycobacteria and HIV infections include interactions with non-tuberculosis mycobacteria. This was first observed in North America where a high incidence of disease with *Mycobacterium avium-intracellulare* (MAI) complex was noted in AIDS patients who commonly had several other opportunistic infections. However, it was soon discovered that in populations with a high prevalence of *M. tuberculosis* infection, TB is the predominant mycobacterial infection in HIV-infected persons. Tuberculosis, in contrast to MAI-related disease, generally occurs as an early, and often the first, clinical manifestation of AIDS.

In Florida (USA) the prevalence of TB among AIDS patients was about 10% among non-Haitians, and over 60% among Haitians. These percentages are very similar to the estimated prevalence of *M. tuberculosis* infection in these populations. This suggests that persons infected with both *M. tuberculosis* and HIV have a very high risk of developing TB.

Several studies in Sub-Saharan Africa, the Caribbean and in some urban areas of the United States (USA) have shown from 20-60% of TB patients to be HIV seropositive. The most likely explanation for this finding is an accelerated progression to TB among persons who harbour infection with *M. tuberculosis* and are also infected with HIV. This interaction of HIV and *M. tuberculosis* infections poses serious problems for TB control programmes in these countries. An upsurge of the TB problem must be expected if measures are not immediately taken to reduce transmission of *M. tuberculosis*, perhaps including steps to reduce progression to TB among dually infected persons.

Increases in the incidence of TB that are thought to be caused at least in part by the effects of the HIV/AIDS epidemic have been noted in several countries, including the USA, Tanzania, Burundi, Uganda, and Zaire.

TB programmes face other new problems in addition to an increase in the number of patients. TB patients usually present with symptoms characteristic for pulmonary disease, such as chronic cough, and can be readily diagnosed by direct sputum smear-microscopy. In HIV-infected patients, however, the clinical picture is often different from that usually seen in adult-type tuberculosis, and includes unusual extra-pulmonary manifestations, from widespread lymphatic involvement to intracranial tuberculomas. In addition, low or midzone pulmonary infiltrates are more common and sputum smears are less likely to be positive. Case-finding and diagnosis by health workers at all levels is therefore more difficult.

When the diagnosis of TB is established at an early stage of HIV infection the response to intensive treatment with rifampicin containing regimens is usually fairly good. In most developing countries, the more effective regimens that include rifampicin and pyrazinamide have not yet been introduced generally because of their high cost. However the optimal duration and adverse reaction rate of such treatment in HIV-infected TB patients is still unknown. In addition, at the more advanced stages of HIV infection adverse drug reactions may be a problem, in particular with thiacetazone.

*M. tuberculosis* is more infectious than other opportunistic infections associated with AIDS, and is therefore of additional concern to the general population. It is transmitted by air and therefore untreated cases of pulmonary TB pose a potential risk to health personnel caring for patients with AIDS, as well as to family contacts. As TB is curable and treatment renders infectious cases non-infectious, prompt detection and treatment are important to prevent transmission in the community.

All of these factors emphasize the need both to strengthen the TB control capacity at national and local levels, and to take immediate action as regards a number of epidemiological, clinical and preventive research questions and issues.

## Recommendations for control programmes

Although research is needed to answer many questions regarding the interaction of TB and HIV, TB and AIDS control programmes can take immediate steps to better control the TB problem. These recommendations will need periodic revision as new information becomes available.

At the national level, programmes for control of AIDS and TB should be coordinated to provide consistent high-quality care to patients with both diseases and to advise infected individuals regarding the risk of disease and methods to prevent transmission to others. **To facilitate this coordination, the inclusion of an expert on TB control in the national committee on AIDS is strongly encouraged.**

The experience of TB experts and staff in integration of their activities within health services, in programme organization and management, and in the training and motivation of health personnel may all be extremely useful to AIDS programmes. Several special aspects of disease control are common to both programmes, such as the need to ensure confidentiality, case notification and reporting, patient and family counselling, and in some programmes strategies for evaluation of household contacts (for TB) or sexual and needle sharing partners for HIV i.e., partner notification.

**Hospitals and clinics that are treating AIDS patients need to be vigilant regarding possible concurrent TB to ensure accurate diagnosis and prompt therapy to prevent further spread of *M. tuberculosis* to contacts. As *M. tuberculosis* can also be spread in hospitals, it is important for health workers to be prompt to begin anti-TB therapy.**

TB in HIV-infected individuals or AIDS patients should be treated according to national policy, preferably with short course regimens. Since the optimal duration of treatment in such cases is not known, patients should be followed up bacteriologically whenever possible. Treatment should be continued for six months after sputum conversion. **Drug intake should be fully supervised, at least in the initial phase with intensive daily therapy.**

The indications for hospitalizing patients for TB are the same whether they are infected with HIV or not. As it is expected that cases with simultaneous AIDS and TB will increase, and that they may pose special clinical problems, hospitals treating TB cases must be prepared to provide adequate care. This includes training health personnel in the management of cases of AIDS and providing diagnosis and treatment for the most common opportunistic infections associated with HIV infection and AIDS. Training is also needed in the diagnosis and treatment of extra-pulmonary TB in HIV-infected persons.

**Prevention of HIV transmission is based mainly on information and health education, which should be provided systematically to all TB patients. Access to voluntary serological tests for detection of HIV infection including pre- and post-test counselling should be offered wherever HIV infection is known to occur. As HIV is transmitted through sexual contact and through blood and, as appropriate chemotherapy rapidly renders persons with TB non-infectious, there is no reason to isolate HIV-infected persons or AIDS patients (with or without TB). Discrimination in dealing with HIV-infected patients, as with TB, should be absolutely avoided<sup>1</sup>.**

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1 Resolution WHA41.24, *Avoidance of discrimination in relation to HIV-infected people and people with AIDS* (1988); in *Progress Report Number 4*, pg. 95. Unpublished WHO document WHO/GPA/GEN/88.3 (1988); available from Global Programme on AIDS, World Health Organization, 1211 Geneva 27 Switzerland.

Adequate safety procedures involving injections, blood, blood products or other body fluids when caring for TB patients should be enforced regardless of a patient's HIV status (*Guidelines for nursing management of people infected with human immunodeficiency virus [HIV]*<sup>1</sup>). The *Guidelines on sterilization and high-level disinfection methods effective against human immunodeficiency virus (HIV)*<sup>2</sup> should be promoted and followed. **Where sterility of needles and syringes cannot be ensured, an entirely oral medication regimen should be used.**

Prevention strategies for TB control include immunization with BCG and chemoprophylaxis. BCG should be administered to infants as early in life as possible, including when the mother is known to be or suspected of being HIV-infected (*Joint WHO/UNICEF statement on early immunization for HIV-infected children*<sup>3</sup>). Evidence remains inconclusive regarding the rate of adverse reactions after BCG immunization among asymptomatic HIV-infected individuals. **BCG should be withheld from individuals with symptomatic HIV-infection<sup>4</sup>.**

Individuals infected with *M. tuberculosis* and HIV have a high risk of developing TB. In countries where the national TB programme strategies include chemoprophylaxis, dual infection with HIV and *M. tuberculosis* should be considered as an indication for chemoprophylaxis.

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## Recommendations for research

The long term objective of the proposed research activities is to curb the anticipated increase in TB in developing countries where both *M. tuberculosis* and HIV infection are highly prevalent. The immediate objectives are to obtain information on the magnitude of the problem and its trend, to develop appropriate diagnostic techniques, and to identify effective treatment and preventive regimens and strategies. Explicit recommendations for both epidemiological and clinical research can be found in the *Report of the WHO Technical Advisory Group on research in AIDS and TB, Geneva, 2-4 August 1988* (WHO/GPA/BMR/89.3).

Epidemiological studies should be undertaken by the national TB and AIDS programmes of countries that have a high prevalence of *M. tuberculosis* and HIV infection, especially African countries south of the Sahara and countries in the Caribbean. They should first determine the prevalence of HIV infection in (a sample of) newly detected TB patients. (For more precision the prevalence of HIV infection could also be determined in matched controls or by comparison with serologic information from sentinel surveillance groups in the same district. A sentinel surveillance system should then be set up to monitor trends in HIV prevalence among new TB patients by periodic sampling.)

**An immediate research priority is the determination of the risk of TB among dually infected persons in order to determine if the risk is sufficiently high to immediately begin intervention (chemoprophylaxis) trials.** This requires further studies in developing countries.

Further epidemiological studies should determine trends in the incidence of TB and of the risk of *M. tuberculosis* infection in the general population according to the level of HIV infection, the infectiousness of *M. tuberculosis* in HIV-infected TB patients, and the effectiveness and safety of BCG vaccination in HIV-infected persons.

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- 1 Published by World Health Organization in collaboration with the International Council of Nurses (ICN), Geneva, 1988 (WHO AIDS Series No. 3).
  - 2 Geneva, World Health Organization, 1988 (WHO AIDS Series No. 2)
  - 3 *Weekly epidemiological record*, **64**: 48-49 (1989).
  - 4 *Statement from Consultation on human immunodeficiency virus (HIV) and routine childhood immunization.* WHO consultation. *Weekly epidemiological record*, **62**:297-299 (1987).

Clinical studies should focus on the symptoms and signs of TB in HIV-infected persons, on the effectiveness of the routinely used tests (smear examination, culture, tuberculin tests, chest X-ray, CSF examination) and on the value of new, especially serological, tests for screening and diagnosis of TB. Alternative treatment regimens should be compared in terms of effectiveness and toxicity in HIV-infected and non-HIV infected TB patients, as regards both pulmonary and extra-pulmonary disease. Whereas it will not be necessary to carry out the proposed clinical studies in all countries concerned, it will be necessary to include different settings (e.g., including HIV-2 affected areas).

Short-course chemoprophylactic regimens should be evaluated in persons found to have both HIV and *M. tuberculosis* infection.

For some studies, detailed protocols will be best prepared jointly by GPA and TUB in cooperation with the national programmes and technical consultants. General guidance will be obtained from experts selected by WHO, IUATLD and national TB and AIDS programmes.

Strengthening of national TB programmes in the countries concerned will require consultant services as well as equipment and supplies (notably for drugs, including short-course chemotherapy). In some countries surveillance and research activities will be undertaken in conjunction with the Mutual Assistance Programme already in operation under guidance of the IUATLD. **In some countries the national TB programmes will require considerable support, both managerial and technical, to strengthen case-finding and treatment and to undertake or strengthen epidemiological surveillance and research.**