GUIDELINES FOR CONTROL OF TUBERCULOSIS IN PRISONS

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Tuberculosis Coalition for Technical Assistance and

International Committee of the Red Cross

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CONTENTS

ACSM	advocacy communication and social mobilization
AFB	acid-fast bacilli
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
BCG	bacillus Calmette-Guérin (TB vaccine)
DOT	directly observed treatment
DOTS	WHO internationally recognized recommended strategy for tuberculosis control
DR-TB	drug-resistant tuberculosis
DRS	drug resistance survey/drug resistance surveillance
DST	drug-susceptibility testing
FDC	fixed-dose combination
GDF	Global Drug Facility
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GLC	Green Light Committee
HIV	human immunodeficiency virus
IEC	information, education and communication
ICF	intensified (TB) case finding
IGRA	interferon gamma release assay
IRIS	immune reconstitution syndrome
IPT	isoniazid preventive therapy
ISTC	International Standards for Tuberculosis Care
Kg	kilogram
LTBI	latent tuberculosis infection
mcg	microgram
mg	milligram
MGIT	mycobacteria growth indicator tube
MDG	millennium development goals
MDR-TB	multidrug-resistant tuberculosis
mm^3	cubic millimeter
MoH	Ministry of Health
MoI	Ministry of the Interior
MoJ	Ministry of Justice
MoL	Ministry of Law
NGO	nongovernmental organization
NTP	national tuberculosis program

PITC	provider-initiated HIV testing and counseling
PTB	pulmonary tuberculosis
SLM	second-line medicine
SOP	standard operating procedures
TB	tuberculosis
TST	tuberculin skin test *or* testing
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNODC	United Nations Office on Drug and Crime
USAID	United States Agency for International Development
UVGI	ultraviolet germicidal irradiation
VCT	voluntary counseling and testing (for HIV)
WHO	World Health Organization
WHO HIPP	WHO Europe Health In Prison Project
XDR-TB	extensively drug-resistant tuberculosis

This third edition of the *Guidelines for Control of Tuberculosis in Prisons* provides general guiding principles for the implementation of the six elements of internationally recommended Stop TB strategy which in combination will accelerate the achievement of case detection and treatment targets and will cure and prevent the emergence of drug resistance. The primary audience is health and administrative staff working in prisons who need to be educated on the magnitude and implications of the TB problem and on the need for effective intervention. It is also intended for national TB program (NTP) managers who collaborate with prison health services in the implementation of the Stop TB Strategy. The document expands on the problems of TB-HIV co-infection and multidrug-resistant TB (MDR-TB) in prisons and contains updated information on diagnostic and treatment approaches. Thus, it replaces the first guidelines published in 1997. The second edition of the guidelines, published in 2000, is still a valid and complementary document.

Recommendations based on the field experiences of prison sector NTPs and their partners in various regions have been incorporated into this third edition. The depth of the document does not extend to a detailed outline of operational activities, because such activities should be developed as standard operating procedures (SOPs) by each country, ideally under the framework of a national strategy endorsed by the prison and public health sectors.

The term *prisoner* is used throughout to describe anyone held in criminal justice and correctional facilities during the investigation of a crime, anyone awaiting trial or conviction, and anyone who has been sentenced. It also refers to persons detained for reasons related to immigration or refugee status.

1. OVERVIEW

At no time in history has tuberculosis (TB) been as prevalence as it is today. More than 9 million new cases occurred in 2006 alone. The increasing world population and other factors, especially HIV infection, have contributed to the increased morbidity. Similarly, TB deaths have continued to rise during the past three decades; the most recent estimate (2006) stands at 1.5 million.[1]

Global and national efforts have been effected to confront TB, mainly through the implementation of the World Health Organization's (WHO) recommended Stop TB Strategy, including DOTS. Components of the Stop TB Strategy are presented in this chapter and addressed throughout the document taking into account the context of prison settings. One notable challenge involves the disproportionate incidence of TB that arises among most populations at risk, including prisoners. This inequity results from characteristics inherent to the group itself, their environment, and their ability to access services. Imprisonment in some settings can be closely related to inadequate judicial and health policies. Factors that contribute to increased morbidity and mortality in these settings include increased prison population rates, delayed legal processes, meager prison budgets that preclude adequate nutrition and access to health services, overcrowded spaces, poor ventilation, violence, and weak or nonexistent links to the civilian health sector.

TB in prisons affects the general population through transmission that occurs when prisoners are moved (upon being released or transferred to another facility) and via prison staff and visitors—a phenomenon that is better documented and understood now.[2–7] Consequently, analysts recognize that public health strategies to curb TB should be uniform and comprehensive to include prisons, since they are communities that have higher TB prevalence and incidence rates.

Linking prisons to the national and local TB control programs will result in enhanced overall TB control and contribute significantly to achieving the TB targets of the Millennium Development Goals (MDG). These targets include reducing TB prevalence and mortality by half of rates in 1990 and beginning to reverse TB incidence by 2015.

The Stop TB Strategy (table 1) was launched in 2006 to complement DOTS, considering the challenges posed by TB/HIV, MDR-TB, high-risk groups (prisoners), and the lack of involvement of health care providers in public and private sectors. The strategy calls for an increased access to quality care and empowerment of patients and affected communities to demand and contribute to effective care. It also underscores the need to strengthen health systems to improve service delivery and in doing so, recognizes the relevance of conducting operations research (to improve program performance) and biomedical research (i.e., rapid diagnostics, vaccines, new medicines).

Table 1. The Stop TB Strategy

Element	Implementation
Vision	A world free of TB
Goal	To dramatically reduce the global burden of TB by 2015 in line with the MDG and the Stop TB Partnership targets
Objectives	• To achieve universal access to high-quality diagnosis and patient-centered treatment • To reduce the suffering and socioeconomic burden associated with TB • To protect poor and vulnerable populations from TB, TB/HIV, and MDR-TB or drug-resistant TB • To support development of new tools and enable their timely and effective use

Targets	• MDG 6, Target 8 – halt and begin to reverse the incidence of TB by 2015
	• Targets linked to the MDGs and endorsed by the Stop TB Partnership:
	  • By 2005, detect at least 70% of new sputum smear-positive TB cases and cure at least 85% of these cases
	  • By 2015, reduce TB prevalence and death rates by 50% relative to 1990
	  • By 2050, eliminate TB as a public health problem (<1 case per million population)

Each of the six elements of the Stop TB Strategy (box 1) relate implicitly and explicitly to prisons. HIV and MDR-TB are exceptionally high in prisons and complicate management in a setting already plagued by extreme poverty, inferior budgets and resources, poor health infrastructure, and competing agendas (i.e., security, violence). In most cases, the organization of prison health services within other ministries (e.g., Ministry of Justice [MoJ], Ministry of the Interior [MoI], Ministry of Law [MoL]) has resulted in insufficient involvement or delay in enrollment of prison health staff in DOTS training and TB control programmatic activities. Moreover, besides being deprived of their civil liberties, in some countries prisoners may also be deprived of access to quality health care. The substandard care offered to TB patients in prisons results in underdiagnosis and underreporting of cases, continued transmission, poor treatment outcomes, and development of drug resistance. These negative consequences merit an urgent response, including research to improve health service delivery in prisons.

TB control programs in prisons need to be established and implemented in collaboration with the NTP and penitentiary health systems; thus, prisons' health services should be integrated into the general health system and the NTP's network for training, supervision, monitoring and evaluation, and laboratory services. NTP should also consider prisons when planning and budgeting. This cooperation would guarantee the application of nationally accepted standard TB control procedures and activities, increase prisoners' access to equitable care, and improve sustainability.

Improvement of TB control and health care in general should be more actively promoted, such as the case of the European region, where considerable progress has been achieved. Currently, 36 countries in the region have committed to the WHO Health in Prisons Project (WHO HIPP). Based on their best practices, this initiative advocates for strong linkage of prisons to the national public health programs; actively involving administrative and security staff, as opposed to limiting the focus to health staff; recognition by the public health system of the crucial role and leadership of prison authorities to achieve health targets and overall improved health of prisoners; and recognition by decision and policy makers that prisons perform a vital public service and that inadequate prison health can considerably affect general public health. TB control is a good example of the public health approach in which national health authorities and prison administration can effectively collaborate to decrease the burden of the disease in the community and penitentiary services likewise.

Box 1. Components of the Strategy and Implementation Approaches

1. Pursue high-quality DOTS expansion and enhancement through—
- a. Political commitment with increased and sustained financing
- b. Case detection through quality-assured bacteriology
- c. Standardized treatment with supervision and patient support
- d. An effective pharmaceutical supply and management system
- e. Monitoring and evaluation system and impact measurement

2. Address TB/HIV, MDR-TB, and other challenges
- a. Implement collaborative TB/HIV activities
- b. Prevent and control MDR-TB
- c. Address prisoners, refugees, and other high-risk groups, as well as special situations

3. Contribute to health system strengthening.
- a. Actively participate in efforts to improve systemwide policy, human resources, financing, management, service delivery, and information systems
- b. Share innovations that strengthen systems, including the Practical Approach to Lung Health
- c. Adapt innovations from other fields

4. Engage all care providers
- a. Use public-public and public-private mix approaches
- b. Use the *International Standards for Tuberculosis Care (ISTC)*

5. Empower people with TB and their communities through—
- a. Advocacy, communication, and social mobilization
- b. Community participation in TB care
- c. Patients' Charter for Tuberculosis Care

6. Enable and promote research
- a. Program-based operational research
- b. Research to develop new diagnostics, medicines, and vaccines

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2 TUBERCULOSIS: THE GLOBAL BURDEN AND PRINCIPLES OF CONTROL

One third of the world's population is infected by *Mycobacterium tuberculosis*, the bacterium that causes TB. There were an estimated 9.2 million new TB cases and 1.5 million TB deaths in 2006, including 0.2 million deaths among people infected with HIV. TB remains a major cause of morbidity and mortality in many countries and a significant public health problem worldwide. The global incidence of TB was estimated to be 139 cases per 100,000 in 2006. Ninety-five percent of these cases and 98 percent of TB deaths occur in developing countries, affecting mostly (75 percent) persons in the economically productive age group (15–50 years).[1]

About 8 percent of TB cases worldwide are attributable to HIV.[1] This proportion is increasing as the HIV pandemic spreads. HIV infection increases both the likelihood that people will develop TB and the rate at which infections are acquired and disease develops. The impact of HIV has been greatest in countries of Southern and East Africa, where up to 40 percent of adults may be infected with HIV and the incidence of TB has increased by four to five times within 10 years. Other significant risk factors, including smoking,[2] diabetes,[3–4] malnutrition,[5] and overcrowding, may have an equally important impact at a population level depending on exposure.

The development of drug resistance is of increasing importance in TB control programs because it is much more difficult and expensive to treat than fully drug-susceptible TB. An estimated 500,000 cases of MDR-TB arise each year among both new and previously treated TB cases. Also, extensively drug-resistant TB (XDR-TB) has been reported from many countries. Drug resistance emerges where TB control programs are weak, defaulter rates are high, and cure rates are low. For this reason, TB programs are advised to concentrate on achieving high cure rates, increasing case detection rates, and ensuring good treatment outcomes for patients with drug-sensitive TB as well as ensuring treatment of patients with MDR-TB.

Major progress in global TB control followed the widespread implementation of the DOTS strategy in countries with a high burden of TB. Building on achievements, the major task for the next decade is to achieve the MDG and related targets for TB control. Global statistics indicated, however, that DOTS alone would not be sufficient to achieve global TB control and elimination. Meeting these targets will require a coherent strategy that enables existing achievements to be sustained; effectively addresses the remaining constraints and challenges; and underpins efforts to strengthen health systems, alleviate poverty, and advance human rights.

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The Global Prison Population

The world's prison population is increasing by varying rates among countries based on socioeconomic and political (including war) factors. The estimated number of people detained on any given day, worldwide, is over 9 million.[1] Almost half of these are in three countries: the United States, China, and the Russian Federation. These data include primarily prisoners who are serving their sentences but also include people detained in police stations, remand centers (under investigation or on trial), centers for internment detention (i.e., asylum seekers), secure hospitals, and prisoner of war camps. The turnover of prisoners (anyone under custody of the state) is high. On any given day, four to six times the estimated 9 million incarcerated persons pass through prisons.

Prison staff and visitors should be considered part of the prison population with respect to the transmission of infectious diseases.

Until recently, prisons were often overlooked by the national public health sector. Health statistics from the prisons were either not assessed or not included in national health statistics, creating biases in the epidemiology, morbidity, and mortality reported.

Prisoner Demographics

Prisoners do not represent a homogenous segment of society. Many have lived on the margins of society, are poorly educated, and come from socioeconomically disadvantaged groups. They are young (15–44 years). An overwhelming majority are male; women prisoners represent less than 5 percent of the total prison population. In many cases, they belong to minority or migrant groups.

Offenders commonly live in unhealthy settings and do not have the means to, or the habit of, keeping themselves healthy. They may have unhealthy habits or addictions, such as alcoholism, smoking, and drug use, which contribute to their poor health and are risk factors for developing TB, too. For these reasons, they enter prison already ill or with a higher risk of becoming ill compared to the general population.

In some countries, while they are incarcerated, prisoners live under harsh and unhealthy environments and suffer from malnutrition, intense psychological and physical stress, and violence. Family relationships are, in many cases, uncertain and deteriorated. These factors can adversely affect prisoners' immune systems and make them more vulnerable to becoming ill with multiple diseases.

Prisoner Hierarchies and Prisoner Behavior

Prison culture varies among countries and even among prisons within a particular country. The unofficial hierarchy of prisoners represents a power structure parallel to the official prison administration. This unofficial hierarchy may be as powerful as—or in some prisons even more powerful than—the official authority. Prison administrations may tolerate and condone the parallel power structure since it helps to maintain order.

These power structures are often not immediately apparent, but the established rules and laws have direct implications, both negative and positive, for the health care of patients. A patient's position within the power structure may affect health care workers' decisions about whether and how to treat them. There may be discrimination in admission to the hospital ward or prison clinic, unfair selection of patients for treatment, or misuse of medicines. High-status prisoners may not accept a low-status prisoner in the same prison hospitalization area. Prison health staff may not be motivated, or even allowed, to visit certain prison areas, which makes directly observed treatment (DOT) and contact investigation difficult to implement. Prison health personnel are often not in a position to enforce separation of prisoners based merely on medical grounds because the custodial staff might "respect" the internal hierarchy to maintain peace and quiet in the prison.

In contrast, prisoner-established hierarchies, in some instances, facilitate the implementation of disease control activities. Leaders in these groups can influence prisoners to seek care for illnesses and comply with treatment. They can promote and even contribute to the organization of treatment of patients within their circles of influence. Prisoners at the top of the internal chain of command can also assist prison health staff in disseminating adequate and accurate health information to the general prison population.

These starkly different contexts, in different countries and different prisons, show that health professionals need to assess and then take into consideration the realities of the establishment in which they work. These realities may be self-evident to full-time prison health staff, but in many places, health professionals from the civilian population only occasionally work in prisons. If they do not fully appreciate the situation in the prison, they could easily be manipulated by the prisoners.

Health Care Delivery in Prisons

The ministry responsible for the prison system varies from country to country. It may be the MoJ, the MoI, the Ministry of Security, or another ad hoc institution. Often health services in prisons are organized vertically and independent of the Ministry of Health (MoH). In these settings, prison health staff are hired by the penitentiary services. The tendency to shift the responsibility of prisons from the MoI to the MoJ has been implemented in several countries in the past 20 years, and prison health care services have been reorganized under the MoH (e.g., in the United Kingdom, Norway, and France).

Because prisons are generally underfunded, health care services within prisons are also underfunded. Consequently, the penitentiary system often neglects this aspect of imprisonment. Planning for health care delivery is usually based on perception. Needs assessments to determine the human resources, equipment, and pharmaceutical supplies necessary to provide adequate health care are not common practice in prisons, resulting in major funding gaps. The principles of equivalence, if not of equity, of health care for all are frequently disregarded in the case of prisoners. An account of one region's approach to improving prison health services shows that prison health can be improved in political and public health agendas and is worthy of consideration in other regions.[2]

Failure of prison authorities to control a treatable and preventable disease may contribute to prisoners venting their anger against the prison system. Subsequently, such outbursts can lead to prison security problems.

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The Burden of TB in Prisons

Prisons are not mere static venues holding large populations. They represent dynamic communities where at-risk groups congregate in a setting that exacerbates disease and its transmission, including TB. Prevalence rates of TB in prisons usually exceed prevalence rates in the specific country substantially. As shown in table 2, TB rates of over 3,000 per 100,000, as compared to the general population, are not unusual. These figures, however, do not control for sex and age. TB incidence rates are also extremely high in prisons, and TB mortality in prisons is elevated. TB case fatality in prisoners has been reported high in many settings. For example, published data from Azerbaijan indicates of 24 percent case fatality rate.[1] Any prison sentence served in a prison that has such a high TB incidence, prevalence, and mortality rate may, in fact, become a death sentence.

Table 2. Prison Case Notification Rates Compared to Country TB Prevalence, Selected Countries

Country	Country Prevalence Rate (number per 100,000 per year)	Prison Case Notification Rate (number per 100,000 per year)
Prison notification rates found through passive case finding		
France[3]	8.6	41.3
Spain[4]	18.2	2,283.0
Azerbaijan[5]	94.2	4,667.0
Moldova[6]	149.0	2,640.0
Russia[7]	109.0	7,000.0 (Tomsk)
Thailand[8]	208.0	1,226.0
Rwanda[9]	79.3	3,363.0
Brazil[10]	77.0	1,439.0 (Rio de Janeiro)
USA[11]	10.4	156.0 (New York)
Prison prevalence rates found through active case finding		
Georgia[12]	144.1	5,995
Malawi[13]	209.0	5,142
Russian Federation[14]	240.0	9,930
Brazil[15]	10.4	3,532

Sources: Internationally published papers, cited by endnotes, provided the data for this table.

Drug-Resistant TB

Resistance to isoniazid and rifampicin, the two strongest bactericidal anti-TB agents, precludes use of the most potent standard TB regimens and disallows the use of short-course therapy contained in the DOTS strategy. MDR-TB, which is defined by resistance to at least isoniazid and rifampicin at the same time, is difficult to treat and can occur with or without resistance to other medicines. According to WHO, approximately 500,000 cases of MDR-TB emerge every year.[2] The number of MDR-TB cases in prisons is often proportionally higher than that found in the general population of a given country. Drug-resistant TB reflects problems with either patient management (i.e., poor patient support and supervision for the continuation of therapy) or program management (i.e., deficiencies in pharmaceutical management, infection control, and supervision of staff duties). For further study, please refer to the "Suggested Reading" list at the end of this chapter.

At least 7 percent of all MDR cases are also XDR-TB cases.[2] XDR-TB involves infection with a strain that is resistant to isoniazid and rifampicin plus any fluoroquinolone medicine and at least one of the injectable agents (amikacin, capreomycin, or kanamycin). Treatment efficacy for this "super-resistant" strain using medicines that are currently available is significantly worse than treatment efficacy of drug-susceptible TB.

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HIV/AIDS in Prisons

At the end of 2007, an estimated 33.2 million people worldwide were living with HIV infection. In the same year, 2.5 million new infections and 2.1 million AIDS-related deaths had occurred.[1]

HIV prevalence among prisoners is believed to be higher than that of the general population although supporting data are limited; available data show that HIV prevalence among prisoners is 6 to 50 percent higher.[1] Many HIV-infected prisoners have come from sections of society that have a higher than average HIV prevalence (e.g., drug users) and therefore enter prison already infected with HIV. Those who enter prison uninfected with HIV have an increased risk of acquiring HIV due to certain risky behaviors including men having sex with men and sharing needles for drug use or sharp objects for tattooing.

HIV Transmission in Prisons

Whether acknowledged by authorities or not, smuggling of drugs into prisons, drug use by prisoners, and sex between men all occur in prisons in many countries. Cohort studies have reported recent incarceration as being associated with a significant increase in HIV incidence rates.[2] Denying or ignoring these facts hinders the prevention of HIV transmission in prisons.

Injection Drug Use

A common route of HIV transmission in prison is intravenous drug use. Preventive measures by prison authorities include penalizing possession and trafficking of illegal drugs; however, drug abuse still exists in prison settings.[3] Many who enter prison are already drug users, [4,]and others may be newly exposed to drugs upon arrival.[5,6,7] Moreover, studies from Greece and Brazil illustrate that the risk of engaging in injecting drug use increases with every year a person is in prison.[5, 10] Injecting drug users often share needles, syringes,[7,8] or homemade injecting equipment and rarely sterilize them, thereby contributing to the transmission of HIV.[9,10]

Sexual Transmission

In prisons, HIV is also commonly transmitted sexually. Men in prison may have anal sex with other men, and condoms are not generally available. In some countries the distribution of condoms is illegal among prisoners, because sodomy is a misconduct punishable by law. Providing condoms to prisoners, as well as other measures to avoid transmission of the HIV virus, is thus a complicated issue. The risk of HIV transmission by unprotected anal sex is high, especially if the sex is forced (rape).[11] Prisoners are vulnerable, both to the power of prison authorities and often also to the demands (including sexual demands) of other prisoners and staff, who may be violent.[12] Factors that exacerbate this vulnerability include overcrowding, an atmosphere of punishment and violence, and sometimes systems of enslavement within prison hierarchies. Vulnerable prisoners and their spouses are at increased risk of HIV transmission.

Furthermore, commercial sex workers from the community enter some prisons for work. Although it is neither legal nor the norm, in some settings, prison authorities allow this practice to generate revenues for themselves (i.e., a percentage of the commercial sex workers' income is shared with prison staff). Similarly, the conjugal visit arrangements in some countries can be permissive, so it is possible for prisoners to contract sexually transmitted diseases, including HIV, through other heterosexual contacts and subsequently spread it to their spouses.

Workplace Hazards

Prison officers may also be at increased risk of HIV infection. Exposure to HIV infection may happen through an accidental prick with a used drug-injection needle during searches or through sexual contact with prisoners.

TB/HIV Co-infection

Undiagnosed and untreated TB is frequently found among persons living with HIV/AIDS. Survey data in high-burden settings show that up to 10 percent of people living with HIV may have undiagnosed TB at the time of undergoing voluntary counseling and testing (VCT). TB, the most common opportunistic infection in people living with HIV, is a leading cause of death in this group. Only 1 in 10 persons infected with TB who are HIV negative will develop TB in their lifetime. By contrast, among persons infected with both TB and HIV, 1 out of 10 will develop TB each year. In high-burdened TB settings, 30 to 40 percent of people living with HIV will develop TB in their lifetime, in the absence of isoniazid preventive therapy (IPT) or antiretroviral therapy (ART).[15]

The risk of developing TB is significantly higher in the first year after becoming HIV-infected and gets progressively higher over time (WHO stages 3 and 4). These patients may be a source of infection to others. TB outbreaks affecting HIV-infected prisoners and health care workers because of exposures in health care facilities have been reported in industrialized countries. Furthermore, the diagnosis of TB in the presence of HIV infection is complicated by increased numbers of patients with pulmonary TB who are acid-fast bacillus (AFB) smear negative or who suffer extrapulmonary forms of disease (i.e., lymphatic, pleural, renal, bone, skin, or central nervous system TB).

TB control programs in prisons, as in the general population, need to address the distinct characteristics of TB in HIV-infected patients, especially in settings with a high burden of TB and HIV, such as prisons. TB/HIV co-infection rates in prison have been found to be 10 to 20 percent higher than those found in the civilian population.[15] Basic strategies include improving case detection of TB among people living with HIV, providing IPT for those without active TB, and providing diagnostic counseling and testing for HIV to patients diagnosed with TB. ART is also an important protective factor in co-infected individuals (see also chapter 12).

Risk of TB in Persons with HIV infection

The risk of TB is increased among patients who have underlying HIV, AIDS, or both. The magnitude of this risk varies according to the following:

- Prevalence of TB in the population (active and latent TB)
- Degree of immunosuppression caused by HIV
- Likelihood of exposure to infectious TB cases
- Accessibility of TB prophylactic treatment to people living with HIV (i.e., treatment of latent TB infection [LTBI])

Some countries have low TB prevalence, but both TB and HIV are associated with distinct groups (e.g., prisoners, injection drug users) and minority ethnic populations, a fact that cannot be overlooked and warrants proper intervention.

Prevalence of and Mortality Due to HIV Infection among TB Patients

The WHO *Global Tuberculosis Control 2008* report estimates that 8 percent of all TB cases are co-infected with HIV.[16]. Yet, this figure varies by region and different countries, ranging from as low as 1 percent in the western Pacific region to 38 percent in Africa; this number increases to more than 60 percent in southern Africa where 20 percent of persons are infected with HIV. Fourteen percent of TB patients in most industrialized countries are co-infected with HIV.

TB mortality is higher in settings with high HIV prevalence. Overall, TB-case fatality rate among HIV-infected patients reaches 40 percent. Final treatment outcome depends on availability of antiretrovirals, early treatment, and proper clinical management and effective care of TB-HIV co-infected individuals. [17]

Effects of HIV Infection on the Course of TB

The strongest risk factor for the development of TB is infection with HIV. In immunocompetent hosts who are infected with *M. tuberculosis,* the bacilli are contained in granulomas through cell-mediated mechanisms. This condition leads to LTBI. Persons with LTBI are not infectious and are asymptomatic due to a low bacillary load.

When a person's immunity is severely compromised, as in HIV-positive individuals, TB bacilli multiply exponentially and TB develops, either by recently acquired TB infection or reactivation of LTBI. As mentioned above, the risk of disease after infection is 10 percent per year among people living with HIV without ART, compared to 10 percent per lifetime among those who are HIV negative. Evidence also shows that TB infection among HIV-infected patients progresses to TB more rapidly than those without HIV infection. Studies also suggest that HIV-infected individuals are more likely to become infected after exposure to *M. tuberculosis*. This likelihood is supported by the occurrence of TB outbreaks among groups of HIV-positive patients after exposure to an infectious (i.e., smear positive) TB case. [18]

TB re-infection (i.e., TB that is caused by infection with a different species after a previous, resolved episode) is a phenomenon associated with HIV infection. This threat is particularly pronounced in settings where TB is highly endemic.

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Prisons Receive TB

Incarcerated offenders often come from communities with TB prevalence rates higher than the community at large and bring with them unhealthy lifestyles and addictions. Because of ignorance, neglect, or a lack of means, these offenders may enter prisons with untreated TB.[1]

Prisoners thus constitute a high-risk population for TB in almost every country. Not only do they bring TB into prisons, but they often create conditions for drug resistance by entering with partially treated TB or by interrupting treatment upon arrival. For these reasons, all prisoners should be screened upon entry or, in low TB incidence countries, be asked about symptoms of TB; however, this practice is often not implemented properly or enforced adequately.

Prisons Concentrate TB

Many prisons all over the world are overcrowded well beyond their official capacities. Overcrowded prisons facilitate the spread of TB because prisoners are in close contact with one another, often for 12 hours or more a day without access to the outside. Rates of overcrowding vary from system to system. In some countries, prisoners' living spaces in the cells are less than 1 square meter per person, their bunks are stacked three tiers high, or they must sleep in turns; however, they may have access to the outside for most of the daytime period. Elsewhere, there may be somewhat more space per person, yet the prisoners are locked inside their cells for much longer periods, thereby spending less time outside.[1]

Overcrowding, poor ventilation due to inadequate infrastructure (lack of windows) or covering of windows by prisoners (to block cold air from entering the room in cold climates or by hanging of clothes on bars), and prolonged confinement inside cells are all factors conducive of transmission of airborne diseases. Furthermore, many prisoners are heavy smokers, adding to the unhealthy atmosphere in overcrowded cells, and standards of hygiene are often poor. Living together in cramped quarters, with little or no ventilation, is another major factor for contracting TB.

New prisoners are often put into cells without an accurate health check and, in many settings, without routine screening for TB. A prisoner with undetected TB may thus be pooled with other prisoners in a unhealthy cell setting, putting all its occupants at risk of contagion. These daily conditions of prison life promote TB transmission.

Prisons Disseminate TB

In many countries, moving prisoners from one prison to another is common. Prisoners also circulate within prisons because authorities transfer prisoners from one part of the prison to another. Prisoners with undetected TB can thus disseminate the disease to other parts of the prison or even to different prisons.[1]

In many countries (often those with high TB burdens), the lack of organization, adequate budgets for prison health, laboratory capacity, trained staff, or a combination of all these shortcomings result in entry screening being erratic or not being done at all. On weekends, for example, when no trained health care staff are present, screening may not take place and no enforceable system may be set up for having the weekend entries called up for screening later in the week. Since prisoners themselves often do not seek medical help immediately and are thus not detected, they can and do disseminate the disease to fellow prisoners (and staff).

TB transmission may be a particular problem among unsentenced prisoners who are awaiting charge, trial, or sentence, or who are still being investigated and among health care staff and visitors. Facilities in remand prisons and similar holding centers are often poor with limited or nonexistent health care services. Overcrowding in such centers tends to be extreme. Delays in the judicial process often prolong what should be a short stay. Since remand prisoners are often not considered part of the prison population, services may not be available to them.

For these reasons, prisons often have ideal conditions for TB to disseminate with relative ease within the system and toward the outside through contact with prison staff and visitors.

Prisons Increase the Risk of Delayed Diagnosis and Poor TB Treatment Results

Delayed Case Finding and Treatment

Several factors contribute to delayed TB diagnosis in the prison system. Initial screening specifically targeting TB is rarely applied. Prison health staff members conduct a medical check-up of prisoners upon entry into the prison. Because of a limited number of health staff and an overwhelming number of prisoners entering concurrently, however, health staff are limited by time; thus, they merely perform a general anamnesis, focusing on current and past history of chronic disease (e.g., hypertension, asthma, diabetes, mental disease) and a rapid physical examination (i.e., vital signs only).[2,3] In the majority of cases, health staff do not ask questions regarding current signs and symptoms of TB. Therefore, infectious patients often go untreated and spend weeks or even months infecting other prisoners in an overcrowded setting before they are detected.

The diagnosis and care of TB patients is usually the responsibility of the MoH's NTP, which is not always, or is to varying degrees, linked to prison health services. Not infrequently, diagnoses need to be confirmed by an outside laboratory within the public health or private sector, and treatment can be dispensed (after proper registration) only by the NTP. Communication between these organizations can be difficult, and the transfer of patients, sputum, or medicines from one department to another provides ample opportunity for delays and glitches. Such snags are of particular concern when dealing with HIV-infected individuals, who are frequently sputum-smear negative or have extrapulmonary TB. In such cases, chest radiography or bacteriology examinations, which require referral to a facility outside the prison, are needed.

In many instances neither prisons nor families have the resources to cover transportation or hospital fees. Consequently, delays in establishing a diagnosis lead to high mortality in this group.[3]

Standard TB guidelines are often not well known or understood by prison health staff who may continue to insist on radiography for diagnosis, without confirmation through sputum examination. In other instances, they may overlook the importance of getting good quality early-morning sputum for analysis or may not properly instruct patients on how to produce a good sample, as opposed to saliva, resulting in acquiring samples of saliva instead of sputum for direct microscopy examination.

Other factors leading to delay involve corruptive practices. Access to health care does not always depend on medical criteria but, in some settings, on bribes or other influences including a hierarchy of prisoners among themselves.

Frequent Interruptions or Incomplete Treatment

Prison transfers are common, and they usually lead to treatment interruptions. Transfers can be short when a prisoner is absent for a day such as when he or she has to appear in court, or if he or she is sent to the punishment cells where there is no access to medical care. Interruptions can be longer if the prisoner's file does not follow him or her upon transfer to a different prison. Furthermore, transfers may occur at night or during the weekend, when the prison health staff are absent; therefore, neither treatment nor a referral form is given to the prisoner for the continuation of therapy in the receiving facility. The transfer destination of highly dangerous prisoners is often classified and unannounced for security reasons, making it difficult for health staff to track down the patient.

Similarly, treatment is often interrupted when a prisoner is released. Release can be granted at any time, including through presidential amnesties, and unless there is effective coordination between the administration and health staff, the prisoner leaves without a proper referral to the local health center. In some cases, health personnel give anti-TB medicines, in part or fully, to the prisoner to complete treatment at home in an unsupervised manner. When a referral is given to prisoners, they commonly provide false addresses so that they cannot be traced by local health center staff whom they mistrust.

The following factors are associated with increased poor treatment outcomes among prisoners:

- Factors related to the patient—
    - Severe malnutrition
    - Serious comorbid disease, infections, and immunodeficiency (such as HIV/AIDS, late-stage diabetes mellitus, hepatic insufficiency, renal insufficiency)
    - Negative attitudes of patients related to seeking care and adhering to therapy
    - Drug addiction and mental illness, two important risk factors for poor adherence
    - Repeated treatment default

- Factors related to the health services in prisons—
    - Delayed diagnosis and treatment initiation, including poor access to diagnostics and medicines; no active case finding (i.e., entry screening and contact investigation)
    - Weak or nonexistent linkages and coordination with public health sector and nongovernmental organizations (NGOs)
    - Inadequate or intermittent TB treatment, supplied in some cases by prisoners' families
    - Unsupervised TB treatment
    - Failure of health staff to recognize the severity of the situation including increased risk of death, drug-resistance, or drug-interactions, and to manage these complications

Corruptive Environments

Prisoners' behavior and prison environments vary within and among countries because of socioeconomic, cultural, and even religious characteristics. Consequently, issues that may become problematic for TB control in some contexts may not be a real concern in others.

In some instances, bribery and commercialization of anti-TB medicines have been identified. Prisoners may try to hoard anti-TB medicines for their own use, and a black market can develop. Prisoners may use anti-TB medicines as an alternative prison currency. They may sell the medicines to the guards, give them to their relatives during family visits, or use them in gambling or paying debts. Either individually or under pressure from gang bosses, TB patients may try to keep their anti-TB medications. They deceive health staff by keeping tablets in their mouths or hands to smuggle them back to their cells. The more influential prisoners can obtain the medicines by various means.[1]

One way of obtaining the medicines is to pressure prisoners lower in the hierarchy who are receiving treatment to hand over their tablets. These inadequately and haphazardly treated prisoners may develop drug-resistant strains of *M. tuberculosis*, which they then spread to their fellow prisoners. Another way is to get on a TB treatment program without having TB. A prisoner may bribe a doctor to register him or her as a tuberculosis patient or may bribe a laboratory technician to record a positive sputum smear. Alternatively, a prisoner may exchange a negative sputum sample for a positive sample from a prisoner with tuberculosis to obtain potential benefits such as better food and accommodation, less strict security, and better visiting rights. Prisoners treated in the sick wards may sometimes decide not to complete their treatment so as *not* to be cured and therefore not be sent back to whatever initial prison setting they came from.

These deceptive practices are not the norm in settings where prisoners and staff are more conscientious of the disease severity and the importance of treatment; thus, patients in these settings are motivated to comply with therapy. Deception is also less likely to occur in settings where TB is highly stigmatized because most people from such countries do not want to suffer the disease for fear of being shunned or, more

importantly, being assaulted by other prisoners for having a transmissible disease. Finally, the lack of or fewer incentives for TB patients in some countries prevents the internal commercialization of medicines in these settings.

Comorbidities

Confinement is particularly associated with high-risk behaviors for acquiring sexually transmitted and blood-borne infections. These behaviors, which are closely interrelated, are frequently present before and continue during incarceration; others may initiate post-entry.

Drug Dependence

Substance abuse, together with mental and communicable diseases, has been highlighted as a grave problem that prisons face. Drug addiction is another negative characteristic that is overrepresented among the prison population. In surveys in European countries, 50 percent of prisoners reported using illicit drugs.[4] In this context, drugs are part of daily life activities including smuggling, sale, consumption, and conducting financial transactions in which drugs become currency. This environment results in drug-induced deaths and emergency consultations, debt, violence, and unsafe practices that are propitious for HIV, hepatitis B, and hepatitis C transmission (e.g., needle sharing). Significantly, the first outbreak of HIV in Thailand in 1988 is assumed to have started among injecting drug users who had been incarcerated.[4]

Although aware of the encroaching problem, prison authorities are faced with the paradox of having to deal with a problem that should not exist at all. Consequently, they may ignore the issue or minimize it. Exceptional prisons, however, are making a dent by acknowledging the issue and introducing drug-rehabilitation and harm-reduction programs. The WHO Regional Office of Europe and the WHO HIPP have developed recommendations on this subject.

Viral Hepatitis

Like other transmissible diseases, hepatitis B and hepatitis C are more prevalent in prisons than in the general population. Hepatitis B and C, which are highly concentrated in human blood and body fluids, are able to survive outside the human body and, thus, are easier to contract than HIV, especially by sharing needles and syringes and by sexual, transvaginal, and parenteral routes.

Different blood-borne infections tend to affect the same populations. A cross-sectional study conducted in two prisons in Spain illustrates the extent of HIV and hepatitis B and C co-infection among injection drug users. The prevalence rates of hepatitis B and C co-infection and of HIV, hepatitis B, and hepatitis C co-infection were 42.5 and 37.0 percent, respectively.[5] In a study in correctional facilities in Maryland in the United States, 65 percent of HIV-positive prisoners were also infected with hepatitis C.[6]

Given that the same groups are at risk, prison provides an invaluable opportunity for integrated approaches to HIV and hepatitis B and C prevention and care, including screening and vaccination for hepatitis B.

Prison as an Opportunity for Effective TB Control

Prisons could be ideal environments for TB control. In planning and implementing effective TB control, prison health services could take advantage of the special features of the prison environment. Having prisoners all in one place should facilitate identification of prisoners with TB, promotion of adherence to treatment, and accurate recording and reporting. Some prisoners have had little access to health care in the community. For these people, a prison with effective health care services could provide an opportunity for access to health care, including TB care.

Highlighting the problem of TB in prisons may make prison authorities more aware of the other common health problems in prisons. Mobilization of resources for TB control could pave the way toward better funding of prison health services. Implementation of DOTS and incorporating the elements of the Stop TB Strategy in prisons could therefore serve as the entry point for improved health services in prisons in general. The opportunity for effective TB control in prisons is also an opportunity to contribute to effective TB control in the wider community.[7] A benefit of effective TB control in prisons is decreased transmission of TB, including drug-resistant tuberculosis, to the wider community. To control TB effectively, DOTS needs to be implemented in prisons. Experience in a Spanish setting showed that implementation of DOTS led to decreased incidence of TB.[7] To this end, it is crucial to ensure patients' adherence to treatment in prison and after being released from prison.[8]

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7. CASE FINDING AND SCREENING IN PRISONS

Detecting TB through Case Finding and Screening

Case detection and treatment success are core elements of TB control. If conducted promptly, effectively, and systematically, these elements could lead to the reversal of a growing TB incidence and to the reduction of TB prevalence and mortality. Consequently, DOTS, the Stop TB Strategy, and the Global Plan to Stop TB 2006–15 are all oriented toward these two fundamentals.

In terms of case detection, DOTS traditionally relies on the passive detection of cases or passive case finding. Passive case finding examines TB suspects (i.e., persons who have had a cough for two or more weeks) among persons who spontaneously visit health centers seeking relief for respiratory symptoms. Passive case finding assumes the complete access to TB diagnostic services, otherwise it may result in delayed case finding because of patients' health-seeking behaviors (e.g., failing to recognize the symptoms of TB or using traditional or non-TB medicines to merely relieve symptoms) or because of providers' failure to recognize TB. In some prisons, passive case finding is further compounded by corrupt practices that may limit a prisoner's ability to seek care. Furthermore, prisoners in most countries tend to be heavy smokers, so that merely triaging "coughing" may be insufficient.

In circumstances or populations at increased risk of developing TB (e.g., people living with HIV, other immunosuppressed individuals, and specifically prisoners), case finding has to be conducted actively to avoid gaps and delays in diagnosis and treatment initiation. *Active case finding* involves screening prisoners at different points during incarceration and using various methods, including symptom-based screening, chest radiography, tuberculin skin testing (TST), immunoglobulin gamma interferon assay (IGRA), or a combination of these methods.

In prisons, passive and active case finding should be implemented simultaneously and systematically. A combination of these two approaches will increase case detection substantially. Some of the advantages and disadvantage of conducting passive and active case finding are listed in box 2.[c]

Passive case finding must be complemented with active case finding or screening. Selection of diagnostic methods and the combination of passive and active finding, including frequency of active case finding, largely depend on the prevalence of TB, HIV, or both in the community and the prison setting and on the availability of resources. Countries must conduct operational research to improve TB case detection and adopt the most effective TB case detection strategy.

[c] World Health Organization (WHO). 2008. *Global Tuberculosis Control 2008: Surveillance, Planning, Financing*. Geneva: WHO, p. 57.

Box 2. Advantages and Disadvantages of Passive and Active Case Finding

Passive Case Finding

Advantages

- Identifies cases missed through other case finding measures (e.g., entry-screening, contact investigation, point mass screening, or surveys)
- Identifies incident cases who develop TB after entry
- Is relatively less expensive and simpler for programs to implement

Disadvantages

- Relies on patients' readiness to attend medical services for evaluation (self-referral)
- May result in delayed case finding and treatment initiation, with prolonged transmission to others
- May result in advanced disease that can be more difficult to treat
- May be biased by internal regulating mechanisms among prisoners (e.g., bullying or corruption) leading to a denial of access to the medical ward to certain subgroups by the "prisoner bosses"

Active Case Finding

Advantages

- Increases case notification; links the prison health system to the NTP and feeds data into the system
- Reduces delays more quickly and, consequently, reduces transmission through immediate removal of infectious cases by separating them from the general prison population and providing effective treatment
- If done early, makes it easier to treat patients detected in the early stages of TB rather than later when severe and incapacitating symptoms of advanced disease which is more difficult to treat prompt patients to seek care
- Is likely to find prevalence rates much higher than the prevalence rates outside the prison, which can be a useful tool for advocacy and for obtaining the necessary funds to deal with the problem
- Avoids bias in triage by internal prisoner procedures

Disadvantages

- Increases duties and workload of the health staff in prison, which are already limited in number and are not sufficiently motivated
- Is a burden on the penal and public health care system, which needs to support active case finding activities; high cost deems these activities unsustainable
- Overburdens the capacity of local health centers and hospital laboratories to respond to increases in smear and culture examinations
- Diverts funds from other DOTS activities
- Leads to potential over-diagnosis of TB, if diagnosis is based on radiography only

When to Screen for TB in Prisons

Entry Screening

Entry screening occurs when prisoners enter the prisons. Frequently prisons institute mandatory medical examination of prisoners upon entry, but invariably this exam is merely a general check-up (i.e., anamnesis and rapid physical examination).

Entry screening in prisons, by contrast, is aimed at detecting undiagnosed active TB, so patients can initiate therapy and transmission can be interrupted inside the prison. Entry screening also is aimed at identifying patients who were receiving TB therapy before imprisonment to ensure that they complete their treatment. Overall, the purpose is to detect and decrease the prevalence of active TB.

The process of screening for TB at entry should be documented on a specific form. (See the sample form in annex 1.) The entry TB screening form would also facilitate monitoring and evaluation of TB control practices in prisons. Entry screening should be followed up with standard procedures for diagnosis and treatment among those suspected of having TB. In some instances, new prisoners entering prison are kept for a few days in quarters segregated from the main prison population, usually for administrative reasons of classification. This segregation is an opportune time to check for TB. Studies repeatedly demonstrate that TB-specific entry screening yields large numbers of undiagnosed cases and cases that discontinued treatment due to incarceration.[1] Consequently, it represents a window of opportunity to identify and initiate treatment early and, hence, to reduce TB prevalence and poor treatment outcomes, including drug resistance inside prisons.

Mass Screening and Prevalence Surveys

Some countries implement periodic (e.g., annually or every six months screening among all prisoners in a facility to detect undiagnosed cases. In some settings, mass screening is also conducted in the context of cross-sectional prevalence surveys. Although this strategy has been useful in finding previously undetected disease,[2–5] it is not recommended as a sole means of finding active TB cases in a prison. Therefore, the mass screening should be complemented with other strategies (e.g., entry screening and ongoing passive case finding) to ensure that prisoners with TB who entered prison or cases that occurred between the periodic surveys are detected effectively. In addition, periodic mass screening may not be sustainable in many highly endemic and resource-limited countries. Moreover, it may overwhelm the capacity of laboratories and of physicians to read chest radiographies. Logistical barriers have also been cited.[3] Thus, this activity is reserved for areas where resources permit. In general, case detection should be thought of as a systematic practice, including entry screening, contact investigation, and passive case finding (incident cases detected post-entry).

The implementation of entry screening and contact investigation requires careful planning and coordination. Health and security staff, with support from prison authorities (i.e., directors and administrators) and prisoner leaders, should develop a plan in which both entering prisoners and contacts of an active TB case found post-entry—

- Are promptly identified and located
- Undergo symptom assessment
- Undergo diagnostic evaluation if they are TB suspects (i.e., if they have had a cough for two or more weeks) with sputum smear microscopy and according to national guidelines.

Prison volunteers can assist health and security personnel in conducting these activities. Their engagement and trust in the TB control program would facilitate the process and make it more sustainable.

How to Screen for TB in Prisons

The specific aim of screening for TB is to identify persons who should be evaluated for TB through sputum smear microscopy and according to national and international guidelines. In congregate settings, including prisons, radiography is recommended as a screening tool when resources permit, always followed by sputum microscopy to confirm the diagnosis of TB. Nevertheless, different screening approaches are employed based on estimated TB rate and availability of resources.

Symptom-Based Screening

In some countries, health staff working in prisons focus on questioning prisoners about the presence of combination of symptoms consistent with TB (e.g., cough, sputum production, fever, night sweats, weight loss, general weakness, hemoptysis, and chest pain) to identify persons who should be evaluated for TB. This procedure is consistent with the identification of TB suspects implemented by TB control programs in the community but carried out as a more dynamic approach. Emphasis is placed on finding sputum smear-positive patients because they are most likely to transmit the disease, especially in a densely populated and high-risk environment.

When performing symptom-based screening in prisons, staff should use a TB form to capture relevant information, regardless of the point or situation in which it is done (e.g., in the context of a TB survey in prisons, entry screening, contact investigation, or outbreak investigation). Information required on the form should include both TB symptoms (presence, duration) and questions about previous TB treatment. This form documents the process of screening and allows for future evaluation of the program. The TB questionnaire should not replace the existing intake medical check-up form but rather should complement it. Thus, it needs to be brief and concise to avoid overburdening the health staff.

TB symptom screening alone may be insufficient in some cases because it may fail to detect some pulmonary TB cases. Studies report a sizeable percentage of TB patients who reported no symptoms before being diagnosed even though they turned out to

be ill with pulmonary TB.[7–10] Nonetheless, TB symptom screening is adequate in prisons with minimal risk for TB (e.g., no cases in the last year or a small prison population). Moreover, it is a simple, rapid, and cheap tool for identifying those prisoners who require a full work-up for TB. It can be completed by nonmedical staff in prisons, including volunteer prisoners and security staff.

Screening through Chest Radiography

Screening all prisoners at entry with chest radiography is beneficial for identifying undiagnosed active TB. This approach, used mainly in industrialized countries, can complement symptom screening when feasible. Studies show its utility in finding prisoners who would have been missed by symptom screening alone.[7] Prisoners with abnormal chest radiography are then followed up with sputum examination. The strategy has also been demonstrated to reduce delays in the diagnosis of TB, reducing the time of exposure to other prisoners.[11] In addition, it is a cost-effective measure for case detection.[12]

Unfortunately, in resource-limited settings, chest radiography screening is not readily available because of cost and logistical barriers. Implementing it requires equipment and a continuous supply of reagents and maintenance. Trained and experienced personnel have to read the films. Prisoners in facilities without radiography machines have to be transported outside the prison, which is complicated by legal and security issues.

Despite implementation constraints (i.e., cost and logistics), the high sensitivity of screening through chest radiography compared to symptom-based assessment cannot be ignored.[13] As an entry screening strategy in prisons, chest radiography should not replace symptom assessment to identify persons who should undergo further evaluation for active disease; however, it can be used together with a symptom questionnaire. This approach could be limited to prisons where TB, HIV, or both are highly prevalent. It can also be considered for prisons housing groups at risk for HIV (e.g., injection drug-users). TB control programs should prioritize these facilities to expedite TB diagnosis and treatment, thus reducing HIV-related TB morbidity and mortality.

Contact Investigation

In congregate and overcrowded settings such as prisons, contact investigation to detect TB patients is crucial and should be prioritized and carried out in an active and prompt manner. Except for low TB incidence countries, contact investigation is carried out mainly to identify and treat active cases of TB. International and national TB guidelines recommend screening for TB among contacts of sputum smear-positive (i.e., infectious) pulmonary TB cases. Guidelines implemented in industrialized countries are based on categorization of contacts as close or casual using a concentric circle approach. In prisons, TB contacts are persons who share air for prolonged periods of time with an active TB case.

These include, but are not limited to, the following—

- All prisoners who sleep in the same cell as the TB case
- Prisoners who spend time in closed or poorly ventilated work areas (e.g., carpentry and handicraft shops, garment factories, bakeries) that operate inside the prison
- Prisoners who interact with the TB patient during recreational activities (e.g., playing cards or chess, watching TV)
- Prison staff who come in contact with a TB case
- Visitors

The goal is to identify TB suspects among contacts listed and investigated and to examine them for active TB according to the general country guidelines; contacts that are diagnosed with active TB are considered secondary TB cases to the index or source case. The index patient should be interviewed about his or her social network and daily or weekly activities during the infectious period to identify different groups of contacts who might be exposed. The next step, classifying the contacts exposed according to the degree of exposure and susceptibility, will allow for prioritization to start the contact investigation and evaluate those at highest risk for developing disease.

Diagnostic Tools to Evaluate LTBI

In some settings, including low to middle TB incidence countries and among those co-infected with HIV, early diagnosis of LTBI is important to initiate chemoprophylaxis. LTBI has been traditionally diagnosed by the administration of TST. IGRA is a second, more specific laboratory tool. TST and IGRA are used for the detection of LTBI, whereas the history, physical examination, radiography, sputum smear, and culture are mainly used for the identification of cases of active pulmonary TB or, in the case of LTBI, to exclude active pulmonary TB.

Tuberculin Skin Testing

TST with purified protein derivative is the most common method of testing for infection with *M. tuberculosis*. Its use is limited to detecting individuals with latent TB infection who would benefit from prophylactic treatment in certain settings (e.g., people living with HIV). LTBI is defined as infection with *M. tuberculosis*, manifested by a pre-defined TST reaction or by a positive IGRA test without any sign of clinically or radiologically active disease or by both. In developing countries, the use of TST is not often recommended for three reasons—

- The priority for TB control programs in those areas is to detect and treat infectious cases
- The prevalence of TB infection is high
- Bacillus Calmette-Guérin (BCG) vaccination, which affects interpretation of TST, is used extensively

Interferon Gamma Release Assay

Recently, two in vitro T-cell based blood tests have been developed that measure interferon-gamma production. IGRAs operate on the basis that T-lymphocyte blood cells previously sensitized by an infection with *M. tuberculosis* release high levels of interferon gamma when stimulated in vitro with specific *M. tuberculosis* peptides, which are absent in *Mycobacterium bovis* BCG and most nontuberculosis mycobacteria.

IGRAs offer a reasonable sensitivity and a higher specificity in comparison with TST. IGRAs require a quality-assured laboratory, and the specifications for blood sampling and transport necessitate proven logistics. In rare cases, IGRAs cannot be interpreted ("indeterminate result") and give false-negative results when the sample does not contain any living or stimulated T lymphocytes. This result may be caused by the following:

- A technical laboratory error (e.g., storage in a refrigerator or freezing before incubation resulting in cell anergy)
- Incorrect transport
- A patient who has severe lymphopenia or immunosuppression

The sensitivity of IGRAs, however, surpasses that of the TST for immunosuppressed patients. Further studies need to be conducted to determine the role of IGRA in early detection of TB infection in prison settings.

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Clinical Features of TB

Symptoms

The most common symptom of pulmonary TB is a persistent, productive cough, often accompanied by other nonspecific symptoms. Although the presence of a cough for two to three weeks is nonspecific, traditionally having a cough of this duration has served as the criterion for defining suspected TB and is used in most national and international guidelines. Cough is not specific to pulmonary TB, however, especially in an unhealthy prison environment. Cough is common in smokers and in patients with acute upper or lower respiratory tract infections. Most acute respiratory infections resolve within three weeks, so a patient who has had a cough for more than three weeks is a pulmonary TB suspect and must submit sputum for diagnostic microscopy.

Patients with pulmonary tuberculosis (PTB) may also have other respiratory or constitutional (general or systemic) symptoms. The most important respiratory symptoms are hemoptysis, chest pain, and breathlessness. The most important constitutional symptoms are fever, night sweats, tiredness, and loss of appetite.

Physical Signs

The physical signs in patients with PTB are nonspecific. They do not help to distinguish PTB from other chest diseases.

Collection of Sputum Samples for Diagnosis

A goal of TB control programs is to adequately identify and examine 100 percent of the TB suspects. A pulmonary TB suspect should submit at least two sputum samples for microscopy. Usually two sputum samples would be enough to establish a diagnosis of TB. Secretions build up in the airways overnight, so an early morning sputum sample is more likely to contain tubercle bacilli than a sample taken later in the day. Health workers should advise TB suspects to cough and clear the back of the throat and then to give a good cough to bring up sputum. *TB suspects should submit sputum samples under supervision by health or security staff.* Samples should be collected in a well-ventilated area, and staff observing need to take adequate precautions to avoid contagion by standing away from or behind the suspect and by using a respirator (e.g., FFP II or III or N95 respirator), if available.

Sputum cups or containers should be labeled with the suspect's name, cell number, and date the sample was collected. Health staff should fill out a sputum smear examination request form for the laboratory with information on the suspect. Samples, with the corresponding laboratory request form, should be transported the same day to the designated laboratory for processing. If not, sputum specimens should be refrigerated. If refrigeration is not an option, samples should be stored for a maximum of three days in a dry place, away from heat and light.

In addition, health staff in prisons should keep a TB suspect register or log in which all TB suspects identified, either though active or passive case finding, are registered. Information in this register includes name, dates seen in clinic, prison cell number, dates of sputum collection, and results of sputum examination. The NTP should regularly supply prisons with sputum containers, recording and reporting forms, and other provisions required, as they do for other facilities in their network (e.g., health centers and district hospitals).

When appropriate, NTPs can provide training on sputum smear and fixation techniques to prison health staff, security staff, or both. These procedures could be performed in an adequate (i.e., well-ventilated and -illuminated) space within the prison clinic. Hence, fixed slides would be transported to the referral laboratory for staining and reading. The process would reduce the workload of the staff at the referral laboratory and the time of reporting of results. If this modality is implemented, quality control (of smearing and fixing procedures) should be ensured.

Taking sputum samples from prisoners should always be done under direct supervision, so as to avoid any doubts about whose sputum is being tested and to check for quality of the sample.

Direct Sputum Smear Microscopy

Direct smear microscopy examination of sputum is the most commonly used method for diagnosing TB. It is not a definitive (i.e., confirmatory) test, but it detects most infectious pulmonary TB cases and allows monitoring of patients' response to treatment. (See also chapter 9, "Standardized Case Definitions.") Direct smear microscopy tests for the presence of AFB in sputum, stained and observed under a light microscope. These samples can also be observed under fluorescent microscope, including newer, less expensive types.[1] TB bacteria retain the stain even after washing with alcohol-acid solutions, deeming them AFB. Among the methods for staining, the Ziehl-Neelsen, or ZN, technique is used most frequently. Direct smear analysis is not a sensitive test for detecting TB bacilli in sputum. It requires a high volume of bacilli in the specimen to be positive and an experienced reader. Still, it is comparatively inexpensive, fast, does not require sophisticated equipment, and can be performed by trained technicians in primary care settings. Consequently, it is the method of choice for diagnosis in low-resource settings.

Sensitivity for detecting TB bacilli in sputum increases substantially if sputum is concentrated and stained with fluorescent solutions (e.g., auramine O). Slides are then observed under a special microscope that uses a halogen lamp. This technique requires lower magnification while examining the slides and reduces the time of observation. Thus, more slides can be read in less time. Conversely, higher capital and running (including maintenance) costs are involved, making it less accessible for programs in low-resource countries.

Culture

The isolation of TB bacilli in sputum (and other clinical specimens) through culture, with further biochemical or molecular tests for identification, constitutes the definitive diagnosis of TB. Sensitivity of culture is substantially higher than that of smear microscopy; sputum smear microscopy detects only up to 50 percent of culture-confirmed pulmonary TB cases.[2] Therefore, the importance of its use to confirm disease should be emphasized, especially among HIV-infected individuals, who are frequently smear-negative.[3] Additionally, this method allows for identification of drug-susceptibility patterns, crucial for guiding therapeutic management. Therefore culture and drug-susceptibility testing (DST) shall be considered for all TB patients who are suspected to be infected with multidrug resistant strains. Culture is part of the routine work-up when evaluating TB suspects in industrialized countries.

Important factors limit its widespread use in developing countries. Traditional culture methods in solid media, such as Lowenstein-Jensen, require decontamination, homogenization, and centrifugation of samples, which implies more equipment (e.g., centrifuge, biosafety cabinets) and higher maintenance costs. Personnel require more training. These procedures produce more aerosols containing the TB bacilli, so laboratory staff have to be adequately protected. Growth of TB bacilli in solid media can be observed within four to five weeks, but may take up to six weeks. More rapid culture results may be obtained through the use of automated or semiautomated methods that make use of liquid media. These include BACTEC-460 and BACTEC-960 (mycobacteria growth indicator tube [MGIT]). *M. tuberculosis* growth can be detected as early as one to two weeks. Again, capital and running costs may render these inaccessible to some TB programs.

Chest Radiography

All pulmonary TB suspects must submit sputum samples for diagnostic smear microscopy. In some instances, however, chest radiography is required to establish the diagnosis of pulmonary TB. The most important indication is when there is clinical suspicion of tuberculosis despite negative sputum smears. The diagnosis of bacteriologically negative (two or more negative smears, at least one culture negative, or both) TB is therefore always presumptive and must be based on other clinical and epidemiological information, including failure to respond to broad-spectrum antibiotics and exclusion of other pathology. *Chest radiography is necessary to document cases of smear-negative pulmonary TB when culture is not available or reliable*. Table 3 outlines the indications that chest radiography is needed.

Table 3. Indication for Chest Radiography during Diagnostic Evaluation of TB

Patient	Presentation
Tuberculosis suspects with negative sputum smears	Patient who continues to cough despite a course of broad-spectrum antibiotic and who has had two negative sputum smears
Patients with sputum smear-positive tuberculosis	Suspected complications in the breathless patient, needing specific treatment (e.g., pneumothorax); with pericardial effusion or pleural effusion, positive sputum smear is rare.
	Frequent or severe hemoptysis (to exclude bronchiectasis or aspergilloma)

Note: Case detection methods in pregnant women should exclude radiographic examination, particularly in the first trimester of pregnancy.

The manifestations of TB on chest radiography vary according to the course of infection in the lungs. Primary tuberculosis refers to initial infection with *M. tuberculosis* after inhalation of droplets in the air that contain the bacilli. Usually, the chest radiography at this point shows no abnormality. In some cases, it may show small areas of nonspecific pneumonitis, and enlarged hilar and paratracheal lymph nodes. Lymphadenopathy occurs in up to 43 percent of adults and 93 percent of affected children.[2] The presence of calcified lymph nodes is characteristic of healed lesions. A small percentage of primary infections progress to severe disease (e.g., miliary TB), especially pediatric cases. Yet, most primary TB resolves without treatment.

Pulmonary TB that has reactivated, or progressed to active disease requiring treatment, shows a different radiological pattern. This pattern is further altered by the presence of HIV. Although radiological characteristics of TB are associated with a patient's immune competency, common findings among HIV-positive and HIV-negative patients are evident (summarized in table 4).

Table 4. Comparison of HIV-Negative and HIV-Positive TB Patients

HIV-Negative TB Patients	HIV-Positive TB Patients

• Infiltrate in apical or posterior segments of upper lobes. Infiltrate may appear as ill-defined alveolar-filling process, fibronodular pattern, or combination of both (80%)
• Cavities (50%)
• Fibrosis with loss of parenchyma (30%)
• Bronchiectasis, bronchial stenosis
	• No abnormalities (12–14%)
	• Findings of primary TB
	  • Hilar, mediastinal lymphadenopathy
	  • Parenchymal infiltrates may be present or not
	  • Miliary disease (19%)
	  • Pleural effusion (10%)

Diagnosis of active TB among prisoners whose sputum smears are negative is one of the major challenges in many settings. The need to transport a prisoner outside the prison to a referral facility for chest radiography has legal and security implications. Approval from higher authorities is required and may take several weeks to obtain. Additionally, transportation costs are incurred for the prisoner and for security personnel escorting him or her, which neither the prison administration nor the prisoner's family can assume. These barriers result in many TB suspects who have negative smear results going without a chest radiography as diagnostic follow-up and, consequently, without TB treatment. Among TB suspects with confirmed or suspected HIV, this occurrence is common. Many of these individuals die before having the opportunity to begin therapy.

This challenge may be addressed by increasing funds to prison or NTP budgets through government and donor (e.g., the Global Fund to Fight AIDS, Tuberculosis and Malaria [GFATM]) mechanisms to cover these costs. A second option, sometimes preferred by prison authorities, involves bringing diagnosis to the prison rather than moving the prisoner for diagnosis outside the prison. For this approach, mobile radiography units have been recommended. These units can visit prisons as needed.

Figure 1 summarizes the diagnostic steps during the evaluation of pulmonary TB among HIV-negative individuals or those living in areas with low HIV prevalence. Chapter 12 reviews the approach to assessing TB in HIV-infected patients.

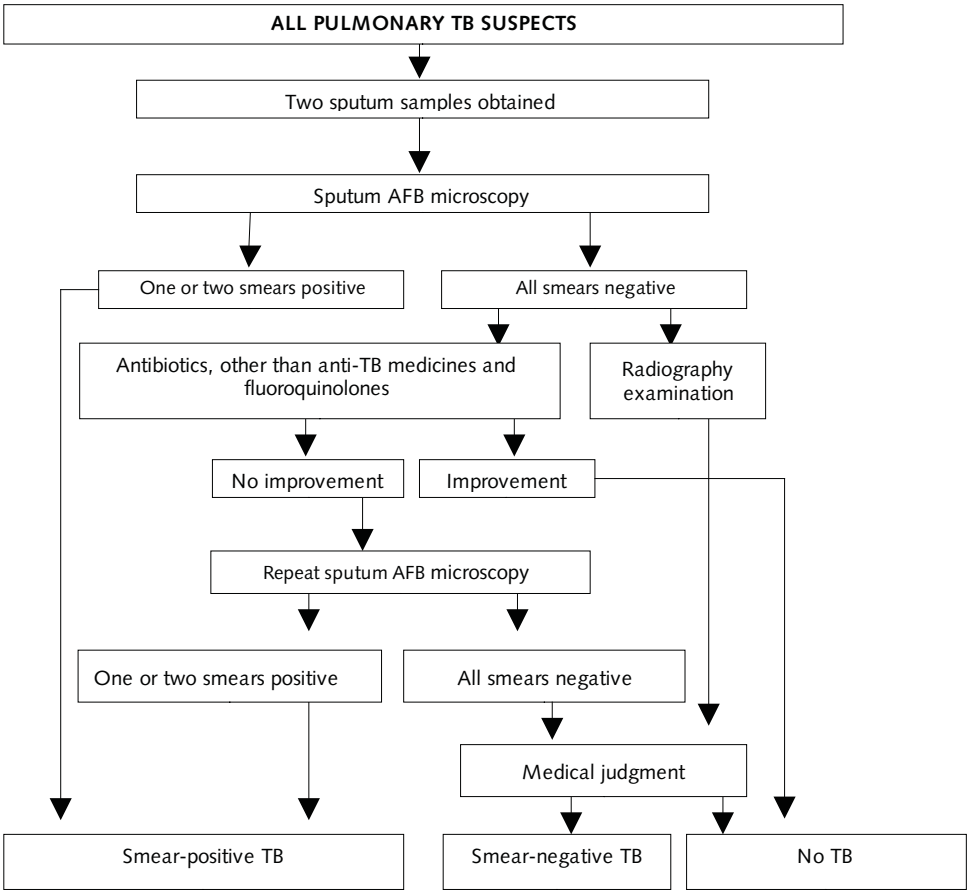

Figure 1. Standardized diagnostic algorithm for pulmonary TB suspects who are HIV negative or living in low HIV prevalence areas

Extrapulmonary TB

TB outside of the lungs is known as extrapulmonary TB. Potential sites for extrapulmonary TB include peripheral lymph nodes, pleura, bones and joints, genitourinary tract, peritoneum, gastrointestinal tract, and the central nervous system. Patients usually present with constitutional features (i.e., fever, night sweats, weight loss) and local features related to the site of disease. Extrapulmonary TB occurs more frequently among patients with severe immunosuppression (70 percent in patients with advanced HIV) than those patients with normal immunity (15 percent).[3]

Since a definitive diagnosis of extrapulmonary tuberculosis is often difficult, the diagnosis may be presumptive (i.e., excluding other conditions). The degree of certainty of diagnosis depends on the availability of diagnostic tools (e.g., biopsy for smear,

culture, and histology of body tissue or fluids). Many patients with extrapulmonary tuberculosis also have coexistent pulmonary TB, so sputum examination for AFBs and a chest radiography may be warranted.

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The diagnosis of TB refers to the recognition of an active case (i.e., a patient with symptomatic disease due to *M. tuberculosis*) according to the following definitions—

- TB suspect: Any person who presents with symptoms or signs suggestive of TB, in particular, a productive cough of duration longer than two weeks, often accompanied by other nonspecific symptoms, such as fever, night sweats, and weight loss.
- Case of TB: A patient in whom TB has been confirmed bacteriologically or diagnosed by a clinician

A diagnosis of TB should be followed by case management specifications based on the type of TB (e.g., TB case definition), which is necessary for the following—

- Treatment prescription according to standardized regimens
- Patient registration and reporting
- Cohort analysis of treatment outcomes
- Epidemiological surveillance

Case definitions for TB take into account the anatomical site of disease, the results of bacteriological and other tests, the history of previous treatment, and the severity of disease.

Anatomical Classification

TB is categorized by anatomical site of disease—

- Pulmonary TB: The disease affects the lung parenchyma. Pulmonary TB is the most common form.
- Extrapulmonary TB: The disease affects other sites including lymph nodes, pleurae, meningeal, pericardial, peritoneal, spinal, intestinal, genitourinary, larynx, spine, bones and joints, and skin.

A patient diagnosed with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.

Bacteriological Classification

"Smear-positive" and "smear-negative" are the most useful bacteriological classifications of pulmonary cases, because they correlate with infectiousness. Where culture facilities are available, the culture diagnostic results are included in the bacteriological classification. In such situations, definitions of bacteriologically confirmed (definite) cases and bacteriologically unconfirmed cases will be used.

A *bacteriologically confirmed case* of pulmonary TB is defined by the following—

- At least one smear examination positive for AFB (sputum smear positive case)

OR

- One culture positive for *M. tuberculosis* complex

A case of pulmonary TB that does not meet either of these two criteria is defined as a *bacteriologically unconfirmed case*. In addition, in keeping with the recommendations of the ISTC, diagnostic criteria should include the following—

- At least two sputum specimens negative for AFB (smear negative case)

AND

- Radiological abnormalities consistent with active pulmonary TB

AND

- No response to a course of broad-spectrum antibiotics among those not used in the treatment of TB

AND

- Decision by a clinician to treat with a full course of anti-TB chemotherapy

For HIV-positive cases (or for setting with high HIV prevalence), the treatment with broad-spectrum antibiotics is not recommended in the algorithm for the diagnosis of sputum smear or culture negative TB cases. (See "Diagnostic Algorithm" in chapter 12.)

History of Previous Treatment: Category of Patient for Registration on Diagnosis

To identify patients who are at increased risk of acquired drug resistance and to prescribe appropriate treatment, a case should be defined according to whether or not the patient has previously received TB treatment. This distinction is also essential for epidemiological monitoring of a TB epidemic at different levels (e.g., global, regional, country, local). The following definitions are used:

- *New:* A patient who has never had treatment for TB or who has taken anti-TB medicines (for treatment of active TB) for less than one month
- *Relapse:* A patient previously treated for TB who has been declared cured or who had completed treatment and is diagnosed with bacteriologically confirmed TB
- *Treatment after failure:* A patient who is started on a re-treatment regimen after having failed previous treatment
- *Treatment after default:* A patient who returns to treatment with positive bacteriology, following interruption of treatment for two or more months
- *Transfer in:* A patient who has been transferred from another TB register to continue treatment
- *Other:* All cases that do not fit the above definitions

Severity of TB

Bacillary load, extent of disease, and anatomical site are considerations in determining TB severity and the appropriate treatment. Involvement of an anatomical site results in classification as severe disease if there is a significant acute threat to life (e.g., pericardial tuberculosis), a risk of subsequent severe handicap (e.g., spinal tuberculosis), or both (e.g., meningeal tuberculosis).

Miliary or disseminated TB is a severe form of disease. The following forms of extrapulmonary tuberculosis are classified as severe: meningeal, pericardial, peritonitis, bilateral or extensive pleural effusion, spinal, intestinal, and genitourinary. Lymph node, pleural effusion (unilateral), bone (excluding spine), peripheral joint, and skin TB are classified as less severe.

Recording TB Patients by Anatomical, Bacteriological, and Previous TB History Classifications

Health staff in prisons will fill out information on each TB patient diagnosed in the basic management unit's TB register (at the prison). This book includes information on the type of patient by anatomical site (i.e., pulmonary or extrapulmonary case), by sputum smear status (i.e., smear-positive or -negative), and by designation as a new versus previously treated patient. This register allows health staff to monitor therapeutic response through sputum smear analysis at months two and five and at the end of treatment. It also contains information on the outcomes of therapy (i.e., cured, competed, defaulted, died, transferred out) and HIV status. See "Recording Standardized Treatment Outcomes" in chapter 11 for more information.

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Aims of Treatment

The aims of tuberculosis treatment are to—

- Cure the patient of TB
- Prevent death from active TB or its late effects
- Prevent relapse of TB
- Decrease transmission of TB
- Prevent the development and transmission of drug resistance

Tuberculosis Treatment Regimens

Anti-TB medicines have three primary properties: bactericidal activity, sterilizing activity, and the ability to prevent resistance. The essential anti-TB medicines possess these properties to different extents. Isoniazid and rifampicin are the most powerful bactericidal medicines active against all populations of TB bacilli. Rifampicin is the most potent sterilizing medicine available. Pyrazinamide and streptomycin are also bactericidal against certain populations of TB bacilli. Pyrazinamide is active only in an acid environment. Streptomycin is bactericidal against rapidly multiplying TB bacilli. Ethambutol is used in association with more powerful medicines to prevent the emergence of resistant bacilli. Daily treatment is recommended in prison settings. Table 5 shows the essential anti-TB medicines and their recommended dosages.

Table 5. Recommended Doses of First-Line Anti-TB Medicines for Adults

Drug	Recommended dose			
	Daily		3 times per week	
	Dose and range (mg/kg body weight)	Maximum (mg)	Dose and range (mg/kg body weight)	Daily maximum (mg)
Isoniazid	5 (4-6)	300	10 (8-12)	900
Rifampicin	10 (8-12)	600	10 (8-12)	600
Pyrazinamide	25 (20-30)	–	35 (30-40)	–
Ethambutol	15 (15-20)	–	30 (25-35)	–
Streptomycin[b]	15 (12-18)	–	15 (12-18)	–

Source: Adapted from World Health Organization. 2003. Treatment of Tuberculosis: Guidelines for National Programmes, 3rd ed. Geneva: WHO.

[b] Patients aged over 60 years may not be able to tolerate more than 500–750 mg daily, so some guidelines recommend reduction of the dose to 10 mg/kg per day in patients in this age group. American Thoracic Society. 2003. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of American Treatment of Tuberculosis. *Am J Respir Crit Care Med* 167:603-662. Patients weighing less than 50 kg may not tolerate doses above 500–750 mg daily (WHO Model Formulary 2008).

The use of fixed-dose combinations (FDCs) is recommended for treatment of all TB cases. FDCs have the following advantages over individual medicines (single-medicine formulations)—

- Prescription errors are likely to be less frequent.
- The number of tablets to be ingested is fewer, which may encourage adherence.
- Patients cannot choose only some of the prescribed medicines to take (when treatment is not observed).

Poor bioavailability of rifampicin has been found in some FDCs. Therefore, use of pharmaceutical combinations of assured quality is essential. These medicines can be obtained through the Stop TB Strategy's Global Drug Facility (GDF).

New Cases

The standard treatment regimen recommended for new cases with either pulmonary or extrapulmonary TB consists of two phases. The initial phase uses four medicines: rifampicin, isoniazid, pyrazinamide, and ethambutol administered for two months. The initial phase is followed by a continuation phase with two medicines: rifampicin and isoniazid for four months as detailed in table 6.

Table 6. Standard Regimens for New TB Patients

TB Treatment Regimens				
Intensive phase treatment		**Continuation phase**		**Comments**
Medicines	**Dosing Frequency**	**Medicines**	**Dosing Frequency**	
Two months of isoniazid, rifampicin, pyrazinamide, and ethambutol	Daily[a]	Four months of isoniazid and rifampicin	Daily[a]	a = Optimal
	Daily[b]	Four months of isoniazid and rifampicin	3 times a week[b]	b = Acceptable alternative for any new TB patient
	3 times a week[c]		3 times a week[c]	c = Acceptable alternative EXCEPT for patients who— Are living with HIV OR Live in HIV prevalent settings

Patients with a large bacillary load (sputum smear-positive pulmonary TB) and many HIV-infected patients with smear-negative pulmonary TB have an increased risk of selecting resistant bacilli. Short-course chemotherapy regimens with four medicines in the initial phase reduce this risk. Such r egimens are highly effective in patients with susceptible bacilli. The same four-medicine regimen, including ethambutol, should be used during the initial phase of treatment for patients with smear-positive pulmonary, smear-negative pulmonary, and extrapulmonary TB.
Supervised or directly observed treatment (DOT) for the daily administration of medicines for treatment of all new cases is imperative in prison settings.

The preferred continuation phase regimen is four months of rifampicin and isoniazid administered daily. The primary advantage of this regimen is the low rate of treatment failure and relapse for patients with fully susceptible TB or TB with initial isoniazid resistance. The use of rifampicin requires measures to support patients in adhering to treatment and preventing development of rifampicin resistance. Since outcomes for ethambutol are poorer in patients who have HIV infection, the preferred option is isoniazid and rifampicin rather than ethambutol and rifampicin for HIV-positive patients. Daily treatment is feasible in congregate settings.

Previously Treated Cases

Drug resistance is more likely to develop in previously treated patients (i.e., patients who have been treated for longer than one month) who continued to be or who became sputum smear (or culture) positive.

The *Global Plan to Stop TB 2006-2015* sets a target that by 2015, all previously treated patients should have access to DST at the beginning of treatment. The purpose is to identify MDR as early as possible so appropriate treatment can be given.

The approach to the initiation of retreatment depends on the country's laboratory capacity, specifically when (or if) DST results are routinely available for the individual patient.

- Countries using rapid DST will have results available within hours or days, and can use the results to decide which regimen to start for the individual patient
- Countries using conventional methods will have results available within weeks (if using liquid media) or months (if using solid media). Because of this delay in receiving DST results, countries using conventional methods will need to start an empiric regimen while awaiting results of DST.
- For countries which do not yet have DST routinely available for individual retreatment patients, an interim approach is described below.

Countries will need to use a mix of approaches if they are in a transition where some areas of the country do not yet have DST results routinely available and others do, or some laboratories use rapid and others use conventional DST methods.

Previously treated patients in settings with rapid DST—With line probe assays, MDR can be essentially confirmed[c] or excluded within hours to days, which allows the results to guide the regimen at the start of therapy.

Previously treated patients in settings where conventional DST results are routinely available for individual patients—Obtaining specimens for conventional culture and DST should not delay the start of therapy. Empiric regimens, often based on drug-resistance surveillance data, are used while awaiting the results of conventional DST (liquid or solid media), and should be started promptly. This is especially important if the patient is seriously ill or the disease is progressing rapidly. Placing a patient on an empiric regimen pending DST is done to avoid clinical deterioration. Also, once empiric therapy begins to render the patient less infectious, the risk of transmission to contacts decreases.

While awaiting the results of conventional DST, WHO recommends the country's standard, empiric MDR regimen for patient groups with high levels of MDR (see "Treatment of MDR-TB" in chapter 14) and the eight-month first-line drug regimen for patient groups with medium or low levels of MDR (table 7).

For many countries, drug resistance surveys will show that patients whose prior course of therapy has failed have a high likelihood of MDR so this group will receive a standard MDR regimen. When DST results become available, regimens should be adjusted appropriately. If the patient's DST results show susceptibility to isoniazid and rifampicin, treatment is changed to the six-month rifampicin containing regimen used for new patients.

Often drug resistance surveys show that those relapsing or returning after default will have a medium or low likelihood of MDR, so they will receive the eight-month retreatment regimen of first- line drugs, as described in table 7. However, levels of MDR in these patient registration groups vary by setting.

Previously treated patients in settings where DST is <u>not</u> routinely available for individual patients—In many countries, there is not yet laboratory capacity to routinely conduct DST for each previously treated patient (or the results arrive too late to guide therapy). Even though DST is not yet routinely available for individual patient management in these countries, the NTP may be able to collect or access some information on levels of MDR-TB in previously treated patients, by using data from a drug resistance survey, a national or supranational reference laboratory. These data are critical for ascertaining the level of MDR in retreatment patients.

If a very high level of MDR is documented in a specific group (such as patients who have failed a retreatment regimen), the NTP manager should urgently seek means to routinely obtain DST on all such patients at the start of treatment, in order to confirm or exclude MDR. If this cannot yet be achieved with any in-country laboratory, most NTPs

[c] Line probe assays detect resistance to rifampicin alone or in combination with isoniazid resistance. Overall high accuracy for detection of MDR is retained when rifampicin resistance alone was used as a marker for MDR. WHO. 2008. Molecular line probe assays for rapid screening of patients at risk of multidrug-resistant tuberculosis. Policy Statement. Geneva: WHO.

can make arrangements to send these patients' specimens to a supranational reference or other international laboratory for DST while the country rapidly builds domestic laboratory capacity.

A country may face a short gap in time before a domestic or an international laboratory can perform DST on specimens from patients who are members of a group shown to have very high levels of MDR-TB. Under this exceptional circumstance, an NTP may consider a short-term policy of directly starting patients from such a group on an empiric MDR-TB regimen without confirmation of isoniazid and rifampicin resistance. This is a temporary measure, while the country is building the laboratory capacity to perform routine DST for individual retreatment patients. Groups of patients whose likelihood of MDR is medium or low will receive the eight-month retreatment regimen with first-line drugs.

Table 7. Recommended Treatment Regimens for Previously Treated Patients (Re-treatment Regimen)

TB Patients	TB Treatment Regimens	
	Initial Phase	Continuation Phase
Relapses Treatment after default	Two months of isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin Followed by one month of isoniazid, rifampicin, pyrazinamide, and ethambutol	Five months of isoniazid, rifampicin, and ethambutol
Treatment failure of Category I In settings where representative drug resistance surveillance (DRS) data show low rates of MDR-TB or individualized DST show drug-susceptible disease	Two months of isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin Followed by one month of isoniazid, rifampicin, pyrazinamide, and ethambutol	Five months of isoniazid, rifampicin, and ethambutol
Treatment failure of Category I or failure of subsequent courses of therapy	Specially designed standardized[a] or individualized regimens with the use of SLMs	

The use of streptomycin carries a risk of HIV transmission when it is injected with inadequately sterilized re-usable syringes and needles. Therefore, streptomycin and other injectables should be used only in settings where the use of disposable or sterile needles and syringes is assured.

Support to TB Patients, Including DOT

For anti-TB therapy to be effective, appropriate medicines must be used in appropriate doses and ingested correctly for appropriate durations. Adherence to treatment is crucial to achieve cure. Factors that may lead patients to interrupt or stop treatment must be addressed. Services providing TB care in prisons should offer support to patients to ensure that treatment will be completed. Close liaison between the prisons and the NTP is necessary to ensure that prisoners with TB complete treatment after release. Involving NGOs working in communities and with hard-to-reach populations can facilitate this process. The NGOs can have an active role in tracing released prisoners, delivering DOT, and counseling them.

A relationship of trust and confidence between the prisoner with TB and prison health staff promotes adherence to treatment. Respecting patients and being considerate at every contact is vital for prison health staff. Adherence to treatment requires that the patient understand the disease and what is necessary for successful treatment and cure. At the time of a patient's registration to start treatment, setting aside enough time to meet with the patient is important. This initial meeting is a prime opportunity to advise, counsel, and educate the patient on the following—

- The importance of cough hygiene (e.g., cover the mouth when coughing and sneezing)
- DOT
- How to recognize potential side effects
- The need for follow-up through sputum smear monitoring
- The use of isolation measures

A new meeting with the patient at the end of the initial phase of treatment will allow for an explanation of progress and the need for the continuation phase.

Many TB patients receiving self-administered treatment will not adhere to treatment. Some patients stop treatment once they feel better, once they have taken their medicines for the first few weeks, or if unpleasant side effects occur. Prisoners, in particular, may find the motivation to complete treatment difficult; they have more immediate worries than the dangers of not receiving a full course of TB treatment.

Since predicting who will or will not surely adhere to treatment is impossible, DOT is necessary to ensure adherence. DOT has been used in TB control programs worldwide to facilitate adherence and improve treatment outcomes. DOT also allows early identification of toxic side effects of medicines and other problems that may affect adherence. In this intervention, the swallowing of medicines is directly observed by another person accountable to or supervised by health services (e.g., a nurse or prison guard).

Prisoners with TB must receive the whole treatment (initial and continuation phases) under direct observation. They should not self-administer treatment during the continuation phase. Self-administration of treatment in the continuation phase could lead to diversion of medicines to the prison black market. Although not always the case, prisoners with TB may use various tricks to avoid swallowing their tablets. They may do this on their own initiative or under coercion from other prisoners who are more senior in the hierarchy. They can then smuggle the tablets back to their cells. Prison administrative authorities and health staff need to be aware of the problems in ensuring DOT and maintain close supervision. Thus DOT in prison should be understood as a means to improve treatment adherence. It does not mean coercion, which has no place in the care of prisoners with TB.

Role of Prison Volunteers in DOT

Ideally, DOT should be delivered by the health staff. Unfortunately this option is not possible in some prisons that have no medical staff at all or that have staff who work only for short periods. In such cases, trained and sensitized prison security staff can conduct DOT. Moreover, some prisons have benefited from the active involvement of prisoners in TB program activities, including DOT. These prisoners, who need to be educated on basic aspects of TB and DOT, may be selected by prison medical or administrative staff based on their willingness to assist the program, good behavior, and being highly regarded by patients and the general prison population. Close supervision of the process of DOT by prisoners is imperative, especially in the beginning, to prevent prison program volunteers from corrupting the system (e.g., by commercializing or selling anti-TB medicines). In addition, prison program volunteers need to be continuously sensitized, educated, and motivated to ensure their support to the program.

TB treatments *must* be administered by DOT. Strict and individual monitoring of medicine intake is absolutely necessary.

Treatment Regimens in Special Situations

Pregnancy and Lactation

Each woman should be asked before starting TB treatment if she might be pregnant. Female prisoners in the second phase of their cycles, without contraception, may not know they are pregnant and should be thoroughly questioned. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the fetus and the newborn. Of the first-line medicines, isoniazid, rifampicin, and ethambutol can be given safely during pregnancy. Streptomycin may cause ototoxicity in the fetus and is contraindicated.

Most anti-TB medicines appear in low concentrations in breast milk at levels that do not produce toxicity in infants. Breast-feeding is not contraindicated. Mother and baby should stay together, and the baby should continue to be breast-fed in the normal way but should be given prophylactic isoniazid for at least three months beyond the time the mother is considered to be noninfectious. BCG vaccination of the newborn should be postponed until the end of isoniazid prophylaxis.

Oral Contraception

For female prisoners who are sexually active (e.g., conjugal visits are allowed in some places or female prisoners may have illicit sexual relations with male guards) and have access to oral contraception through the prison clinic or other sources, the prisoner must be informed that rifampicin interacts with oral contraceptive medications and may decreased their protective efficacy against pregnancy. Following consultation with a clinician, a woman receiving oral contraception may choose between two options while receiving treatment with rifampicin: either an oral contraceptive pill containing a higher dose of estrogen (50 mcg) may be taken or another form of contraception may be used.

Liver Disorders

Isoniazid, rifampicin, and pyrazinamide are all associated with hepatitis. Of the three medicines, rifampicin is least likely to cause hepatocellular damage, although it is associated with cholestatic jaundice. Of the three agents, pyrazinamide is the most hepatotoxic.

Provided the prisoner has no clinical evidence of chronic liver disease, patients who carry the hepatitis virus or who have a history of acute hepatitis or excessive alcohol consumption can receive the usual short-course chemotherapy regimens. Hepatotoxic reactions to anti-TB medicines may be more common among these patients, however, and should therefore be anticipated.

Established Chronic Liver Disease

Patients with liver disease should not receive pyrazinamide. Isoniazid plus rifampicin plus one or two non-hepatotoxic medicines such as streptomycin and ethambutol may be prescribed.

Recommended regimens are the following—

- Two months on streptomycin, isoniazid, rifampicin, and ethambutol in the initial phase followed by six months on isoniazid and rifampicin in the continuation phase

OR

- Two months on streptomycin, isoniazid, and ethambutol in the initial phase followed by 10 months of isoniazid and ethambutol in the continuation phase

OR

- Nine months on rifampicin and ethambutol

Acute Hepatitis (e.g., Acute Viral Hepatitis)

Uncommonly, a patient has TB and concurrently acute hepatitis unrelated to TB or TB treatment. Clinical judgment is necessary. In some cases, TB treatment can be deferred until the acute hepatitis has resolved. When treating TB during acute hepatitis is necessary, the combination of streptomycin and ethambutol for three months is the safest option. If the hepatitis has resolved, the patient can then receive a continuation phase of six months of isoniazid and rifampicin. If the hepatitis has not resolved, streptomycin and ethambutol should be continued for a total of 12 months.

Renal Failure

Isoniazid, rifampicin, and pyrazinamide are either eliminated almost entirely by biliary excretion or metabolized into nontoxic compounds. These medicines can therefore be given in normal dosage to patients with renal failure. Patients with severe renal failure should receive pyridoxine with isoniazid to prevent peripheral neuropathy.

Streptomycin and ethambutol are excreted by the kidney. When facilities are available to monitor renal function closely, streptomycin and ethambutol may be given in reduced doses. Thioacetazone is partially excreted in the urine; however, since the margin between a therapeutic dose and a toxic dose is too narrow, patients in renal failure should not receive this medicine. The safest regimen for patients with renal failure is two months on isoniazid, rifampicin, and pyrazinamide in the initial phase followed by four months on isoniazid and rifampicin in the continuation phase.

Signs of Complications and Risk of Death among Tuberculosis Patients

Complications and death among TB patients are major risks. Failure of diagnosis and treatment is the main cause of death among patients. Approximately 50 percent of TB patients without treatment die after two to four years from the onset of disease, and close to 75 percent die after five years. Consequently, the main cause of death is late TB diagnosis and treatment. When TB patients are diagnosed and treated promptly, the cause of death is not often attributed to TB, but is associated with other comorbid conditions. Box 3 outlines symptoms that might require hospitalization of a TB patient.

Box 3. When to Hospitalize

Patients with the following medical conditions, signs, and symptoms should be hospitalized for treatment, because of the increased risk of morbidity and mortality—

- Severe malnutrition
- Serious comorbid disease and immunodeficiency, such as HIV/AIDS or late-stage diabetes
- Respiratory insufficiency
- Moderate to severe hemoptysis
- Serious adverse effects to anti-TB medicines
- Strong suspicion of serious extrapulmonary TB (i.e., miliary TB, TB meningitis, or multisystem TB)

Suggested Reading for Chapter 10

B. Blomberg, S. Spinaci, B. Fourie, and R. Laing. 2001. The Rationale for Recommending Fixed-Dose Combination Tablets for Treatment of Tuberculosis. *Bulletin of the World Health Organization* 79(1): 61–68.

British Thoracic and Tuberculosis Association. 1976. Short-Course Chemotherapy in Pulmonary Tuberculosis: A Controlled Trial by the British Thoracic and Tuberculosis Association. *Lancet* 3: 1102–04.

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H. Reyes. 2007. Pitfalls of TB Management in Prisons, Revisited. *International Journal of Prisoner Health* 3(1): 43–67.

H. Reyes and R. Coninx. 1997. Pitfalls of Tuberculosis Programmes in Prisons. *British Medical Journal* 315: 1447–50.

Tuberculosis Coalition for Technical Assistance. 2006. *International Standards for Tuberculosis Care (ISTC)*. The Hague: TCTA.

WHO. 1999. *Fixed-Dose Combination of Tablets for the Treatment of Tuberculosis.* Geneva: WHO.

Patients with sputum smear-positive pulmonary TB should be monitored by sputum smear examination. These TB patients are the ones for whom bacteriological monitoring is possible. Monitoring the patient's response to treatment by chest radiography is considerably less reliable in comparison to bacteriological methods. For patients with sputum smear-negative pulmonary TB and extrapulmonary TB, clinical monitoring is the usual way of assessing the response to treatment. Sputum culture can be used to confirm or exclude treatment failure and to determine the drug-susceptibility pattern in failure cases. Culture is also used to monitor the response to treatment in MDR-TB patients.

New Sputum Smear-Positive Pulmonary TB Patients

Response to treatment should be monitored by sputum smear examination. In general, two sputum specimens should be collected for smear examination at each follow-up sputum check. Sample collection should be done without interrupting treatment.

Sputum smears should be performed at the end of the second month, during the fifth month, and in the last month of treatment. Negative sputum smears indicate good treatment progress, which encourages the patient and the health worker responsible for supervising his or her treatment. Table 8 shows when sputum smears should be performed in new sputum smear-positive PTB.

Table 8. When to Perform Sputum Smears for New Smear-Positive PTB Patients

Sputum Smear Examination	Category I Treatment (Six-Month Regimen)
At the end of the initial phase	At the end of the second month
In the continuation phase	At the beginning of fifth month
At the end of treatment	At the end of the sixth month

At the end of the initial phase of treatment, most patients will have a negative sputum smear. Such patients will then start the continuation phase of treatment. If a patient has a positive sputum smear at this time, it may indicate one of the following:

- That the initial phase of therapy was poorly supervised and that patient's adherence was poor
- That the rate of sputum smear conversion is slow (e.g., if a patient had extensive cavitation and an initially heavy bacillary load)
- That the patient may have drug-resistant TB that does not respond to first-line treatment

A small proportion of patients may be slow converters. Whatever the reason, if the sputum smears are positive at the end of the initial phase, the sputum samples should be sent for a culture examination, and the initial phase should be prolonged for another month. If drug resistance is suspected, rapid DST tests are recommended. After the prolonged initial phase, another sputum smear examination is done. The patient then starts the continuation phase. Sputum smears will be checked again at the beginning of the fifth month of treatment, and those that are still positive during the fifth month constitute treatment failure.

Treatment failure can also be declared earlier if the patient is found to harbor an MDR strain at any point during treatment. If possible, culture and DST (or molecular tests) should be conducted to confirm whether treatment failure is due to MDR-TB (i.e., isoniazid plus rifampicin resistance). If culture and DST are not available, the patient should be reregistered as a treatment failure and started on a re-treatment regimen, with Category II. If DST results confirm presence of multidrug resistance, treatment with SLMs should be started (see "Treatment of MDR-TB" in chapter 14).

Access to culture facilities and DST should become a priority for settings with a high prevalence of drug resistance. In such settings, culture and DST should be used to evaluate cases of treatment failure or those suspected of having drug-resistant disease.

Previously Treated Pulmonary Sputum Smear-Positive Patients

Sputum smear examination is performed at the end of the initial phase of treatment (at the end of the third month), during the continuation phase of treatment (at the end of the fifth month), and at the end of treatment (at the end of the eighth month). Table 9 provides a timeline for monitoring response to therapy in sputum smear-positive cases that were previously treated (i.e., receiving an eight-month treatment regimen).

Table 9. When to Perform Sputum Smears for Previously Treated Smear-Positive PTB Patients

Phase	Month
At the end of the initial phase	At the end of the third month
In the continuation phase	At the end of the fifth month
At the end of treatment	At the end of the eighth month

If the patient is sputum smear-positive at the end of the third month, the sputum samples should be sent for a culture examination, and the initial phase should be prolonged for another month. If drug resistance is suspected, rapid DST is recommended. If the culture and sensitivity results show drug resistance, the patient should be referred to a specialized unit for treatment with SLMs (see "Treatment of MDR-TB" in chapter 14).

New Sputum Smear-Negative Pulmonary TB Patients (Category III)

Sputum smear-negative patients should be monitored clinically; body weight is a useful progress indicator. Sputum smears should be checked only at the end of the second month in the event that the disease worsens because of nonadherence to treatment or drug resistance, that an error was made at the time of initial diagnosis (i.e., a true smear-positive patient was misdiagnosed as smear-negative), or both. In the event of positive sputum smear after the second month of treatment, case management should follow one of sputum-positive cases (described above).

Extrapulmonary TB

Response to treatment can be monitored only through clinical observation. As in pulmonary smear-negative disease, the weight of the patient is a useful indicator, as is improvement of other systemic signs and symptoms.

Recording Standardized Treatment Outcomes

At the end of the treatment course for each individual patient, the prison tuberculosis coordinator records the treatment outcome on the patient's treatment card and in the prison tuberculosis register. Table 10 provides the standardized definitions of treatment outcomes.

Table 10. Recording Treatment Outcome in Smear-Positive PTB Patients

Outcome	Definition
Cure	Patient who is sputum smear-negative, culture negative, or both in the last month of treatment and on at least one previous occasion
Treatment completed	Patient who has completed the full course of prescribed chemotherapy but for whom results of negative smear, culture, or both are not available
Treatment failure	Patient who, while on treatment, is bacteriologically positive at five months or later during the course of treatment Patient who is found to harbor an MDR strain at any point during the treatment
Death	Patient who dies for any reason during the course of treatment
Default	Patient whose treatment was interrupted for two or more consecutive months
Transfer out	Patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known

Note: Treatment success is defined as the sum of patients who are cured and those who have completed treatment.

All six outcomes are evaluated in sputum-smear positive patients. In smear-negative PTB and extrapulmonary TB patients, cure and treatment failure cannot be assessed with the use of sputum smear but can be assessed with the use of bacteriological culture (if available). Outcome indicators such as treatment completion, death, default, and transfer out, however, should be recorded for these patients in the prison TB register.

Monitoring and Managing Drug Toxicity

Monitoring of TB Patients for Significant Adverse Effects of Anti-TB Medicines

Most TB patients complete their treatment without any significant adverse effects from the medicines. A few patients, however, do develop adverse effects. Clinically monitoring patients during treatment is, therefore, important so that adverse effects can be detected promptly and managed properly. Routine laboratory monitoring is not necessary.

Health and prison personnel can monitor adverse effects of medicines by teaching patients how to recognize symptoms of common adverse effects and stressing the need to report if they develop such symptoms. Staff can also monitor adverse effects by asking about symptoms when patients report to collect their medications.

Prevention of Adverse Effects of Medicines

Health personnel can prevent some medicine-induced side effects, for example, isoniazid-induced peripheral neuropathy. This effect usually presents as a numbness, tingling, or burning sensation of the feet and occurs more commonly in pregnant women and in people with HIV infection, alcohol abuse, malnutrition, diabetes, and chronic liver disease. These patients should receive preventive treatment with pyridoxine (10 mg daily) along with their anti-TB medicines.

Adverse Effects of Anti-TB Medicines

The adverse effects of essential anti-TB medicines are listed in table 11, and those of SLMs are provided in "Management of Adverse Effects" (table 19) in chapter 14.

Table 11 provides a symptom-based approach to the most common adverse effects of the essential anti-TB medicines. Adverse effects are classified as minor or major. In general, a patient who develops minor adverse effects should continue the TB treatment, although sometimes at a reduced dose, and should receive symptomatic treatment. If a patient develops a major side effect, the treatment or the offending medicine is stopped. Further management depends on the nature of the adverse reaction. Patients with major adverse reactions should be managed in a hospital.

Table 11. The Adverse Effects of Essential Anti-TB Medicines

Side Effect	Medicine Probably Responsible	Management
Minor side effects		Continue anti-TB medicines Check medication doses
Anorexia Nausea Abdominal pain	Pyrazinamide Rifampicin	Give medicines with small meals or last thing at night
Joint pains	Pyrazinamide	Give aspirin.
Burning sensation in the feet	Isoniazid	Give therapeutic dose of pyridoxine (100 mg daily).
Orange or red urine	Rifampicin	Advise patients when starting treatment that this commonly happens and is normal.
Major side effects		Stop responsible medicine(s) Hospitalize patient
Itching Skin rash	Thioacetazone	Stop anti-TB medicines
Deafness (no wax on auroscopy)	Streptomycin	Stop streptomycin; use ethambutol
Dizziness (vertigo and nystagmus)	Streptomycin	Stop streptomycin; use ethambutol.
Jaundice (other causes excluded) Hepatitis	Isoniazid Pyrazinamide Rifampicin	Stop anti-TB medicines
Confusion (Suspect medicine-induced acute liver failure if jaundice is present)	Most anti-TB medicines	Stop anti-TB medicines Perform urgent liver function tests and a prothrombin time test
Visual impairment (other causes excluded)	Ethambutol	Stop ethambutol
Shock Purpura Acute renal failure	Rifampicin	Stop rifampicin

Management of Medicine-Induced Hepatitis

Most anti-TB medicines can damage the liver. Isoniazid, pyrazinamide, and rifampicin are most commonly responsible; ethambutol is rarely responsible. When a patient develops hepatitis during TB treatment, the treatment may be, but is not necessarily, the cause. Ruling out other possible causes is an important step before deciding that the hepatitis is medicine-induced.

If the diagnosis is medicine-induced hepatitis, the anti-TB medicines should be stopped and withheld until liver function tests have reverted to normal. Sometimes, performing liver function tests is not possible; in these situations, wait an extra two weeks after the jaundice has disappeared before recommencing TB treatment. Asymptomatic jaundice without evidence of hepatitis is likely due to rifampicin.

Once medicine-induced hepatitis has resolved, the same medicines are reintroduced one at a time. If the hepatitis produced clinical jaundice, however, avoid pyrazinamide. A suggested regimen in such patients is a two-month initial phase of daily streptomycin, isoniazid, and ethambutol followed by a 10-month continuation phase of isoniazid and ethambutol.

A severely ill TB patient with medicine-induced hepatitis may die without anti-TB medicines. In this case, treat the patient with two of the least hepatotoxic medicines: streptomycin and ethambutol. After the hepatitis has resolved, restart the usual TB treatment.

Suggested Reading for Chapter 11

WHO. 2008. *Tuberculosis Handbook*. Geneva: WHO.

Collaborative TB/HIV activities by NTPs and national HIV/AIDS programs should prioritize prisons, where prevalence of both diseases is often higher. The goal of these activities in prisons, as in any community, is to decrease the burden of TB and HIV. Specific objectives of the collaborative activities are threefold—

- Establish a mechanism for collaboration between both programs
- Decrease the burden of TB in people living with HIV/AIDS
- Decrease the burden of HIV in TB patients

Given the existing constraints that limit the movement of prisoners outside prisons for diagnosis and care, and given that the same health staff deal with all diseases inside a prison, prisons can implement one-stop, integrated TB/HIV care.

Mechanisms for Collaboration between Both Programs

An adequate mechanism should exist for collaboration between TB and HIV/AIDS programs at the local level and district public health services, and both should include prisons in their workplans. That is, all activities implemented in the community should also be made available for prisoners. Prison health representatives should be invited to participate in planning and strategizing meetings of the coordinating TB/HIV body. Their input is essential for the implementation of collaborative activities in these settings.

Surveillance of HIV Prevalence among TB Patients

Conducting HIV surveillance among TB patients is critical to understanding the trends of the epidemics and in developing appropriate interventions to address the problem. In prisons where the HIV prevalence among TB patients is not known, the program should carry out periodic or sentinel surveys to assess the situation. It is recommended that provider-initiated voluntary HIV testing and counseling of TB patients be implemented.[1]

Joint Planning and Mobilization for TB/HIV

Either by devising a joint TB/HIV plan or by incorporating TB/HIV components in their respective national, district, and local plans, the TB and HIV/AIDS programs should communicate and coordinate activities in prisons to prevent duplication of work and competition for resources. Prisons authorities and health staff also need to be engaged in planning. The roles and responsibilities of each program and of the prison staff need to be clearly defined, understood, and monitored.

Coordinated TB/HIV activities in prisons need to be embedded in the national, district, and local workplans of both programs; funding should be reflected accordingly in their budgets, based on agreed-upon tasks and responsibilities. More frequently, countries are including prison activities in their proposals to international funding mechanisms (e.g. GFATM).

TB/HIV Capacity Building

Capacity building of public health and prison personnel is crucial for delivering quality and effective TB/HIV interventions in prisons. The TB and HIV programs should provide joint preservice and in-service training for prison staff on TB/HIV activities as they do for public health personnel. The programs also need to ensure sufficient capacity (e.g., laboratory, medicines, referral mechanisms, and support systems) to deliver TB/HIV activities. The prison setting offers the advantage that the same health staff carries out all health-related activities and programs; thus, a one-stop approach can be implemented for TB/HIV activities.

Community Involvement in Collaborative TB and HIV Activities

NGOs and other groups, including churches may carry out different types of programs in prisons. These groups can get actively engaged in supporting TB/HIV activities in prisons. HIV/AIDS support groups can be involved in TB education and counseling and in identifying TB suspects. NGOs and similar groups can be mobilized to advocate for resources and opportunities to conduct TB/HIV activities.

Decreasing the Burden of TB in People Living with HIV

This strategy is commonly referred to as the three I's, which stand for—

- Intensified TB case finding (ICF)
- IPT for HIV-infected individuals
- Infection control

Establish ICF among Those Living with HIV/AIDS

ICF for tuberculosis involves screening for symptoms and signs of TB in settings with high HIV prevalence, with the objective of early diagnosis and treatment of persons living with HIV/AIDS and groups at risk high for HIV. In prisons, all persons living with HIV should be screened for TB either at the time of HIV diagnosis or before staring ART; these junctures are when TB is most likely to be detected. In addition, ICF should be carried out regularly thereafter (e.g., every six months)[2] and can be done with the aid of a simple questionnaire, often the same form used during entry screening of prisoners. If none of the listed symptoms is present, then the likelihood of TB is small; further screening may not be needed.

Studies have demonstrated that ICF and treatment among HIV-infected individuals prevents transmission[3] and mortality,[4] reduces the risk of nosocomial transmission due to earlier detection, and presents a chance for delivering IPT to those individuals without active TB.[5]

Providing IPT

HIV-infected individuals with LTBI can receive IPT to prevent them from developing active forms of TB. IPT has been demonstrated to reduce the risk of progression from latent infection to active TB by up to 60 percent. Its efficacy on survival and duration of the protection conveyed remains limited.[2]

IPT is part of the package of care for persons living with HIV/AIDS. The benefit of IPT has been studied among patients with a positive tuberculin test (TST). Many countries however, do not use or have access to TST. The lack of TST should no preclude programs from implementing IPT. In such settings IPT can be started without TST results[6] as part of the package of care for persons living HIV/AIDS. It is crucial, prior to initiating IPT, to rule out active tuberculosis based on the algorithm in Figure 2. IPT is given daily through self-administration for 6 to 9 months.

Implementing infection control measures in prisons

In congregate settings, including prisons, where TB and HIV are more prevalent, measures to prevent transmission are mandatory. These measures are aimed at reducing the exposure of prisoners, health and security staff, and visitors to *M. tuberculosis*; they are classified as programmatic, administrative, environmental and engineering, and personal protection. Of particular concern is the convergence of HIV infection and MDR-TB. Studies and surveillance data document the links between these epidemics, and evidence is clear that institutional outbreaks of MDR-TB have primarily affected HIV-infected persons.[7] In this context and with recent occurrence of XDR-TB among HIV patients, implementing infection control measures is an urgent matter that can no longer be neglected. A plan for infection control needs to be devised and funds for its implementation need to be mobilized. Chapter 18 discusses infection control measures in greater detail.

Decreasing the Burden of HIV in TB Patients

HIV Counseling and Testing of Prisoners with TB

A prisoner with TB may be well aware of the possibility of also having HIV infection. Offering counseling and voluntary HIV testing to prisoners with TB is important because of the following possible benefits—

- Prisoners may want to know their HIV status
- Access to ART is increasingly available in many countries, including in prison populations
- Better diagnosis and management of other HIV-related illnesses can be achieved when the HIV status is known
- Because some anti-TB medicines are more suitable for HIV-positive individuals, a better selection of medicines is possible when HIV status is clear
- Prisoners can be given health education to reduce high-risk activities and avoid further HIV transmission

Confidential counseling is essential before and after HIV antibody testing. The prisoner must understand what the test involves and what the implications of testing are, and he or she must give explicit informed consent. The counselor provides support. Counseling is a dialogue between the counselor and the person who is counseled. The Joint United Nations Programme on HIV/AIDS (UNAIDS) advocates against compulsory HIV testing. In a prison setting, a policy of compulsory HIV testing of prisoners with TB would be counter-productive because it would deter prisoners from seeking care, decrease HIV case-finding, and reduce the credibility of prison health services. Provider-initiated HIV testing and counseling (PITC) is recommended by WHO.[8] With PITC, prisoners can "opt-out" or decline testing when asked by a health care provider. The 2004 UNAIDS/WHO policy statement recommends that PITC be—

- Done for all patients, irrespective of epidemic setting, whose clinical presentation suggests underlying HIV infection
- Included as part of standard care for all seeking health care in generalized HIV epidemic areas
- Carried out more selectively in concentrated and low-level epidemics

Preventing HIV Transmission within Prisons

Since HIV is common in prisons and fuels TB, decreasing HIV transmission can contribute to TB prevention. The behaviors mainly responsible for HIV transmission in prisons are injecting drug use, sex between men, and piercing and tattooing with unhygienic tools. These behaviors are unacceptable to the legal and political authorities, and to the mass of social, cultural, and religious opinion in many countries. Authorities may deny that these activities take place, but denial does not solve the problem of HIV transmission in prisons and beyond prisons into the wider community, and furthermore, it presents a significant barrier to discussing ways to decrease HIV transmission in prisons. To respond to the challenge of HIV transmission in prisons, prison authorities must first acknowledge the occurrence of intravenous drug use and sex between men. Acknowledgment does not mean condoning or encouraging such activities but rather accepting a reality that exists in prison settings everywhere. TB and HIV/AIDS programs should collaborate to implement comprehensive HIV strategies that target sexual, parenteral, and vertical transmission of HIV.

Measures to reduce the sexual spread of HIV include promoting safer sexual behaviors and practices. The provision of condoms and the prevention of rape, sexual violence, and coercion are recommended. Evidence in many settings shows that condom access in prisons is not a threat to security or operations and does not lead to increased sexual activity. This measure is acceptable for both prisoners and staff.[9] To help minimize violence, prison staff training should include how to avoid unnecessary force or brutality and how to respect the rights, dignity, and well-being of prisoners. Additionally, all TB patients receiving care in prison clinics should be screened through a symptom-based approach for sexually transmitted infections and treated accordingly.

The measures for decreasing parenteral HIV transmission include ensuring the use of sterilized injections and surgical equipment in prison clinics.

Harm-reduction measures among injecting drug users are controversial and include the following—

- Providing substitution therapy (e.g., methadone for heroin addicts) or medically supervised detoxification
- Providing sterile needles and syringes in exchange for used ones
- Enabling prisoners to sterilize injecting equipment by providing full-strength liquid bleach
- Educating prisoners about HIV and drug-injecting (e.g., through the use of fellow prisoners or outreach workers who are themselves injectors or previous injectors)

Needle and syringe programs in prisons can challenge legal statutes and public opinion. Nevertheless, they have proven to be successful in the community. Currently, they are being implemented in prisons with different levels of funding and infrastructure in eastern Europe and central and southern Asia. Moreover, in these prisons, needle and syringe exchange programs are accepted by prisoners and have been shown to reduce sharing of syringes, thus reducing the risk of HIV and hepatitis B and C transmission. Contrary to expectations, these programs are not associated with increased drug use or injection in the prison nor have needles been used as weapons. Consequently, WHO and the United Nations Office on Drugs and Crime (UNODC) recommend that they be introduced in settings with high HIV prevalence among injection drug users.[9] Alternate options include distribution of bleach for disinfection of needles and syringes.

Co-trimoxazole Preventive Therapy

Administering prophylactic co-trimoxazole reduces mortality among smear-positive TB patients who are HIV-positive.[10] It also reduces hospitalization and morbidity among persons living with HIV/AIDS.[11] For tuberculosis patients, co-trimoxazole prophylaxis should be initiated irrespective of the CD4 cell count.

Effective HIV Treatment, Care, and Support

Equity to care for prisoners includes access to ART as part of comprehensive HIV/AIDS care. ART improves the quality of life and survival of those affected by HIV/AIDS. The availability of ART can be an incentive for people to get tested for HIV. ART also reduces the incidence of TB among persons living with HIV/AIDS.[12]

ART is becoming more available in developing countries and those in transition. As national HIV/AIDS programs scale up ART delivery, they need to consider increasing access to prisoners, including the high standard of care (e.g., specialist consultations, CD4 and viral load testing, and support systems) for prisoners equal to that implemented among the general population. Improved levels of care will be facilitated if prison departments are represented as part of the national HIV/AIDS coordinating committee. Prison departments should also be involved in the planning for scaling-up ART, so that funds are properly earmarked for prisons for all aspects of ART delivery (i.e., development, training, laboratory examinations, and monitoring and evaluation) and so that overall close communication and coordination are established to foster an equal partnership.

Diagnosis of TB Infection and Disease among People Living with HIV

Clinical Features

The clinical characteristics of TB may change in the context of HIV co-infection. Whereas TB may occur at any time during the course of HIV infection, symptoms and clinical patterns similar to those found in non-HIV individuals occur when CD4 counts are relatively high.[13] As an individual's immunity is suppressed (i.e., CD4 counts are lower), more severe forms of TB develop (e.g., extrapulmonary, meningitis, disseminated disease)[14] with particular signs and symptoms according to the site affected. In some cases, pulmonary and extrapulmonary TB occur concomitantly. Significantly, confirmed cases of TB have been found in individuals without symptoms at all.[15] Due to its diverse manifestations and potential differential diagnosis, HIV complicates the diagnosis of TB. Thus, TB should always be considered when dealing with confirmed or suspected HIV-positive persons.

Bacterial Examination and Radiographic Findings

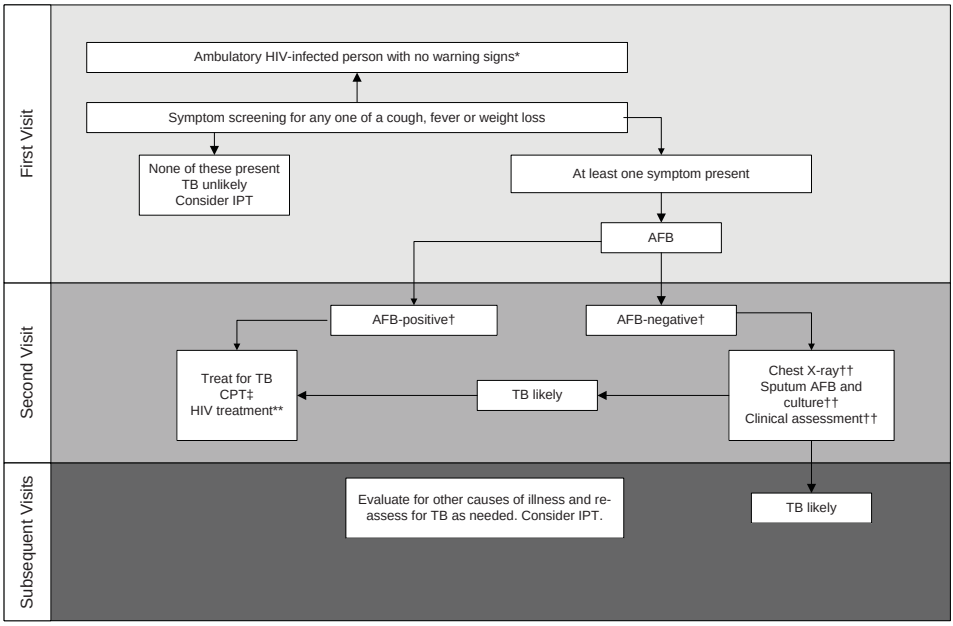
Although not always the case, multiple studies have shown how HIV-positive patients with confirmed TB are more likely to have smear-negative sputum, compared to individuals who are HIV negative. This important feature warrants that HIV-positive patients or those suspected of HIV infection be further evaluated for TB through sputum culture and chest radiography. Blood cultures of *M. tuberculosis* have also been shown to be a helpful diagnostic tool among patients with advanced HIV infection.

Chest radiography is essential when evaluating TB in the setting of HIV. Typical findings, including apical infiltrates and cavitations, are present in individuals with preserved immunity. As HIV infection progresses, and CD4 count drops, radiographic findings include hilar and mediastinal adenopathy, less or no cavitation, and involvement of middle and lower lobes of the lungs. In severe TB, miliary patterns are found in chest radiography.

Diagnostic Algorithm

Figure 2 illustrates the diagnostic approach for screening for tuberculosis for ambulatory persons living with HIV. WHO has issued another useful document with algorithms for the diagnosis of smear negative and extrapulmonary tuberculosis, based on HIV prevalence and resources;[16] it is available online at http://whqlibdoc.who.int/hq/2007/WHO_HTM_TB_2007.379_eng.pdf.

Of crucial importance is the acceleration of TB diagnosis, so that treatment is initiated as early as possible. TB is associated with increased mortality among people living with HIV, especially soon after exposure, before treatment is started, and during the first weeks or months after diagnosis.[17] It may also be related to subsequent opportunistic infections.



*Warning signs include any one of: respiratory rate > 30/minute, fever > 39 °C, pulse rate > 120/min and unable to walk unaided.
†AFB-positive is defined as at least one positive smear and AFB-negative as two or more negative smears.
‡CPT = Co-trimoxazole preventive therapy. Administer as per national guidelines.
** HIV treatment includes CD4 and clinical staging, as well as referral for HIV treatment
††The investigations within the box should be done at the same time wherever possible in order to decrease the number of visits and speed up diagnosis. If culture is not available, then the decision should be made based on chest X-ray and clinical assessment, as per national guidelines.

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Figure 2. Algorithm for TB screening for ambulatory people living with HIV

TB Treatment in HIV-Positive Patients

Response to Treatment

Studies show that TB patients who are co-infected with HIV respond well to the treatment regimen used for HIV-negative patients, that is, a regimen that includes isoniazid, rifampicin, ethambutol, and pyrazinamide for two months (initial (intensive) phase), followed by at least four months of isoniazid and rifampicin (see chapter 10 for dosing and other treatment recommendations). Patients improve clinically and tend to become sputum-negative soon after initiating therapy, granted that treatment is supervised. Relapse rates among HIV-infected patients are comparable to those among HIV-negative patients. In studies, relapse was not significantly associated with HIV infection. Instead, it was associated with drug-resistance and cavitary disease. Recent studies indicate earlier start of antiretrovirals can decrease the case fatality.

Toxicity

Co-infected TB/HIV patients seem to suffer more adverse reactions to first-line TB medications, particularly when using rifampicin-containing regimens. Patients who are receiving TB and ART at the same time are more likely to suffer adverse reactions, probably because of the coinciding toxicities. The most common side effects are peripheral neuropathy, rash, and gastrointestinal symptoms. Peripheral neuropathy is common among patients receiving isoniazid and stavudine or didanosine. Table 12 lists common adverse effects of TB and HIV medicines.

Table 12. Medicine- or Disease-Related Adverse Events

Adverse Event	TB or HIV Medicine Probably Responsible	Other Etiologies Possibly Associated with HIV
Hepatitis	Pyrazinamide, isoniazid, rifampicin, rifabutin, nevirapine, protease inhibitors, trimethoprim-sulfamethoxazole, paraminosalicylic acid (PAS), ethionamide	Viral hepatitis HIV-associated cholangiopathy Immune reconstitution syndrome (IRIS) Cytomegalovirus Epstein-Barr virus
Skin eruptions	Pyrazinamide, isoniazid, rifampicin, rifabutin, nevirapine, efavirenz, abacavir, trimethoprim-sulfamethoxazole, streptomycin	Eosinophilic folliculitis Scabies Psoriasis vulgaris Atopic dermatitis IRIS
Nausea and vomiting Diarrhea	Pyrazinamide, isoniazid, rifampin, rifabutin, zidovudine, ritonavir, Amprenavir, indinavir, trimethoprim-sulfamethoxazole, paraminosalicylic acid (PAS), ethionamide	Pancreatitis Cytomegalovirus Cryptosporidiosis
Hematological abnormalities (e.g., leukaemia, anemia, thrombocytopenia)	Rifampin, rifabutin, zidovudine, valgancyclovir, trimethoprim-sulfamethoxazole, isoniazid (rare)	HIV-related bone marrow suppression Idiopathic thrombocytopenic purpura Autoimmune hemolytic anemia
Visual disturbances	Ethambutol, rifabutin, voriconazole	Cytomegalovirus Retinitis IRIS Toxoplasmosis Varicella zoster virus Fungal infections

Adverse Event	TB or HIV Medicine Probably Responsible	Other Etiologies Possibly Associated with HIV
Neuropathy	Isoniazid, zalcitrabine, didanosine, stavudine, ethionamide, dapsone	Alcoholism Cytomegalovirus
Seizures	Isoniazid, cycloserine, fluoroquinolones, efavirenz	Central nervous system lesions (e.g., lymphoma, toxoplasmosis) Meningitis
Flu-like syndrome Sleep and psychiatric disturbances	Rifampicin, efavirenz, cycloserine	Acute HIV infection

Thiacetazone is associated with a high risk of severe, and sometimes fatal, skin reactions in HIV-infected individuals. Patients with known or suspected HIV infection should not receive thiacetazone.

Concomitant ART

In addition to increased toxicity, other complications to treating patients for TB and HIV simultaneously can arise, including medicine interactions, compliance issues, and the possibility of IRIS. For these reasons, patients must be managed by specialized or adequately trained personnel.

Medicine Interactions

In principle, TB patients who are living with HIV should receive the same TB treatment regimens as HIV-negative TB patients. Rifampicin, however, is associated with major interactions with HIV medicines, which may complicate management of co-infected patients receiving concomitant therapy. Specifically, rifampicin reduces the serum concentration of protease inhibitors and non-nucleoside reverse transcriptase inhibitors. Rifabutin has a similar effect but to a lesser extent. See table 11 (chapter 11) and table 12 (above). Rifamycins also interact with azoles. In a study, ketoconazole reduced the level of rifampicin, which may lead to acquired rifampicin mono-resistance.[18]

Recommended Medicine Regimens

Because of the complexity of managing co-infected patients with TB and ART regimens, consulting infectious disease specialists directly is highly recommended. Although when to start ART during TB treatment is not altogether clear, the common criteria are based on the level of immunosuppression (measured by CD4 count). WHO's recommended approach to initiating ART during TB treatment and treatment schemes is summarized in tables 13 and 14. Before taking responsibility for implementing ART in prison settings, staff must be fully aware of these issues, and strict adherence to treatment should be insisted upon.

Table 13. Procedure for a TB Patient Not on ART and CD4 Not Available[19]

Patient Clinical Status	How to Manage—When to Consult or Refer to Doctor or Medical officer
Patient has sputum smear-positive pulmonary TB only (no other signs of clinical Stage 3 or 4) and is gaining weight on treatment.	Start TB treatment. Reassess after initial phase of TB treatment to determine whether to start ART during TB treatment or after completing it.
Patient has sputum smear-negative pulmonary TB only (no other signs of clinical Stage 3 or 4) and is gaining weight on treatment.	Start TB treatment. Reassess after initial phase of TB treatment to determine whether to start ART during TB treatment or after completing it.
Patient has any pulmonary TB and has signs of clinical Stage 4 or thrush, pyomyositis, recurrent pneumonia, persistent diarrhea, new prolonged fever, or is losing weight on treatment, or patient shows no clinical improvement.	Start TB treatment, and refer the patient at once to the district medical officer for an ART co-treatment plan. ART probably needs to be started immediately.
Patient has extrapulmonary TB.	Start TB treatment, and refer the patient at once to the district medical officer for an ART co-treatment plan. ART probably needs to be started immediately.

Table 14. Procedure for a TB Patient Not on ART and CD4 Available

CD4 Count	How to Manage
If CD4 is <200/mm^3	Start TB treatment, and refer the patient at once to the district medical officer for an ART co-treatment plan. ART needs to be started as soon as TB treatment is tolerated (i.e., between two weeks and two months).
If CD4 is 200–350/mm^3	Start TB treatment. Refer the patient to the district medical officer for an ART co-treatment after initial phase (unless non-TB Stage 3 or 4 conditions are present; in that case, refer at once).
If CD4 is >350/mm^3	Start TB treatment. Defer ART until TB treatment is completed unless non-TB Stage 4 conditions are present.

Any HIV-positive patient receiving an anti-TB medicine regimen containing isoniazid should also receive pyridoxine (10 mg daily) to prevent peripheral neuropathy. Studies in several settings have shown that early start of ART in TB/HIV co-infected individual can reduce mortality considerably.

Immune Reconstitution Syndrome

IRIS is a temporary exacerbation of symptoms or radiographic signs (or both) of TB occurring soon after the start of treatment with ART and anti-TB medicines. IRIS most commonly presents with fever and a worsening of pre-existing respiratory disease or lymphadenopathy after initial improvement on TB treatment in patients who have started on ART in the past three months, although it can occur within five days. It is similar to, but more frequent than, the paradoxical reactions seen in immunocompetent patients on anti-TB therapy.

IRIS appears to be more common if ART is started early in the course of TB treatment. The diagnosis is clinical and one of exclusion, with the differentials including side effects of ART, failure of TB treatment because of drug resistance or poor adherence, failure of ART, or other underlying infection. Most cases resolve without any intervention, and ART can be safely continued. Occasionally, serious reactions, such as tracheal compression due to massive adenopathy or respiratory difficulty, may require the use of corticosteroids.

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FOLLOW-UP OF RELEASED PRISONERS—COMPREHENSIVE DISCHARGE AND REFERRAL PLAN

Discharge planning for soon-to-be-released prisoners is an important part of TB case management. It is essential in ensuring the continuity of TB management and therapy among persons with TB and LTBI. Following release, former prisoners face different problems including housing, employment, registration of residence, not to mention the social stigma attached to TB that still exists in many countries. These competing issues often take priority for prisoners over their health. Discharge planning should be implemented for prisoners with confirmed TB, suspected TB, and LTBI (based on country' policy).

The success of post-release follow-up relies on two factors: a structured system of referral between the prison and the community and interventions to increase adherence to TB treatment. Although these factors should be addressed by the NTP, often they are not.

Interventions from volunteer organizations (e.g., grass-roots organizations, faith-based organizations, international organizations) could help to improve the cure rate of prisoners released under treatment. Efforts to control TB in large cities in the United States in the early 1990s demonstrated that adherence to treatment could be successful using simultaneous incentives and enablers including covering transportation costs, providing daily (canned food) and weekly incentives (food parcels), and developing an active tracing capacity of social workers.[1]

When prisoners on TB treatment are released, they need to be followed up by the local health center, under the TB program of the NTP, or an organization collaborating with the NTP in the community. This follow-up often does not happen, however, especially in countries with the highest TB burden. In a Spanish setting, methadone treatment in drug addicted TB patients released from prison proved to be an effective tool.[2] A host of challenges need to be addressed to curb further TB transmission and lack of cure.

Under ideal conditions, the following practices should be implemented to the degree allowed by prison health staff, health center TB program manager (and district TB program supervisor-NTP), and local social services organization's capacity—

- Discharge or referral planning
- Post-release follow-up
- Notification of unplanned releases and transfers
- Monitoring of referrals

Discharge or Referral Planning

The following steps should be taken as soon as possible after diagnosis, to increase chances for curing prisoners' TB. Box 4 provides some additional tips about the discharge process.

- **Step 1**. Prison health staff as case managers should prepare for the prisoner's eventual release. Case managers should coordinate prisoner follow-up with outside health care providers (e.g., local health center or district TB supervisor from the NTP) to ensure continuity of TB treatment. If possible, prison health

staff should communicate with the TB health staff in the civilian sector about the following factors.

- Where will the prisoner reside after release?
- Will family or other social support be available?
- What kind of post-release assistance will be needed (e.g., housing, social services, TB or HIV/AIDS treatment, substance abuse or mental health services)?
- How well does the prisoner understand the importance of follow-up, and does he or she know how to access health care services?

- **Step 2**. Prisoners should receive education and counseling about TB. Peer educators have been demonstrated to be effective participants in this process. Peer educators can emphasize the importance of adhering to therapy and of notifying health staff in prisons if the prisoners are close to release or will be transferred to another penal facility.

- **Step 3.** While participating in treatment in prison, prisoners with TB should be asked to provide the following information—

  - Names, addresses, and telephone numbers of relatives and friends
  - Where he or she plans to live and seek health care. A prisoner may give incorrect location information for him- or herself and contacts because he or she fears recrimination, harassment, stigmatization, and even deportation. This misinformation represents a significant challenge to post-release health care. To avoid this possibility, prison health staff need to do the following—

    - Stress the difference between TB and criminal offence. Prison health staff and peer educators need to emphasize that the prisoner was not incarcerated for having TB; it is a separate health issue, unrelated to the offence.
    - Educate the prisoner's family and friends during visiting days about the consequences of defaulting on TB treatment. Inform visitors of the need to encourage patients to visit the health center and to continue therapy if released from the prison clinic or if transferred to another facility. During this educational and awareness raising session with a prisoner's family and friends, confirm the address and contact information provided by the prisoner.

Box 4. Tips for Discharge or Referral Planning

- Prison health staff as case managers should be capable of establishing rapport with prisoners to help prisoners understand and appreciate the importance of TB follow-up.
- Families and friends visiting the patient in prisons must be educated and made aware of the importance of adhering to treatment and consequences of default.
- Fellow prisoners may be trained as peer educators to support treatment adherence measures. Peer educators can be effective in assisting this process.

Post-Release Follow-up

When release dates are known, the following measures can contribute to an easy transition—

- A functional mechanism for following up referrals needs to be established with support from both prison and public health sectors. Such mechanisms must clearly outline the defined roles and tasks that will ensure successful referrals.
- Wherever possible, the prisoner should be introduced (preferably face to face) to the TB program manager or district TB program supervisor who is responsible for treatment and care in the community (local health center staff and district NTP).
- Setting post-release appointments at the local health center has been demonstrated to improve compliance.
- Prison health staff should complete a referral form (part of the NTP's information system forms) for the prisoner to provide to the local health center staff where he or she will continue treatment in the community. A copy should be kept in the prison and a second copy sent to the regional area or district NTP manager. The same procedure applies to prisoners who are transferred to another prison.
- A referral register is a useful tool to monitor and evaluate referrals. Feedback information should be entered in the referral register. This register is kept at the prison or by the area (province, district) NTP supervisor, or at both locations.
- Under limited conditions, prisoners with TB should be given a supply of medication at release that is adequate to last until the next medical appointment. Under many circumstances, prisoners will sell or barter TB medications outside prison, so this practice needs to be assessed and determined on an individual basis.

Depending on local resources and capacity, prison and NTP local staff can work with advocacy groups or private or government-funded programs to facilitate a safe, supported transition into the community. Substance use, mental health conditions, and poverty affect health care, medication adherence, housing opportunities, social relationships, and employment. These hardships will most likely be the greatest barriers to continuity of care for TB. Mental illness can be a significant barrier when service

providers have not been trained to interact with mentally ill patients. Persons who are mentally ill or use illicit drugs may have difficulties keeping medical appointments. Collaboration between prison staff and the NTP (or other appropriate agency) can facilitate, when resources permit, placement of newly released prisoners in substance abuse or mental health treatment programs to improve the likelihood of social stabilization and continuity of care.

NGOs and churches working in prisons can play a pivotal role in assisting with following up prisoners undergoing TB treatment after release from prison. They should be sought out and convened during planning and monitoring activities. Establishing partnerships with them that include well-defined tasks and responsibilities is essential. Box 5 describes prisoner release field experience in three settings.

Box 5. Field Experience: Preparing for Prisoner Release

Republic of Georgia

In the Republic of Georgia, the International Committee of the Red Cross started a pilot project in coordination with the MoJ, using the existing parole regulation that compels released prisoners to register regularly. This opportunity will be used to provide education and incentives to increase adherence and should ideally decrease the defaulter rate.

Cambodia

In Cambodia, Prison Fellowship–Cambodia implements a project to assist with the transition of prisoners back into society. Upon the prisoners' release, the organization provides services that include free medical check-ups; assistance with referrals to hospitals, health centers, and other NGOs that provide health care; counseling and mediation with families (including confirming the families' addresses); daily free meals; help in finding accommodation; and teaching skills that will help in finding a job. This organization has been identified as a potential key player to assist the NTP in preventing the interruption or default of TB treatment by released prisoners, including DOT.

Russia

The Russian Red Cross sends in civilian social workers to counsel and prepare prisoners who will be released on post-release care. The prisoners trust the civilian psychologists and social workers, who are not seen as part of the prison system.

Notification of Unplanned Release and Unplanned Transfers

Administrative procedures should be in place at the prison for the unscheduled discharge of prisoners being managed or treated for TB. Prison health staff should be notified of all scheduled and unscheduled releases as information becomes available. Prompt remedial steps need to be taken in collaboration with the local and regional (i.e., area, district) NTP supervisors to guarantee that the released TB patients (or patients transferred to another facility) visit the local health center and continue therapy there. For this notification, prompt communication via telephone, text messages, and other rapid methods are encouraged. The patient's treatment card (or a copy of it) must be sent to the receiving health care facility that will follow-up with the patient.

Monitoring of Referrals

Any strategy to follow up released prisoners requires allocation of human and financial resources, monitoring mechanisms, and a solid coordination with the NTP. Two indicators are useful for monitoring of released prisoners:

- Rate of registration of referrals in TB treatment units
- Treatment completion rate of referred patients

Data to calculate these indicators can be obtained from referral forms, the patient referral register, and the basic management unit TB register.

Endnote for Chapter 13

1. CDC. 1993. Approaches to Improving Adherence to Antituberculosis Therapy--South Carolina and New York, 1986-1991. *Morbidity and Mortality Weekly Report 42*(04): 74-75,81.
2. A. Marco, J. A. Caylà, M. Serra, et al. 1998. Predictors of Adherence to Tuberculosis Treatment in a Supervised Therapy Programme for Prisoners before and after Release. Study Group of Adherence to Tuberculosis Treatment of Prisoners. *European Respiratory Journal* 12: 967–71.

Suggested Reading for Chapter 13

WHO Regional Office for Europe. 2007. Status Paper on Prisons and Tuberculosis. Copenhagen: WHO. http://www.euro.who.int/Document/E89906.pdf

Case management of drug-resistant tuberculosis, particularly MDR-TB (and XDR-TB), in prisons should follow the same protocols and guidelines used for patients in the community, that is they should be treated under the drug-resistant TB program that is under the responsibility of the NTP or other recognized NTP partners with experience working with MDR-TB patients and in prisons (see table 15).

Table 15. Components of the DOTS Strategy as Applied to MDR-TB

Component	Elements
Sustained political commitment	• Addressing the factors leading to the emergence of MDR-TB • Long-term investment of staff and resources • Coordination of efforts between communities, local governments, and international agencies • A well-functioning program
Appropriate case-finding strategy, including quality-assured culture and DST	• Rational triage of patients into DST and the drug-resistant TB control program • Relationship with supranational TB reference laboratory
Appropriate treatment strategies that use SLMs under proper case management conditions	• Rational treatment design • DOT • Monitoring and management of adverse effects • Properly trained human resources
Uninterrupted supply of quality assured SLMs	
Recording and reporting system designed for drug-resistant TB control programs that enables performance monitoring and evaluation of treatment outcomes	

Source: WHO. 2008. *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis. Emergency Update.* Geneva: WHO

Pathogenesis of Drug Resistance and Definitions

Although its causes are microbial, clinical, and programmatic, drug-resistant TB is essentially a manmade phenomenon. From a microbiological perspective, resistance is caused by a genetic mutation that makes a medicine ineffective against the mutant bacilli. From a clinical and programmatic perspective, the cause is an inadequate or poorly administered treatment regimen that allows a drug-resistant strain to become the dominant strain in a patient infected with TB. Through random genetic mutation, TB strains may become resistant to any of the anti-TB medicines currently available. During treatment of active disease, at the level of the patient, these resistant strains may be "selected" and propagated through "inadequate" treatment. Inadequate treatment occurs when an insufficient number of anti-TB medicines are used, incorrect medicine dosing is prescribed, interruptions in therapy occur, or therapy of too short duration is given. Once these resistant organisms are selected and multiply, an affected patient will no longer respond to standard TB therapy and becomes an acquired resistance TB case (i.e., someone who has received at least one month of anti-TB therapy). These patients subsequently spread their resistant disease to their contacts who often become sick with the same resistant stain transmitted by the original patient. This type of newly diagnosed case is called a primary resistance TB case. In the prison setting, the propagation of drug-resistant TB is magnified and rapidly becomes a mixture of resistance among new and previously treated patients.

Factors that contribute to the generation of drug resistance can be divided into those related to the health care providers, the medicines used, and the patients undergoing therapy. Prisoners may have had an unfinished course of TB treatment in the past and, due to poor adherence, have a greater chance of contracting drug-resistant TB. Table 16 summarizes most common clinical and programmatic reasons for development of drug resistant TB.

Table 16. The Most Common Causes of Drug Resistance

Health Care Providers: Inadequate Regiments	Medicines: Inadequate Supply or Quality	Patients: Inadequate Medicine Intake
Inappropriate guidelines Noncompliance with guidelines Absent guidelines Poor training No treatment monitoring Poorly organized or funded TB control programs Poor adherence (or poor DOT, unmotivated staff)	Poor quality Unavailability of certain medicines (stock-outs or delivery disruptions) Poor storage conditions Wrong dose or combination	Poor adherence Lack of information Lack of money (no treatment available free of charge) Lack of transportation Adverse effects Social barriers Malabsorption Substance dependency disorders

Source: Adapted from WHO. 2008. *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis. Emergency Update.* Geneva: WHO

Diagnosis of MDR-TB and XDR-TB

An MDR-TB case is defined as a patient who is identified as infected with a strain that is resistant to at least isoniazid and rifampicin. XDR-TB is one that is resistant to isoniazid, rifampicin, plus any fluoroquinolone, and at least one of three injectable SLMs (amikacin, kanamycin, or capreomycin). The only way to confirm MDR-TB and XDR-TB is through DST of first- and second-line medicines, respectively.

In developing countries, DST is mostly done in reference laboratories that are part of the NTP network. DST on solid cultures (egg-based or agar-based) can be performed as direct or indirect tests. The former has the advantage that results are available sooner. Direct tests are also more representative of the patient's original bacteria. When results are not valid using the direct method due to insufficient or excessive bacterial growth or contamination, however, the test must be performed again with an indirect method (pure culture). WHO recommends three types of methods for DST in Lowenstein-Jensen (solid) media: (1) the indirect proportions method, (2) the resistance ratio method, and (3) the absolute concentration method. The indirect proportions method is most popular. Under program conditions, the total turnaround time is 10 to 12 weeks, from inoculation on culture media to determination of resistance patterns.

Other more rapid tests for assessing MDR and XDR-TB, which use solid and liquid media with either automated, semiautomated, or non-automated systems, are becoming more widely used. These systems include BACTEC-460 and BACTEC-960 (MGIT-960), microscopic-observation for drug susceptibility (MODS) testing, and colorimetric methods. Other rapid tests include genetic methods such as the line probe assays that identify genes associated with resistant mutation and bacteriophage-based assays (FAST-Plaque-TB), which identifies growing *M. tuberculosis* in the presence of isoniazid and rifampicin.

In areas where DST is limited due to cost, maintenance, and untrained personnel, only patients suspected of MDR-TB or XDR-TB should be evaluated with culture and DST. WHO's *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis* lists the following groups of patients living in resource-poor settings for whom DST should be prioritized due to an increased risk of drug-resistance[1]—

- Patients who have experienced failure of re-treatment regimens; chronic TB cases
- Individuals who have had exposure to a known MDR-TB case
- Patients who have experienced failure of Category I
- Individuals who have experienced failure of anti-TB treatment in the private sector
- Patients who remain sputum smear-positive at the second or third month of short-course chemotherapy
- Patients who have relapsed and returned after default without recent treatment failure
- Individuals who have had exposure in institutions that have MDR-TB outbreaks or a high MDR-TB prevalence

- Individuals who live in areas with high MDR-TB prevalence (i.e., in prisons in high-prevalence countries)
- Patients who have a history of using anti-TB medicines of poor or unknown quality
- Patients who received treatment in programs that operate poorly (especially programs with recent or frequent drug stock-outs)
- Patients with comorbid conditions associated with malabsorption or rapid-transit diarrhea
- Individuals with HIV, in some settings

Even more important than DST, a meticulous and complete medical history of the patient is extremely valuable when investigating drug resistance. This history should review previous anti-TB treatments taken, results of such treatments, contact with MDR-TB cases, and drug-susceptibility patterns of those contacts. This information can be retrieved by interviewing the patient and cross-checking his or her medical chart and NTP records.

Treatment of MDR-TB

Selection of Medicines Used in MDR-TB (and XDR-TB) Regimens

In the WHO consensus guidelines on drug-resistant TB management, medicine choices are grouped into five distinct categories (table 17). In designing a treatment regimen, all first-line anti-TB medicines (Group 1 agents) with preserved potency should be included. An injectable agent (Group 2) with preserved efficacy should also be incorporated. Fluoroquinolones (Group 3) have demonstrated a bactericidal effect against TB and should be included if resistance testing reveals susceptibility to these agents. Susceptibility to fluoroquinolones has been shown to be an independent predictor of cure among MDR-TB patients. The number of Group 4 agents added depends on the number of agents available from the previous groups. Thiacetazone should be avoided in TB patients with HIV given its association with severe skin eruptions, including Stevens-Johnson syndrome in individuals with HIV. Group 5 agents have unclear efficacy and should not be used routinely.

Table 17. Groups of Anti-TB Medicines

Grouping	Medicines
Group 1—First-line oral anti-TB agents	Isoniazid, rifampicin, ethambutol, pyrazinamide, rifabutin
Group 2—Injectable anti-TB agents	Kanamycin, amikacin, capreomycin, streptomycin
Group 3—Fluoroquinolones	Levofloxacin, moxifloxacin, ofloxacin
Group 4—Oral bacteriostatic SLMs	Ethionamide, protionamide, cycloserine, terizidone, P-aminosalicylic acid
Group 5—Anti-TB agents with unclear efficiency or unclear role in MDR-TB treatment (not recommended by WHO for routine use in MDR-TB patients)	Clofazimine, linezolid, amoxicillin/clavulanate, thioacetazone, clarithromycin, imipenem

Source: WHO. 2008. *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis. Emergency Update.* Geneva: WHO.

Note: Thioacetazone should be used only in patients documented to be HIV-negative and should usually not be chosen over other medicines listed in Group 5.

Principles of Management

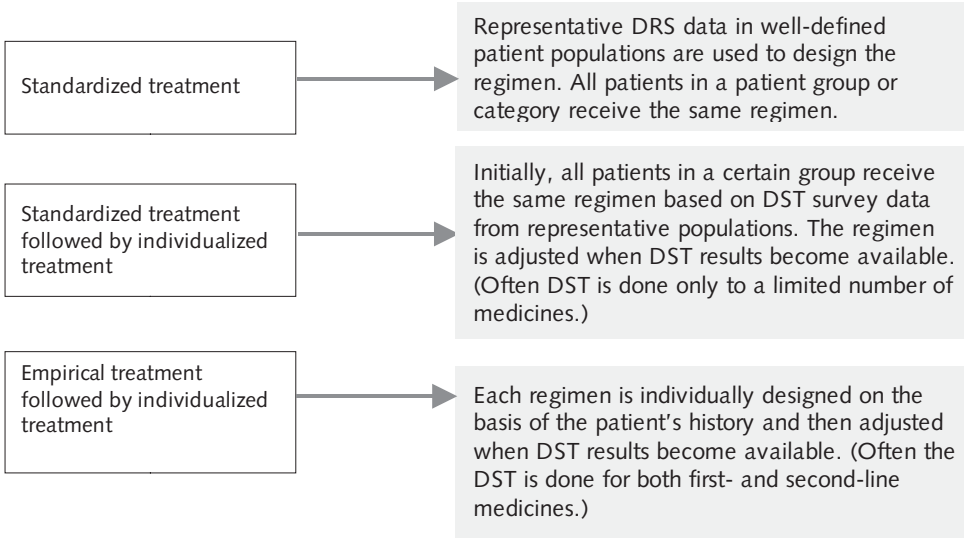
The treatment of MDR-TB is particularly difficult and should be managed by, or in close consultation with, an expert in the field through an MDR-TB control program. Recommended treatment regimens for MDR-TB are identical for HIV-positive and HIV-negative patients, except for the required adjustment of medications and dosages as dictated by concomitant ART. WHO guidelines for selecting treatment regimens for MDR-TB follow several core principles (box 6).

Box 6. WHO Core Principles for Selecting MDR-TB Treatment Regimens

1. The choice of regimen should be made based on the history of prior medicine exposure.
2. The local prevalence of resistance to anti-TB agents should be taken into consideration.
3. *Regimens should include at least four medicines that are almost certain to be effective* for the patient's isolate, based on quality-assured drug-susceptibility testing.
4. Medicines should be administered at least six days a week.
5. Medicine dosing should be based on the patient's weight.
6. An injectable agent (e.g., aminoglycoside or capreomycin) should be used for a minimum of six months, with at least four months of continued injectable therapy after culture conversion. Thrice weekly regimens of injectable agents can be considered after the first two to three months.
7. Treatment should be continued for a minimum of 18 months after culture conversion.
8. DOT should be used throughout treatment.
9. Drug-susceptibility testing, where available, should guide regimen design.
10. Pyrazinamide can be used throughout the treatment course.
11. Early detection of MDR-TB and the rapid initiation of effective treatment are key elements to achieve success.
12. When possible, pyrazinamide, ethambutol, and fluoroquinolones should be given once per day because the high peaks attained in once-a-day dosing may be more efficacious. Once-a-day dosing is permitted for other SLMs depending on patient tolerance; however, ethionamide/protionamide, cycloserine, and P-aminosalicylic acid have traditionally been given in split doses during the day to reduce adverse effects.
13. Treatment of adverse medicine effects should be immediate and adequate to minimize the risk of treatment interruptions and prevent increased morbidity and mortality due to serious adverse effects.

Treatment Strategies

Three options or types of treatment schemes are recommended by WHO (figure 3). These schemes use information obtained from DST results and drug-resistance surveillance within the local population. The latter can also be obtained from drug-resistance surveys.



Source: WHO. *2008. Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis. Emergency Update* Geneva: WHO.

Figure 3. The three treatment schemes recommended by WHO

Standardized Regimens

Certain groups of TB patients suffering from MDR-TB can be treated with standardized schemes that are not based on individual DST results. This approach is used in many developing countries where NTPs cannot afford to do DST on every MDR-TB suspect or where a drug-resistance pattern is epidemiologically well-defined. This strategy can be used to manage patients who are considered at high risk for MDR-TB (e.g., chronic TB cases). In some settings, patients who have failed Category I that included isoniazid and rifampicin in the continuation phase may have developed MDR-TB; they may be considered for treatment with standardized regimen for MDR-TB. Even though standardized regimens are used, NTPs need to conduct DST to identify groups with increased risk of MDR-TB (and XDR-TB), help design standardized regimens, and help to confirm utility of such regimens.

Individualized Regimens

These regimens are more clear-cut because they are based on DST results. Nevertheless, physicians should be cautious when interpreting DST results. DST should support other evidence including past treatment history and exposure to the medicine in question. DST does not predict with 100 percent certainty the effectiveness or ineffectiveness of a medicine. DST of medicines such as ethambutol, streptomycin, and Group 4 and 5 medicines does not have high reproducibility and reliability; these guidelines strongly caution against basing individual regimens on DST of these medicines. Lastly, additional resistance may have developed during the time since the specimen was collected for DST, given that the turnaround time under program conditions is lengthy.

In designing treatment regimens from MDR-TB, whether standardized or individualized, providers should follow the management principles listed in "Principles of Management" above. Table 18 presents steps in designing treatment regimens of MDR-TB patient.

Table 18. Designing Treatment Regimens

Step Number	Step Action	Comment
1.	Use any available— **Group 1: First-line oral agents** Pyrazinamide Ethambutol	Begin with any first-line agents that have certain, or almost certain, efficacy. If a first-line agent has a high likelihood of resistance, do not use it. (For example, most Category IV regimens used in treatment failures of Category II do not include ethambutol because it is likely to be resistant based on treatment history.)
2.	Plus one of these— **Group 2: Injectable agents** Kanamycin (or amikacin) Capreomycin Streptomycin	Add an injectable agent based on DST and treatment history. Avoid streptomycin, even if DST suggests susceptibility, because of high rates of resistance with MDR-TB strains and higher incidents of ototoxicity.
3.	Plus one of these— **Group 3: Fluoroquinolones** Levofloxacin Moxifloxacin Ofloxacin	Add a fluoroquinolone based on DST and treatment history. In cases where resistance to ofloxacin or XDR-TB is suspected, use a higher generation fluoroquinolone, but do not rely upon it as one of the four core medicines.
4.	Pick one or more of— **Group 4: Second-line bacteriostatic agents** P-aminosalicylic acid Cycloserine (or terizidone) Ethionamide (or protionamide)	Add Group 4 medicines until you have at least four medicines likely to be effective. Base your choice on treatment history, adverse effect profile, and cost. DST is not standardized for the medicines in this group.

Step Number	Step Action	Comment
5.	Consider using one of these— **Group 5: Medicines of unclear role in MDR-TB treatment** Clofazimine Linezolid Amoxicillin/clavulanate Thioacetazone[a] Imipenem/cilastatin High-dose isoniazid Clarithromycin	Consider adding Group 5 medicines in consultation with an MDR-TB expert if there are not four medicines that are likely to be effective from Groups 1–4. If medicines are needed from this group, it is recommended to add at least two. DST is not standardized for the medicines in this group.

Source: Adapted from F. J. Curry. 2004. *Drug-Resistant Tuberculosis: A Survival Guide for Clinicians.* San Francisco: National Tuberculosis Center and California Department of Health Services.

[a] Thioacetazone is contraindicated in HIV-infected individuals given the serious risk of life-threatening adverse reaction.

Monitoring of Patients

Patients should be monitored closely for signs of treatment failure. Clinically, the most important way to monitor response to treatment is through regular history-taking and physical examination. The classic symptoms of TB—cough, sputum production, fever, and weight loss—generally improve within the first few months of treatment and should be monitored frequently by health care providers. The recurrence of TB symptoms after sputum conversion, for example, may be the first sign of treatment failure. Monthly smear and culture monitoring should be preformed until conversion, with *conversion* defined as two consecutive negative smears and cultures taken 30 days apart. After conversion, the minimum periods recommended for bacteriological monitoring is monthly for smears and quarterly for cultures. Usually culture conversion occurs within the first two to three months of therapy.[2] If smears or cultures continue to be positive after three months of treatment, the regimen should be reassessed, DOT questioned, and DST performed. After conversion and until the end of treatment, smear and cultures should be done every two months. Response to therapy can also be evaluated by improvement of symptoms and signs (e.g., weight loss, cough, malaise, fever).

Management of Adverse Events

Although rarely life threatening, the adverse effects of SLMs can be debilitating for patients. Patients experiencing high rates of adverse effects may be at increased risk of nonadherence. Therefore, early and effective management of adverse effects should be part of adherence-promotion strategies in the management of drug-resistant TB. In most cases, management of adverse effects can be accomplished using relatively simple and low-cost interventions without compromising the integrity of the drug-resistant TB treatment regimen. Potential side effects of SLMs, and recommended management, are listed in Annex 7.

Nutritional Support

In addition to causing malnutrition, drug-resistant TB can be exacerbated by poor nutritional status. Without nutritional support, patients, especially those already suffering from baseline hunger, can become enmeshed in a vicious cycle of malnutrition and disease. The SLMs can also further decrease appetite, making adequate nutrition a greater challenge.

Vitamin B6 (pyridoxine) should also be given to all patients receiving cycloserine or terizidone to prevent neurological adverse effects. Vitamin (especially vitamin A) and mineral supplements can be given in areas where a high proportion of patients have these deficiencies. If minerals are given (e.g., zinc, iron, calcium), they should be dosed apart from the fluoroquinolones because they can interfere with the absorption of these medicines.

Role of Surgery in Treatment of MDR-TB

Surgical therapy, with resection of involved lung tissue, is considered as adjunctive therapy for those with MDR-TB. Surgery may be particularly useful for those with localized disease who are refractory to pharmaceutical therapy. Surgical intervention for MDR-TB has been shown to be associated with improved outcomes and effective with low complication rates when performed at a center with expertise in this area.[3] Effective anti-TB pharmaceutical therapy remains a critical component, however, and in general should be given for at least two months before surgical intervention and for at least 12 to 24 months afterward.

Endnotes for Chapter 14

1. WHO.*Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis.* 2008. *Emergency Update*. Geneva: WHO.
2. C. Mitnick, J. Bayona, E. Palacios, et al. 2003. Community-Based Therapy for Multidrug-Resistant Tuberculosis in Lima, Peru. *New England Journal of Medicine* 348(2):119–28.
3. R. S. Francis and M. P. Curwen. 1964. Major Surgery for Pulmonary Tuberculosis: Final Report. A National Survey of 8232 Patients Operated on from April 1953 to March 1954 and Followed up for Five Years. *Tubercle* 45(Suppl.): 5–79.

Suggested Reading for Chapter 14

S. Moadebi, C. K. Harder, M. J. Fitzgerald et al. 2007. Fluoroquinolones for the Treatment of Pulmonary Tuberculosis. *Drugs* 67(14):2077–99.

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R. Coninx, G. E. Pfyffer, C. Mathieu, et al. 1998. Drug Resistant Tuberculosis in Prisons in Azerbaijan: Case Study. *British Medical Journal* 316: 1493–95.

Tuberculosis Coalition for Technical Assistance (TCTA). 2006. *International Standards for Tuberculosis Care (ISTC).* The Hague: TCTA. www.who.int/tb/publications/2006/istc_report.pdf.

15. SYSTEMATIC APPROACH TO INTRODUCING A TB CONTROL PROGRAM IN PRISONS

Prison health services are often ill-equipped to respond to the challenge of implementing effective TB control. Health is usually not a priority for prison authorities because they tend to be more concerned with fulfilling another important function of the prison: keeping prisoners *inside* the facility. Recognizing TB as an important health care problem specific to prisons may be the first step to taking the appropriate actions, both preventive and curative. This recognition may also facilitate the allocation of funds required to deal with the problem. Consequently, the NTP needs to take the lead in integrating the Stop TB Strategy activities into prison health services, as well as considering these units when planning, budgeting, supervising, and evaluating their program. Prison administrations and the national TB control program play a crucial part in drawing attention to prison health in general but also in moving TB higher in the political and public health agendas and pushing for wider recognition in political circles that good prison health equals good public health.

Resources available to prisons vary by country and within each country. Consequently, activities recommended under the Stop TB Strategy must be implemented to the extent permitted by available resources and adapted according to the local situation. Generally, prisons with more resources tend to be more independent and function with more autonomy. Smaller prisons and those with more limited budgets rely more on their counterparts from the public health sector.

Some countries are moving to reform their systems so that prison health services become the responsibility of the MoH and no longer that of the MoJ. Under this arrangement, recommendations on the organization of TB control programs in prisons may differ significantly from those outlined in this document and illustrated in figure 4.

Regardless of the situation, prison health services and the NTP should strive for a standardized system, which would facilitate program implementation, evaluation, and scale-up. Figure 4 illustrates how Stop TB Strategy activities can be delivered in prisons through sequential steps; figure 5 shows an organization chart for establishing a prison-civilian network from the central to the local level.

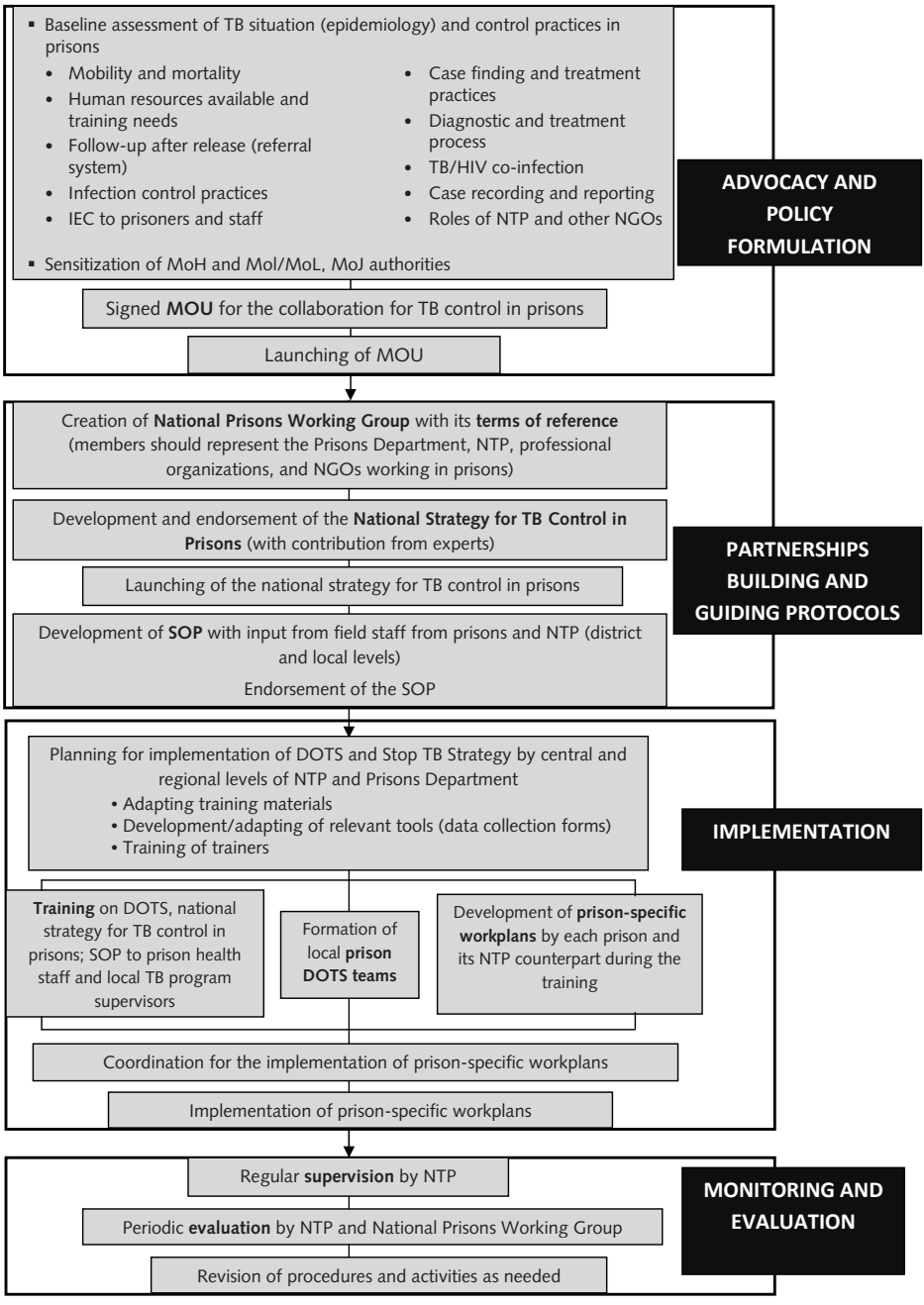

Figure 4. Phases in the development and establishment of a TB control program in prisons

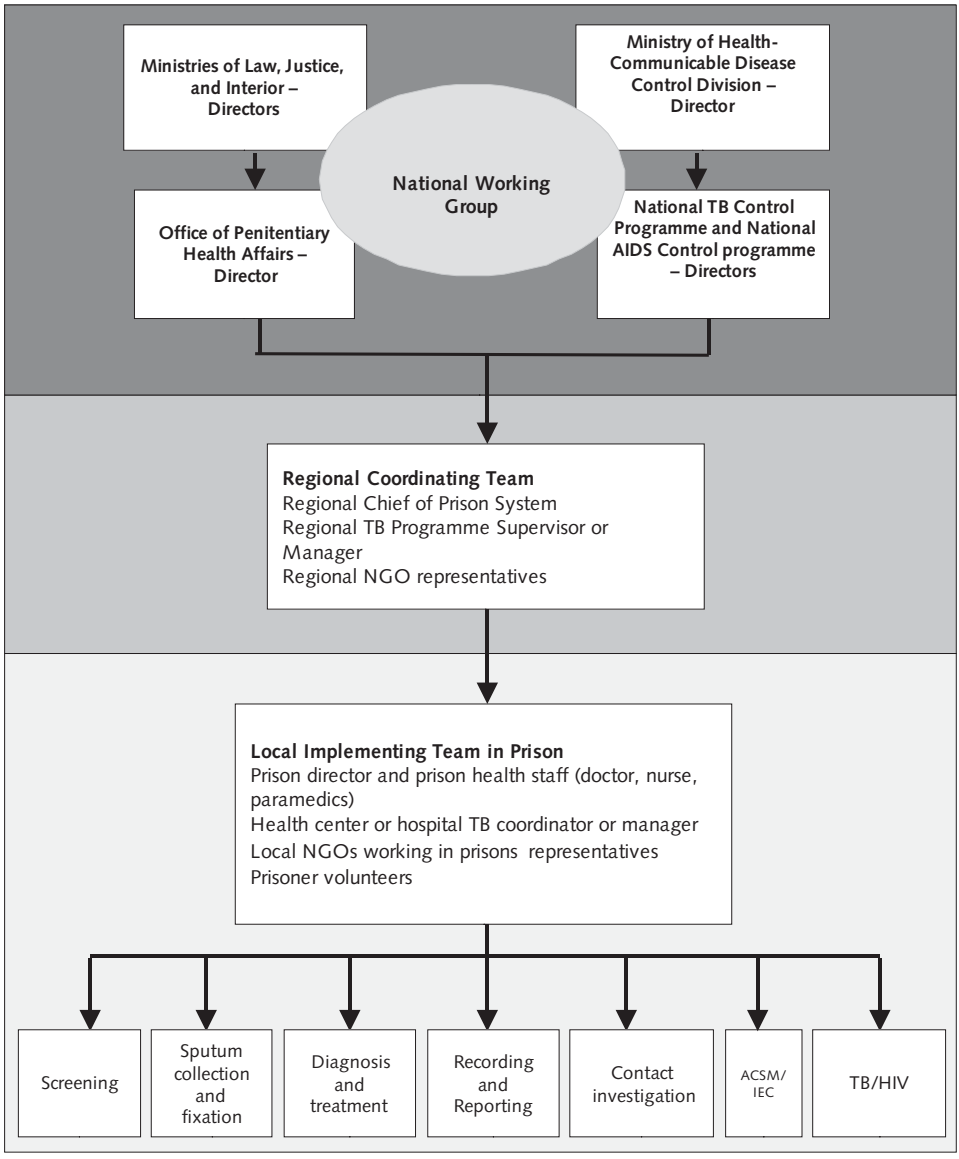

Figure 5. Sample organizational chart

Advocacy, Partnerships, and Policy Formulation

An initial and crucial component of implementing an integrated TB control program in prisons, in line with the new Stop TB Strategy, is to seek and consolidate support from other stakeholders and donor agencies. In addition to the penitentiary sector, other public health programs (e.g., HIV/AIDS programs), professional associations (e.g., academic and specialty societies), and community organizations should be involved. One purpose of conducting advocacy is to establish effective partnerships that will initiate and sustain the implementation of a sound TB control program. These partnerships should bring together key prison sector representatives—from the national and subnational (i.e., regional, provincial, district, and local) levels, the NTP, and academia and other NGOs working in prisons—into a coordinating body or national working group, which would facilitate operations, monitor activities and outputs, and leverage institutional commitment. Stakeholders of this interagency working group share common goals and assume mutual responsibility for TB control in the prison setting.

The TB control program in prisons should be implemented within a formal policy framework. The national working group, though its terms of reference, should actively participate in policy formulation, including the development of a memorandum of understanding or letter of agreement. Additionally, this interagency group would be actively engaged in the development of a national strategy for TB control in prisons (which may or may not be part of a comprehensive public-private mix national strategy) following the issues and recommendation in this document. The national working group should monitor and evaluate strategies and disseminate findings to gain further support for the program.

An important goal is to raise awareness of the problem, engage other partners, and secure the allocation of funds for prison TB control activities within existing government budgets and from donor organizations. Prison TB control should be a strategy incorporated into national, regional, and local budgets as well as into grant applications to bilateral and global funding mechanisms (e.g., GFATM). Funds obtained would close gaps that could hamper implementation of the Stop TB Strategy in prisons. Prisons should have equitable access to resources for different activities (e.g., diagnosis; treatment; and information, education, and communication [IEC]), depending on needs, similar to those available for primary care facilities in the community.

Developing Guiding Protocols and Establishing Local TB Control Teams

Once the TB epidemiology and case management situation in prisons has been assessed through a situation analysis, stakeholders can jointly develop a national strategy for TB control in prisons that will guide the implementation of DOTS and the Stop TB Strategy activities. This guiding document must be endorsed by the MoH and prison counterpart MoI, MoJ, or MoL. An additional helpful tool is an operational plan targeted at local program implementers (e.g., prison health staff and local NTP managers and supervisors). The operational plan would outline steps to be taken by prison health and administrative staff and their local counterparts from the health centers and district level NTPs for case detection, treatment, case recording and reporting, advocacy communication and social mobilization (ACSM), and infection control measures.

This document would define objectives, actors and roles, tasks, tools, and indicators.

Before rolling out the program in prisons, the NTP and stakeholders should adapt available materials for training, data collection, and monitoring and evaluation to the prison context if necessary. Development of new materials may be required for specific issues related to prisons (i.e., screening, contact investigation, infection control measures, flow of information). Ideally, any materials would be validated for content, clarity, and utility in a given context. (See useful implementation tools in table 20.)

Table 20. Practical Tools

Components	Tools
Advocacy	• National strategy for TB control in prisons • National directive (or other policy document) endorsed by MoH and MoJ and other relevant ministries • ISTC • Memoranda of understanding • National prison working group with terms of reference
Planning and implementation	• Baseline assessment form • SOP • Prison-specific workplans • NTP forms and registries
Training and human resource development	• Adapted NTP modules and training curricula • National strategy for TB control in prisons • SOP • Training of trainer modules • Job description for NTP prison officer or coordinator (if applicable)
Monitoring and evaluation	• NTP data recording and reporting forms for case finding, treatment, and laboratory external quality assessment • Patient treatment card to include information on place of diagnosis (i.e., referred from where?) • Referral and defaulter tracing registries • Prison supervision checklist
ACSM plan and materials	• ACSM plan • Flipchart for nurse counseling • Flipchart for patient and family-oriented education • Flipchart for general public in waiting rooms • Wall posters, pamphlets, videos

Training and Developing Prison-Specific Workplans

Training should follow the presentation or launching of the prison DOTS program and target the same stakeholders (i.e., prison and public health staff who attended the socialization meeting). Prison staff should be partnered during the training with their local counterparts from the health center and with the district NTP supervisor in the corresponding community that would support prisons in their TB program. Training should follow the NTP's modules, the national strategy for TB control in prisons, and the SOP. Topics should cover issues specific to prisons including screening at entry; effective contact investigation; referral of prisoners undergoing TB treatment; and IEC to patients, the general prison population, and prison staff. Through training, prison staff will gain skills required to carry out the TB control strategic plan, including the following—

- Increasing case detection and improving treatment outcomes
- Implementing DOT in prisons
- Establishing a sound prison-to-prison and prison-to-health center referral system
- Establishing a systematic and strong prison surveillance system

During the training event, prison TB control teams at the local level can be formed among prison staff and health center and district NTP managers or supervisors. These operational units would be responsible for implementing the program in their respective prisons.

The training event should also be used as an opportunity to develop tailored workplans by each prison DOTS team. Standardized formats and templates for the workplan should be provided by the NTP. Each prison-specific workplan would incorporate the elements outlined in the national strategic plan and operational plan (e.g., for case detection, treatment, recording and reporting, infection control, IEC). This document should list objectives, activities, logistics, outputs, indicators, time frame, responsible parties, and a budget (when applicable). Stakeholders should mobilize resources to implement the activities contained in the workplan and achieve the objectives and targets specified. Prison DOTS teams should update their workplan periodically.

Operational Roles and Responsibilities of Local TB Control Teams

During the planning phase of implementation of a TB control program, the tasks of the health cadre in prisons must be clearly outlined and defined. These responsibilities must be understood and monitored closely, both by prison doctors within the prison and by their local public health counterparts (local and district TB managers or supervisors).

Duties of the Prison Physician or Equivalent (Clinical Officer, Medical Officer)

- Educate and counsel the TB patient.
- Build rapport and an effective physician-patient relationship.
- Investigate the patient's previous TB treatment.
- Determine the treatment according to the standardized NTP guidelines.
- Calculate the dose of anti-TB medicines according to the patient's weight and age.
- Follow up TB cases regularly, or at least three times during the course of treatment—
    - At the beginning of the treatment
    - At the end of the initial phase
    - When completing treatment
- Review the patient's treatment outcome.
- Manage adverse effects to anti-TB medicines.
- Determine the initial severity, risk of death, and any complication during treatment.
- Refer TB patients to the hospital, if needed.
- Ensure that patients who are released or transferred to another prison while undergoing TB treatment are properly referred to a health facility to continue therapy.

Duties of the Prison Nurse or Equivalent

- Organize the administration of treatment.
- Conduct a minimum of three interviews with the TB patient during the course of treatment, at the—
    - Beginning of the treatment (using flipchart)
    - End of the initial phase
    - End of treatment
- Identify risk behaviors that may lead to default.
- Educate and counsel the TB patient.
- Administer treatment, according to the medical indication and standardized treatment.
- Ensure DOT.
- Weigh the patient monthly.
- In coordination with the physician, request sputum smear follow-up (control) exams according to the operational plan and NTP guidelines.
- Fill out the NTP forms used for case finding and treatment (e.g., suspect registry, patient registry, treatment cards).
- Carry out the recording and reporting (e.g., case finding and treatment monitoring, quarterly reports).
- Ensure appropriate use and storage of anti-TB medicines.

- In the event of a transferred-in TB patient, send feedback and communicate the outcome condition to the establishment of origin.
- Organize the referral system of TB patients who are released or transferred to another facility while undergoing therapy and follow up on referrals.

Duties of the Local or District TB Control Program Manager or Supervisor

- Provide training and technical assistance to the prison health staff.
- Help organize the program in prisons.
- Supply the prison clinic with necessary materials and consumables to carry out TB-related tasks (e.g., sputum collection cups, supplies for smearing and fixing slides if applicable, NTP forms and registries, IEC materials).
- For prisons that do not have a TB laboratory on site, coordinate collection of sputum samples with the prison health staff.
- Coordinate reporting of sputum smear examination results to prison health staff.
- Coordinate with the intermediate laboratory the derivation of samples of sputum that require culture (if available).
- Coordinate and assist in monitoring the referrals of prisoners who are released during TB treatment.
- Carry out periodic supervision visits to prisons, include in-service training (fill out supervision log in prison, if possible).
- Ensure that the prison health staff report case finding and treatment outcome information (depending on prison capacity).
- Monitor and evaluate the TB control program in prisons through periodic evaluation meetings with prison staff.

Suggested Reading for Chapter 15

WHO. 2007. *Advocacy Communication and Social Mobilization For Tuberculosis Control, A Handbook for Country Programme*. Geneva: WHO.

Monitoring and evaluation of TB program performance involves assessing activities, monitoring costs and expenditures, determining program coverage, and evaluating treatment outcomes and the epidemiological impact of the program.

The rationale for monitoring and evaluating program performance includes the following—

- Ensuring that training, supervision, logistics, and communication activities are being carried out effectively
- Deciding whether health units are collecting the data needed to assess case notification rates and treatment outcomes
- Identifying technical and operational problems, specifying the reasons for the problems, and taking the necessary corrective actions
- Helping staff to improve standards of practice
- Improving patient care and support, and quality of information

Monitoring program performance requires accurate record keeping and regular reporting of case findings and treatment outcomes. Program performance is evaluated by analysis, interpretation of data on case-finding, and treatment outcomes. Feedback to all staff involved in TB control in prisons enables improvement in program performance in the identified problem areas. To ensure effective monitoring and evaluation, clearly defined indicators are needed. (Annex 7 provides a list of proposed indicators.) Prison staff may need training on recording, reporting, and interpreting data.

Recording and Reporting

Appropriate recording practices are essential for providing effective patient management as well as for comparing epidemiological trends and improving program performance. Effective monitoring depends on appropriate recording and reporting systems.

As recording and reporting systems grow increasingly complex with computers becoming standard, programs are moving into electronic TB registration. Electronic systems have the potential to ensure more complete data entry, easier and better communication and transmission of the data to other levels, and more refined analysis of program performance.

Recording System

The recording system comprises the below elements—

- *TB suspect register:* All TB suspects identified according to the definition used in the chapter 9 should be promptly recorded into the TB suspect register. This log should be kept at every service unit providing care for TB (i.e., in the prison context, each prison clinic should have its own TB suspect book). This register contains information on the suspects (e.g., name, dates of registry and sputum collection, address, and laboratory results). All pulmonary TB suspects entered in this register should have sputum collected and sent to the corresponding laboratory. They should also be listed in the laboratory register.

- *Laboratory register:* The laboratory register, maintained by a laboratory technician, records patient details with a serial identification number, and source of referral. The results of the sputum examination should be recorded in the laboratory register and then sent back to the referring facility or unit.
- *Patient treatment card:* The patient treatment card for each person diagnosed with TB (smear-positive, smear-negative, or extrapulmonary) records basic epidemiological and clinical information, and medicines administration. The patient treatment card is used for recording treatment and for follow up.
- *Basic management unit (district or prison) TB register:* The district or prison TB register is used to monitor progress and treatment outcome for all patients in the prison. The register provides, in one line per patient, the essential information on identification of the patient and status of case management. The register is used by the responsible health worker to provide the district or local health officer with rapid feedback on program performance in the prison.
- Some facilities have additional registers recording the culture results, contact examinations, referrals, and transfers.

Reporting System

The reporting system (aggregated reports) consists of (1) a quarterly report on TB case registration summarizing the numbers of TB patients started on treatment, laboratory tests performed, and HIV tests administered and results obtained; (2) a quarterly report on treatment outcome and TB/HIV activities after all patients in the cohort have completed their course of treatment; (3) a quarterly order form for TB medicines; (4) a quarterly order form for laboratory supplies; and (5) an annual report on program management describing human resource and TB delivery service facilities and the contribution of private sector and community to referral, diagnosis, and treatment.

Cohort analysis refers to the systematic analysis of standard outcomes of treatment. A cohort of TB patients consists of patients registered during a certain period, which is usually a quarter of a year (i.e., January 1 to March 31, April 1 to June 30, July 1 to September 30, and October 1 to December 31). Sputum smear-positive pulmonary TB patients (i.e., the infectious cases) form a separate cohort from sputum smear-negative and extrapulmonary TB patients. In smear-positive pulmonary TB patients, the standard outcomes of treatment reported are cure, treatment completion, treatment failure, death, treatment interruption (default), and transfer out (see table 10 in chapter 11 for definitions). In smear-negative PTB and extrapulmonary TB patients, cure and treatment failure cannot be assessed with the use of sputum smear but can be assessed with the use of bacteriological culture (if available). Outcome indicators such as treatment completion, death, default, and transfer out, however, should be recorded for these patients in the prison TB register. New and previously treated patients form separate cohorts.

The recording and reporting system allows for individualized follow up to help patients who do not make satisfactory progress as well as for a rapid managerial assessment of the overall performance of each institution. A robust system of accountability involving cross-checks between reports, registers, and forms should minimize any risk of false reporting.

Annexes 2-6 contain the following sample forms and registers used for TB control activities—

- Request for sputum smear microscopy examination
- Request for sputum culture and DST
- TB laboratory register (if laboratory in the prison)
- TB treatment card
- TB identity card
- Quarterly order form for TB medicines
- TB treatment referral or transfer
- Register of referred TB cases
- Prison TB control program register
- Quarterly report on TB case registration
- Quarterly report on treatment outcomes

Referral and Transfer

Prisoners with TB may be transferred to the reference treatment facilities for diagnosis, treatment, or special care. Referral and transfer are distinct functions, with different follow-up and related tasks, so clearly differentiating between referral and transfer is important for the purposes of TB control. Transfer of patients without proper follow-up information reflects poor care management of patient movement and requires rapid correction through improved communication. Appropriate forms for referral, back-referral, and transfer are therefore essential for effective information sharing between different health care providers involved in the program implementation.

Referral refers to the process of arranging the movement of a TB patient before registration in the TB register for the purposes of starting treatment in a more appropriate location or for diagnosis in a competent facility. The unit (prison) referring a case should not register the patient in the TB register. A special referral register is helpful, however, to monitor referrals and ensure appropriate follow up. The unit receiving a referred patient is responsible for informing the referring facility about the arrival of the patient and for the care provided. A TB patient listed in a register (i.e., a patient started on anti-TB treatment) could also be referred to another facility in the same unit or outside for other (non-TB) tests or treatment (e.g., surgery or ART).

Transfer refers to the process of arranging the movement of a TB patient who is already listed in a TB register between two treatment units, that is, the patient has started treatment and will continue treatment in another prison (or prison hospital) with a different TB register. The unit that is transferring a patient out is responsible for reporting the treatment outcome in the quarterly report on TB treatment outcomes, after obtaining this information from the unit completing the details of treatment outcomes. The unit receiving a transferred-in patient is responsible for informing the unit that transferred the patient that the patient arrived and on the eventual treatment outcome.

The TB treatment referral or transfer form is an individual patient form used in case of both transfer and referral. Half of the form should be returned to the originating facility upon arrival of the patient to provide feedback and ensure a successful referral.

Prisoners with TB are often released (i.e., discharged) from the prison before completing the treatment. Properly planning the discharge for soon-to-be-released prisoners is essential to ensure continuity and completion of treatment. Refer to chapter 13 for further details.

Laboratory Evaluation

The sputum smear microscopy laboratory should routinely report the following information—

- Number of sputum samples examined and proportion positive
- Number of new smear-positive patients diagnosed
- Results of regular quality assurance tests

Evaluation of Prison TB Control Program Performance

Evaluating a TB program is done in three stages—

- Case finding
- Cohort analysis of results of sputum smear conversion at two or three months
- Cohort analysis of results of treatment outcome

Case Finding

The prison TB coordinator must compile and submit the three-month report on case finding to the NTP. This document reports the numbers of new cases (smear-positive and smear-negative PTB and extrapulmonary TB) and previously treated cases. In general, sputum-smear positive PTB cases constitute about 50 percent of the total TB cases in a population. The remaining cases are sputum smear-negative pulmonary (30 percent) and extrapulmonary (20 percent). If smear-positive cases form less than 50 percent of the total number of TB cases detected by a program, an analysis should be done to find out why. The common explanation is that the program is probably under-detecting smear-positive cases, over-detecting smear-negative and extrapulmonary cases (which may be common in prisons where radiography screening is routinely done), or both. Another explanation may be a high prevalence of HIV infection among prisoners, which points to the need for HIV surveillance or routine testing of all TB cases.

Cohort Analysis of Results of Sputum Smear Conversion at Two or Three Months

The sputum smear conversion rate at two or three months is the proportion of the sputum smear-positive patients registered in one quarter who have become sputum smear-negative two or three months, respectively, after starting treatment. The prison TB coordinator calculates this rate from the laboratory register during supervisory visits to the laboratory. The sputum smear conversion rate is available six months after the start of a particular quarter and is the earliest available indicator of the program performance.

Cohort Analysis of Results of Treatment Outcome

The prison TB coordinator reports the results of cohort analysis for all TB patients (new and previously treated cases) on the quarterly treatment outcome report form. These reports are usually filled out after the last patient from the given cohort has completed the treatment (i.e., 9 to 12 months after the start of a particular quarter).

Supervision

A system of supervision is necessary to support the prison TB coordinator and maintain effective prison TB control program performance. The person providing support to the prison TB coordinator may work at the provincial or regional level of the NTP. The provincial or regional TB coordinator should visit the prison TB coordinator at least quarterly to assess the quality of program performance, identify problems and appropriate solutions, and take the necessary action to overcome these problems.

Identifying Problems and Taking Action

The information management system provides a tool for supervision. Quarterly reports on case-finding and cohort analysis may reveal unsatisfactory performance due to problems in program implementation. Prison TB coordinators must work with NTP staff to identify the causes of these problems. Table 21 shows some possible causes of problems in program implementation and possible solutions.

Table 21. Some Problems, Causes, And Possible Solutions

Problem	Possible Cause	Possible Corresponding Solutions
Too many failures	Trading in medicines of unknown quality	Investigate thoroughly and improve staff supervision.
	Prisoners concealing medicines	Teach prison health staff about prisoners' tricks to conceal tablets, and improve DOT.
	Poor-quality medications being used	Review the tendering and procurement procedures.
	Patients not taking all the medications	Investigate whether the prison has a black market in anti-TB medicines. Make sure that DOT is 100%.
	High level of primary resistance to both rifampicin and isoniazid	Consider a local protocol with rigorous evaluation; for example, submit sputum for culture and DST of all previously treated patients (irrespective of duration of previous treatment) before prescribing treatment.
	Re-treatment patients wrongly receiving the regimen for new patients	Improve supervision of the prison health staff. Check that the prison health staff knows the right regimens for each patient treatment category. Check the regimen prescribed in the register and on the patient treatment card.

	"Sputum swapping" between prisoners to stay in TB facility	Implement directly observed sputum collection to ensure correct specimens, belonging to the right prisoners, are sent to the laboratory.
Too many patients with interrupted treatment	Inadequate health education	Make sure that patients receive proper, continuous health education and that the health messages are relevant and understandable. Help authorities understand the importance of the diagnosis and treatment of TB.
	Unfriendly behavior of the health staff	Pay attention to staff morale and enhance training.
	Failure to follow up patients who interrupt treatment	Make sure staff understand the importance of tracing patients. Improve procedures for tracing patients who interrupt treatment, especially those who have sputum smear-positive PTB.
	Failure to ensure referral of patients on release or transfer	Improve supervision of staff. Review procedures for coordination between the prison health authorities, the NTP, and community health services.
	Prisoners not showing up for treatment and "fetching" them is not possible because of lack of staff	Increase medical staff for adequate follow-up. Find out whether "peer coercion" is responsible for prisoners not showing up (e.g., extortion, discrimination, "internal hierarchy" punishments by prisoner bosses) and take adequate measures.
Too many deaths	High prevalence of HIV	Implement multiple interventions to minimize HIV transmission. Intensify or expand TB case finding and the provision of appropriate therapy for dually infected prisoners, including the management of opportunistic infections and access to ART.
	Late diagnosis of TB	Make sure health workers properly assess symptoms in prisoners attending prison health services; identify TB suspects and send them sputum for smear microscopy. Identify any barriers to access to health services and ways to overcome them. Strengthen ACSM among prison population and staff.

Operations Research

Operations research projects should be promoted and designed to address operational problems that are identified during the assessment, implementation, and monitoring and evaluation steps. Results can be used to enhance the implementation of the Stop TB Strategy in prisons and formulate relevant, evidence-based solutions and policies. These efforts should include other institutions (i.e., universities and research centers) to assist in protocol development, financing, data collection, data analysis, and report writing. The potential contribution of these institutions should be valued and used. Topics that can assist decision makers and program managers in adopting and strengthening sound and evidence-based policies for TB control include the following—

- Understanding the factors associated with diagnostic and treatment delays from the provider and patient perspectives
- Ensuring an efficient referral system between prison and civilian services
- Establishing effective diagnostic practices of providers (use of chest radiography over microscopy)
- Using incentives and enablers for providers and patients
- Understanding the stigma attached to TB
- Designing interventions to implement and improve TB/HIV collaborations
- Knowing the risk factors for MDR-TB

Suggested reading for Chapter 16

WHO. 2003. *Treatment of tuberculosis: guidelines for national programmes*. 3rd ed. Geneva: WHO (revised 2005).

WHO. 2005. *Management of tuberculosis: training for district TB coordinators*. Geneva: WHO.

WHO. 2005. *Management of tuberculosis: training for district TB coordinators. How to organize training for district TB coordinators*. Geneva: WHO.

Enarson, D.A., H. L. Rieder, T. Arnadottir, et al. 2000. *Management of tuberculosis: a guide for low-income countries*, 5th ed. Paris, International Union Against Tuberculosis and Lung Disease.

WHO. 2006. *Revised TB recording and reporting forms and registers – version 2006*. Geneva: WHO.

This chapter describes the pharmaceutical process, from procurement to distribution, of anti-TB medicines. This process is a key aspect of TB control; the uninterrupted supply of quality pharmaceuticals is a component of DOTS. In the majority of cases, most of the steps in this process are exclusive to the NTP. This entity should ensure prompt delivery of TB medicines to prison health staff whenever a case is diagnosed in a prison. Prisons should be responsible for optimal storage and dispensing of medicines to patients through DOT.

A crucial step in the control of TB is the uninterrupted supply of TB medicines, which are of proven quality and safety and have been shown to be efficacious across the national TB program, including in prisons. Penitentiary systems can be quite complex with their elements reporting to different ministries and receiving different funding. Therefore, NTP program managers should include and coordinate all aspects of pharmaceutical management in planning and implementation processes (see figure 6).[1,2]

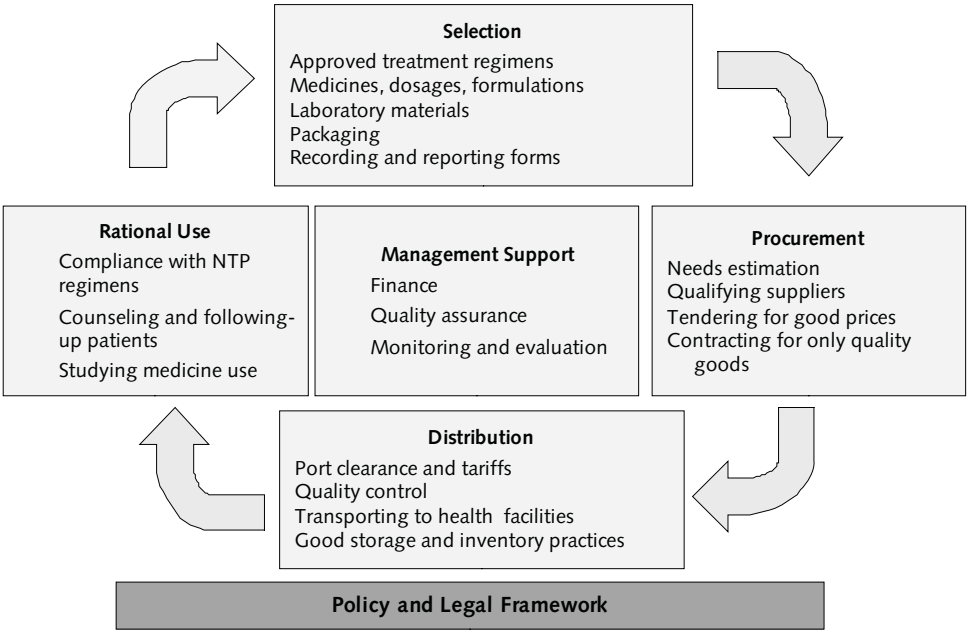

Figure 6. Planning and implementation processes of pharmaceutical management

Policy and Legal Framework

To support the goals of TB control in the country and ensure an uninterrupted supply of quality TB medicines, the government, the MoH, MoJ, MoI, and MoL, advised by the TB central unit, must implement major policy decisions, such as the following[1]—

- National policy that defines the rights of prisoners to diagnosis and treatment, including provision of necessary pharmaceuticals (both first- and second-line medicines)

- Standardized treatment regimens and medicine formulations by levels of TB control
- Sustainable availability of funds for pharmaceutical supply at all levels and institutions that constitute a penitentiary system
- Clear understanding with the penitentiary system, MoH, and NTP regarding the responsibilities for pharmaceutical supply in the penitentiary system (e.g., through detailed memos of understanding)
- Pharmaceutical regulations that ensure the registration, procurement, and use of medicines of proven efficacy and guaranteed quality only

Selection of TB Drugs[3]

Careful medicine selection is one of the most cost-effective ways of promoting a regular supply of anti-TB medicines. The process of medicine selection for NTPs is based on a variety of factors, such as standard treatment guidelines, cost, resistance to TB medicines, access to quality medicines, and management and distribution capabilities.

The TB control managers in prisons must participate in national anti-TB medicine selection processes to ensure that the specific needs of TB control in prisons are addressed. Considerations must be made to determine whether daily or intermittent regimens should be used by the program, and then the appropriate package and presentation must be selected, including whether to use blister packs (versus loose medicines), FDCs (versus single-dose medicines), and patient kits (versus bulk blister of loose pill packing).

For a prison setting, FDCs of TB medicines have clear advantages over single-dose medicines (e.g., the lower tablet load per dose makes direct observation of intake easier, and medicines that are combined in one tablet are less likely to be abused by prisoners or used for indications other than TB). Blistered FDC medicines may be a better choice for a penitentiary system because they are easier than bulk loose tablets to handle and dispense. This feature may be especially important in settings where storage facilities are weak or in humid climates. Conducting inventory checks and accounting for blister-packed medicines are easier with FDCs, too.

Selection of Patient Kits

A TB patient kit (patient pack) may be a good solution for a penitentiary system. A TB kit contains the full course of treatment for a single patient. The benefits of selecting medicines in a kit form are clear—

- Medicines are guaranteed for the duration of the treatment.
- The guaranteed availability of medicines instills trust and promotes adherence by patients.
- Quantification of medicines, dose calculations, and dispensation to a patient are less confusing and more provider-friendly.

Standard Stop TB Patient Kits© can be selected by a penitentiary program and procured ready-made. The Stop TB Strategy's GDF offers two types of preassembled kits: one for Categories I and III, and the other for Category II. Kit packages include medicines needed for both the initial and continuation phases. All medicines are quality assured. Eligible programs may receive these kits as free grants or procure them directly from the GDF.

Patient kits can also be assembled from blister-packed medicines at the health facility level. This process, however, requires special training of staff, an adequate facility and materials for repacking medicines, and clear written step-by-step procedures for kits assembling. Use of loose single-dose tablets for making patient kits is not recommended unless the services of a professional pharmacy are used.

Programs must carefully consider the benefits and limitations of patient kits when making selection decisions. Patient kits may not be suitable for use among prisoner patients that are released from prison shortly after the treatment course has started or in a facility with a high rate of patients transferring out without their kits. For the same reasons, patient kits may not be suitable for use in jails where people are detained for minor crimes or to await trials. In these situations, patient kits will be wasted or will require reconstitution, which is an additional expense for a program (i.e., for training, repacking, and other steps).

The selection process of SLMs differs considerably from selection of first-line treatment because they have a short shelf life (sometimes shorter than the duration of a treatment course), are administered to patients for longer periods than the first-line treatment (up to 24 months), and are much more expensive. Some medicines (e.g., PASER®) require cold chain. Information about pharmaceutical management of SLMs can be found in documents recently elaborated by WHO[4] and Rational Pharmaceutical Management (RPM) Plus, an MSH project funded by USAID.[3]

Procurement of TB Medicines and Other Commodities[5]

In many countries TB medicines are procured centrally for the penitentiary system through the MoH or NTP. In some countries, procurement is decentralized, and the MoJ, the Ministry of Internal Affairs, or both conduct their own procurement. Individual procurement by a penitentiary system may not be efficient because of the small number of patients. To achieve the economy of scale, a penitentiary system should coordinate product selection and delegate the procurement to the MoH.

A TB program achieves effective procurement when it—

- Procures the most cost-effective medicines in the right quantities
- Selects reliable suppliers of quality-assured products
- Ensures timely delivery
- Achieves the lowest possible cost for all medicines

Quantification

The procurement process starts with the quantification process. The procurement plan should cover the pharmaceutical needs for one year plus a reserve stock of up to one year depending on program efficiency. This reserve allows for delays from the supplier, port clearance, distribution, or sudden increases in patient needs. Estimates of medicine requirements and a reserve stock for a fiscal period are based on case notifications of the previous period, the increase foreseen in case detection as a result of the DOTS strategy expansion, the treatment regimens, remaining stocks in pipeline, and procurement and distribution lead times.[3]

Commodities for diagnostics (i.e., the sputum containers, reagents, and laboratory supplies required for microscopy examination) are estimated based on the number of new smear-positive cases detected annually and the smear-positivity rate among TB suspects. Microscopy sputum examination is used for both diagnosis and follow-up examinations. To promote DOTS expansion and improve case detection in countries with high TB prevalence, the GDF now provides TB diagnostics materials (in a kit form) for use in laboratories.[6–8]

Requirements for TB recording and reporting forms used in DOTS programs should also be estimated and included in the procurement plan. Any shortages in supply of TB forms will affect the implementation of DOTS, so consistent availability should be ensured.

Some Procurement Considerations[3]

Registration of medicines. In most countries, first-line anti-TB medicines must be registered with the national drug regulatory authority. The exact formulations and dosage forms that are required by the NTP guidelines might not be registered, however, as they are with first-time use of FDCs. Because many SLMs are widely used antibiotics, checking to see if the legally registered indications also include TB is important, otherwise negative consequences for the program, including costs and delays for registration which can take 3 to 12 months, are likely.

Domestic manufacturing. When countries manufacture TB medicines locally, legislation may be in place to support domestic industry. Although such legislation is good for creating jobs for the local population, domestic manufacturing does not always reflect the needs of national health programs since quality requirements (e.g., inspection for Good Manufacturing Practices) may be waived for domestic products.

Competition in the market. For sound competition at least three, and preferably five, potential suppliers for each needed anti-TB pharmaceutical product are required. Little competition may lead to collusion between suppliers and higher prices. In the local markets where competition is not sufficient or obtaining low-quality medicines is a risk, the program should work with the government toward competitive procurement in the international market (if it is cost efficient) or go for direct procurement from nonprofit international suppliers such as the GDF and the Green Light Committee (GLC).

Regular procurement. Annual procurement on a fixed date is the most efficient way to build up confidence of suppliers and draw prices and costs down, through use of a standardized package of procurement bidding documents and bulk purchase of TB medicines and commodities.

Procurement methods. There are four basic procurement methods that programs may use when procuring TB medicines—

- Open tender—a request for bids that is open to all interested suppliers
- Restricted tender—a request for bids limited to known, reliable, prequalified suppliers
- Competitive negotiation—direct negotiation with a small number of selected sellers to achieve a specific price or service arrangement
- Direct procurement—purchase from a single supplier at its quoted price

With price and quality being the main determinants of sound pharmaceutical procurement, the four methods must be considered carefully because price and quality can vary significantly. The preferable method that is most likely to ensure the quality and good price of anti-TB medicines is a restricted tender among prequalified suppliers. Prequalification may become a time consuming process that also requires the availability of highly qualified staff capable of assessing pharmaceutical dossiers and documents from manufacturers.[9] If such capacity does not exist, it is advisable to turn for a grant of anti-TB medicines or direct procurement from the GDF, which procures its products from prequalified suppliers.[10]

SLMs are expensive and often not immediately available, even in international markets. The GLC of the DOTS-Plus Working Group within the Stop TB Partnership offers a reliable source for these anti-TB medicines.[11] To apply to the GLC, however, countries must comply with specific conditions (e.g., good quality implementation of the DOTS strategy minimum package). Still, the minimum cost of treating a resistant case with SLMs approaches 1,000 U.S. dollars, and the pharmaceutical cost can reach 10 times that amount, an important reason to prevent TB drug resistance by appropriate use of first-line medicines.[4]

Quality assurance. To ensure that patients receive safe and efficacious medicines, NTP must have quality assurance systems in place that address quality issues within each function of the pharmaceutical management cycle, including the selection, procurement, distribution, and use of medicines.[12] Sound quality assurance systems require strong political support and participation of all stakeholders involved in pharmaceutical supply, and specific expertise at the drug regulatory level to be able to evaluate documents pertaining to medicine quality.[13]

Distribution and Storage of Anti-TB Medicines

The most important elements in the distribution of anti-TB medicines and supplies are port clearance, storage, transportation, and inventory control. The NTP should consider that medicines and supplies management constitute an information system as well. Therefore, recording and reporting forms must be provided to the districts and health facilities.

The NTP and the penitentiary system should establish a system for proper storage, distribution, and inventory management of anti-TB medicines and supplies. The distribution cycle should be linked from a central store with overall program reporting and supervision cycles and performed regularly, e.g., quarterly. Frequency of distribution from central to local units will vary, however, depending on the number of detected cases and the availability of storage facilities for medicines.[14]

Each warehouse, storeroom, or health unit should have trained staff to order, receive, and manage stocks adequately.[15] At lower level facilities (i.e., the district level), the TB officer must assist with calculating needs, obtaining the medicines, and distributing them to the health facilities.[16]

Endnotes for Chapter 17

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The impact of HIV infection, the increasing problem of MDR-TB, and the emergence of XDR-TB in settings where health systems and TB control programs are weak have led to a reappraisal of the importance of infection control in health care and congregate settings. Transmission of infectious diseases is a real risk among persons living and working in congregate settings, especially in prisons that serve populations with high TB incidence. In addition, the presence of HIV-infected and immunocompromised patients in prisons and the absence of appropriate infection control policies and practices create a favorable environment for transmission and spread of TB. Therefore, improving TB infection control is urgently needed.

TB infection control is a combination of measures aimed at minimizing the risk of TB transmission. The foundation of such infection control is early and rapid identification of individuals with suspected and known TB and effective treatment of disease. TB infection control, as a component of WHO's revised Stop TB Strategy, is intended to strengthen health systems. It is also an essential part of sound HIV control programs in countries with a high prevalence of HIV.

Developing (TB) infection control capacity should be embedded in broader strategic plans, so that resources are allocated. Clear goals and objectives, activities, and outcomes have to be defined by program managers and prison health authorities. Policy and service delivery areas related to TB infection control may be studied at four levels—

- Programmatic (organizational) control measures, including TB infection control policy development, strategic planning, advocacy, human resource development, monitoring and evaluation, and operational research
- Administrative control measures, including early TB case detection, TB screening, separation or isolation of patients, and cough etiquette and hygiene
- Environmental control measures, including natural and mechanical ventilation and ultraviolet germicidal irradiation (UVGI)
- Personal protection control measures, including respirators and respiratory fit testing

Figure 7 depicts the transmission chain and importance of TB infection control in prisons.

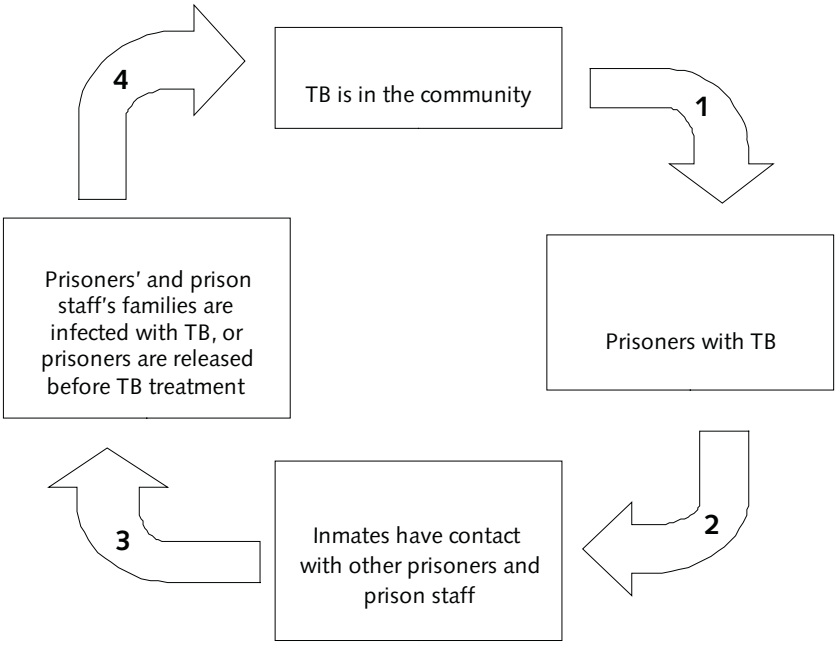

Figure 7. In Indonesia, a simple model of TB infection control in prison was drafted to depict TB transmission chain in prisons and the community

Several infection control measures could be conducted based on figure 7 (refer to the numbers in the arrows)—

1. Preventing spread of infection from community to prison by—

   - Using intensified TB screening for new or transferred prisoners
   - Preparing adaptation blocks or rooms (to be used for two to four weeks) for new or transferred prisoners

2. Preventing TB infection among prisoners (from one TB prisoners to other prisoners) or to prison's staff by—

   - Conducting a contact investigation for TB suspects and cases
   - Improving infection control (i.e., implementing organizational, administrative, and environmental interventions) in prisons
   - Using IEC for prisoners

3. Preventing infection of family members and the community by a released prisoners or prison staff by—

   - Examining prisoners before release
   - Examining prison staff regularly

4. Establishing TB infection control in the community by—

   - Instituting early TB case detection
   - Using effective treatment

Programmatic (Organizational) Measures

The organizational activities are aimed at assessing the TB infection risks in the prison setting, developing policy, budgeting, building human resources capacity, setting up surveillance systems, conducting monitoring and evaluation, and doing operational research.

Ideally, each prison should have a written TB infection control plan with a protocol for the prompt recognition, separation, provision of services, investigation for TB, and referral of patients with suspected or confirmed TB disease. A designated infection control officer is responsible for overseeing the implementation of infection control measures and providing infection control training for health care and other staff members who may be exposed to TB infection.

All staff working in a facility should understand the importance of infection control policies and their role in implementing them. As part of training, each health care worker and staff member, including any lay workers, should receive instruction specific to his or her job description. Training should be conducted before initial assignment, and continuing education should be provided to all prison staff and program volunteers annually.

Consumables for infection control (e.g., N-95 or FFP-II respirators, UVGI) that were considered appropriate for only high-resource settings need to be available in resource-constrained countries that carry the burden of TB cases. In such places, purchasing can be organized centrally through subsidized mechanisms (as is done for pharmaceutical procurement and distribution). Because of cost, these measures can be prioritized and targeted toward high-risk populations and settings, including prisons reference hospitals.

Monitoring and evaluation provide the means to assess the quality, effectiveness, coverage, and delivery of infection control interventions and to ensure continuous improvement of program performance. Monitoring and evaluation should involve collaboration and sharing of indicators between programs (e.g., programs related to TB, HIV, occupational health, and infection control) and should include the link between prison and civilian health services particularly on continuum of care and follow up of released prisoners with TB.

Administrative Measures

Implementing administrative interventions in particular work practices has the highest possible impact on preventing TB transmission and is usually the least expensive. Thus, they are strongly advocated in most settings. The administrative controls include procedures to promptly identify infectious cases of TB, separate those individuals from the rest of the population, and treat them with the minimal delay. Interventions aimed

at reducing TB transmission in congregate settings include screening, physical separation or isolation of patients or TB suspects, instruction in cough etiquette, and introduction of alternative measures of punishment (rather than imprisonment) to decrease overcrowding or decrease the number of prisoners per cell. When building new prisons, airborne infection control measures should be considered to ensure better ventilation.

NTP and prison health officers need to advocate within their respective ministries for the allocation of funds to allow separation rooms for prisoners who have TB or are suspected of having infectious TB. These entities can also seek funds for restructuring or building separation rooms in prisons in their proposals to bilateral cooperation agencies or other donor mechanisms (e.g., GFATM).

Early case detection and effective treatment of TB reduces exposure to other inmates and staff and, therefore, is considered to be the cornerstone of infection control measures. Screening prisoners upon entry into prison and again during contact investigation plays a crucial role as part of early case detection. Passive case-finding is also necessary and should be expedited to prevent delays in diagnosis and treatment initiation.

By the time an individual is diagnosed with TB and starts therapy, he or she would have infected and will continue to infect others during the investigation phase, which may take up to several weeks and even months in prisons. Most pulmonary TB patients are no longer infectious after few weeks of appropriate treatment. Beyond this time, inmates can return to their original cells. Appropriate measures to improve treatment adherence including TB health education and DOT are crucial.

In many resource-restricted countries, which typically have limited medical staff and often severely overcrowded prisons, separation of patients may be difficult to implement. Delays in implementing separation should not, however, delay initiating therapy for the patient. In most cases, the active TB case will already have been in contact with many others for some time. The sooner he or she is treated, the sooner contagion will cease. The contacts should then all be carefully screened. Separation, even when possible in countries with limited staff and loose discipline, may be difficult to enforce because prisoners are notorious for bribing their way into wherever they want to go to see fellow inmates, even into MDR-TB sections. The problem becomes more complex when facing HIV infection and MDR-TB in prisons. Some countries have a specialized center for treatment of MDR-TB. The only solution here is increasing the number of staff, motivating them, and educating both staff and prisoners on the dangers of contagion.

UNAIDS policy opposes the isolation of prisoners on grounds of HIV status alone. HIV-positive prisoners, however, are at much higher risk of developing TB disease. Whenever possible, TB suspects and TB patients should be kept separate from HIV-positive prisoners. Likewise, MDR-TB cases must be separated from other TB patients. Prison health and security staff should educate and counsel TB suspects or patients who are put in these rooms about the reason for separation. They should emphasize that it is a preventive measure and not a punishment.

Furthermore, sputum of TB suspects *must* be collected in well-ventilated areas. Exposing staff and other inmates to aerosols containing TB bacilli coughed up into the air during this procedure should be avoided.

Environmental Controls

Prison health care staff should teach TB suspects and patients simple measures to decrease the risk of transmitting tuberculosis. These measures include covering the mouth with elbow or back of the hand or, even better ,with a tissue when coughing and using sputum pots with lids. Printed education leaflets are a useful supplement to spoken advice. Often, peer educators, trained from within the prisoner population, can be the most effective trainers. A clinician examining a TB patient or suspect should ask him or her to turn his or her head to one side to avoid coughing directly at the health care provider.

Standard surgical face masks prevent the wide spread of aerosols and droplets. These masks decrease the risk that the person wearing the mask can infect other people. Whenever possible, a TB suspect or patient should wear a mask when moving from one part of a prison facility to another.

Natural Ventilation

Good ventilation helps reduce TB transmission indoors. Ideally, prison clinics and cells should have large windows. In prison hospital wards, simple measures to improve outpatient clinics and sputum collection rooms include the following—

- Open windows
- Directional airflow
- Outdoor waiting areas
- Collection of sputum samples outdoors (away from other patients, visitors, and the waiting area)

In existing prison facilities that have natural ventilation, effective ventilation should be achieved by proper operation and maintenance and by reminding prison guards and prisoners of importance of natural ventilation. Natural ventilation rates can be maximized by seeking advice from natural ventilation experts or by maximizing the openings of windows

Mechanical Ventilation

Well-designed, well-maintained, and correctly operated exhaust fans (mixed-mode ventilation) can help to obtain adequate ventilation when sufficient air change per hour cannot be achieved by natural ventilation alone.

In some settings, mechanical ventilation will be needed, for example, where natural or mixed-mode ventilation systems cannot be implemented effectively or where such systems are inadequate given local conditions (e.g., building structure, climate, regulations, culture, cost, and outdoor air quality).To be effective, a minimum of 12 air change per hour must be maintained.

Upper Room or Shielded UVGI

In prisons where natural or mechanical ventilation may not be achieved, e.g., because of cold winters, an additional option is to use an upper room or a shielded UVGI device. Room air cleaners with UVGI may provide a less expensive alternative to more expensive environmental control measures that require structural alterations of a facility. Effective use of UVGI ensures that *M. tuberculosis*, as contained in an infectious aerosol, is exposed to a sufficient dose of ultraviolet-C (UV-C) radiation at 253.7 nanometers to result in inactivation. When introducing environmental interventions, and in particular UVGI, country regulations must be taken into account.

Personal Protection: Face Respirators

In addition to implementation of administrative and environmental controls, health-care workers may use respirators when caring for patients with infectious TB. Respirators (N95 or FFP-II equivalent or higher) provide reasonably good protection against TB by filtering out microscopic droplets and aerosols. The use of respirators provides protection for health care workers in close contact with TB patients. This protection is particularly important when health staff are supervising a cough-inducing procedure (e.g., bronchoscopy) or sputum induction using nebulized hypertonic saline.

Staff must wear the respirators correctly; hence, organizing training and appointing a responsible staff for proper use of respirators may be needed. If possible, respirators should be tested to see if they fit correctly on each staff member's face. Information on how to use fit testing and specification of respirators may be found in specific infection control guidelines.

The second component of the Stop TB Strategy is to protect poor and vulnerable populations from TB, TB/HIV, and MDR-TB. In no other setting are these needs better highlighted simultaneously than in prisons. The convergence of groups with multiple risk factors warrants a particular assessment and response. The strategy outlines five strategic components that, working in synergy, would lead to achieving the overall goal and objectives. The fifth component is to empower people with TB and communities. This goal is expected to be achieved through the implementation of ACSM strategies targeting TB control.

Definitions

The ACSM Working Group of the Stop TB Partnership uses these definitions—

- *Advocacy:* persuading decision makers of the importance of TB action
- *Communication:* using media in all its forms to inform, persuade, and generate action among all people about TB
- *Social mobilization:* actively engaging and empowering the community in the fight against TB

Although the usual basis for the ACSM initiative is the general population, its applicability to prisons cannot be underestimated. Prisons represent highly developed, enclosed communities, and although these entities have their own particularities (i.e., security issues, overcrowding, specific internal hierarchies with their own values and rules, inferior funding, increased risks), the challenges remain the same or even amplified. Prisons, therefore, must provide TB services for prisoners who normally do not have these services available and for TB programs to actively find cases through screening and contact investigation interventions. These services must also include ACSM activities.

Strategic Components

The ACSM subgroup at the country level outlines four key strategies that address (1) improving TB case detection and treatment compliance, (2) combating stigma and discrimination, (3) empowering people affected with TB, and (4) mobilizing political commitment and resources to fight TB. Boxes 7 and 8 describe field experiences related to these strategies.

Improving TB Case Detection and Treatment Compliance

Challenges have arisen because case detection uses a generally passive approach. Normally, patients must present themselves to the health services when symptomatic and adhere to multidrug therapy for at least six months. In reality, studies document that patients and providers delay both diagnosis and treatment initiation[1–4] in the civilian population and in prisons.[5,6]

Determinants of poor compliance with TB therapy have been researched extensively. Poor knowledge and awareness of TB and its treatment are common and are related to

health-seeking and treatment compliance behaviors. Although disproportionately less information is available from prisons compared to civilian populations, studies conducted in prisons confirm clear misperceptions regarding the etiology, prevention, and treatment of TB among prisoners and staff.[7,8]

Box 7. Field Experiences:
How Education Affects Case Detection and Treatment Outcomes

Cali, Colombia
The evaluation of a civilian-based, educational mass media campaign in Cali, Colombia, has demonstrated the impact of education about TB on case detection. The messages disseminated through the campaign focused on the identification of symptoms, attendance to a clinic if a cough of more than 15 days was present, the availability of free diagnostic examination, and the availability of effective and free treatment. Specifically, it aimed at increasing the public's demand for sputum smears at diagnostic centers and reducing the prevalence of stigmatization toward persons living with TB. The results showed an increase in the numbers of persons who underwent sputum testing, sputum specimens tested overall, and TB cases reported.[9]

Honduras
Similar results were observed in Honduran prisons. The introduction of DOTS into the penal system included a strong IEC component that incorporated formal educational mechanisms (e.g., talks, videos, flipcharts, printed materials) and recreational educational activities (e.g., soccer matches with messages transmitted, theatrical skits, song contests, poster contests, question-and-answer games). Parallel to these efforts, the reported TB suspects increased by 320 percent from baseline, and smear-positive case notification increased by 88 percent.[10] At the individual level, patient-based education has contributed to enhanced treatment compliance with improved treatment outcomes. In Honduran prisons, cure rates improved significantly as IEC activities gained momentum. Education on the relevance of adherence was provided to patients and their families during visitations. Peer (prisoner) educators were involved in providing this service.

San Francisco, California
In a randomized control trial in a prison in San Francisco, California (United States), researchers measured attendance at a clinic for continuation of treatment for LTBI within one month post-release. The interventions among inmates included (1) education every two weeks while incarcerated, (2) a cash incentive for attending the follow-up clinic within one month after release, and (3) usual care. Patients in the education group and the incentive group were more likely to attend the clinic for follow up within one month of release compared to controls. Patients in the educational arm were also twice as likely to complete LTBI therapy compared with controls and those who received an incentive.[7,8] Thus, education has a demonstrated efficacy in treatment adherence.

Combating Stigma and Discrimination

Stigma and discrimination, which are among the greatest threats to TB control, are complex to address. Fear of stigmatization and rejection have been associated with delays in seeking care for TB symptoms in multiple studies, and those delays adversely affect the individuals' health outcomes and allow for TB to spread into the family and community. Those afflicted by TB may be rejected and shunned by their family and peers. Because TB is sometimes attributed to the loss of moral values, as in the case of prisoners in Honduran prisons,[7] patients are often blamed. In some societies, TB renders women unmarriageable. Engagements and even marriages have been broken if a woman is diagnosed with the disease, a fact that highlights the unequal burden that women afflicted with TB bear in these countries and societies.

Consequently, symptomatic patients may avoid a diagnosis. Similarly, persons may attribute their ailments to AIDS and, fearful of this diagnosis, delay diagnosis and care, as demonstrated in a study in Thailand.[11] The studies in Honduras and Texas (United States)[8] give proof to stigma being present not only among prisoners but also among staff. In the latter, 43 percent of prisoners (especially women) and 44 percent of staff perceived stigma against TB; 54 percent of correctional officers expressed their fear of working with TB patients.

Once a diagnosis is made, patients may isolate themselves. This secrecy surrounding their illness, and the lack of a supportive social network, increase a patient's likelihood of defaulting from treatment.

Studies that sought to improve our understanding of the development of stigma have elucidated information useful to the design of stigma-reducing education. A study among the general population in Hong Kong on HIV/AIDS, TB, and SARS identified factors that sequentially play into the formulation of stigma—

- The controllability of the disease or the control an individual has over acquiring the disease on his own
- The degree of responsibility an individual has for getting the disease, which in turn leads to determining whether the patient is to blame or not for his disease[12]

In Colombia, a survey illustrated that inaccurate beliefs about TB transmission and fear of patients significantly predicted prejudice.[4] Hence, prisons must incorporate information and education that modifies beliefs (i.e., perceived susceptibility and severity) and attitudes toward those affected with TB, in addition to factual knowledge about the disease. As an example, the educational campaign within Honduran prisons reported a 17 percent reduction in the percentage of prisoners and staff who strongly agreed with the statement "I would be shunned by those people around me if I got TB" after a year of exposure to intensive education that addressed stigma.

Empowering People Affected with TB

In an effort to empower those affected by TB, programs can build upon the wealth of experiences accrued by the HIV/AIDS community. Including affected populations in the planning and implementation of HIV control strategies has allowed for a greater response to tackling the epidemic. Effective communication channels for TB patients to voice their concerns and express their needs are required.

Concerning TB control in prisons, community participation is particularly challenging given the public's, and in some cases policy makers', perceptions of prisoners as antisocial and misfits who cannot be entrusted with a role in disease control. Yet prisoners have been successfully integrated into HIV and TB control programs as volunteers. In the fight against HIV, specialists recommend involving prisoners in the development and dissemination of educational programs. Consistent with this, Honduran prisoners have been engaged as peer educators and treatment observers and have been involved in the identification of TB suspects. During prison IEC campaigns, prison directors, health personnel, and prisoners collaborate in the design and development of the activities. The benefits of this approach are threefold—

- It makes the information and messages more sensitive and appropriate to the prison context and, consequently, the information presented more credible.
- It boosts the sense of ownership among prisoners, which contributes to the continuity of the program.
- It allows for more interaction of ideas, and that interaction helps keep messages and activities changing to avoid desensitization by the target audience.

Mobilizing Political Commitment and Resources to Fight TB

Complementary political commitment lies at the core of efforts to establish and sustain effective TB control strategies in prisons. The common denominator of successful initiatives is the equal participation of decision makers, administrators, and implementers of the public health and penitentiary systems. Policies that support ongoing and sustainable programs should be introduced, along with adequate resources to build the required capacity that would translate such policies into effective practice.

Political commitment must be present at the various levels of the NTP and of the prison system. Within the public health sector, the decentralization that has occurred in many resource-constrained countries has shifted the planning and resource-allocation processes from the central level to provincial and district authorities, limiting in many instances the influence and involvement of the central level. Thus, advocating heavily and fostering awareness continuously are essential for TB services in prisons in the periphery, and decision makers in these levels should become stakeholders in the program to help ensure its continuity.

In most cases, the penitentiary structure continues to operate vertically. Regional and local officials take action if mandated from above; consequently, a positive and committed response from the highest level will have a favorable impact to facilitate the

implementation of TB control activities, including the mobilization of resources.

The involvement of other groups, including prisoners, NGOs, religious organizations, and the private sector has proven to maximize results. The contributions of these groups within TB control programs in prisons should be acknowledged and replicated. In the prison setting, where funding and staffing are less than that available for public health facilities, prisoners may become the human resources for TB services. Capitalizing on them for multiple tasks, including education, counseling, and development of IEC materials, may result in better accepted information and interventions.

Box 8. Field Experiences:
The Role of Partnerships in Mobilizing Resources for Prison TB Programs

Peru
The TB control program in San Juan de Lurigancho prison in Lima, the largest penitentiary facility in Latin America, is a model of integrated TB services where the prison health officials have joined with the NTP to implement DOTS. Understanding the urgency of controlling drug resistance in the prison, prison officials participated actively with the NTP in developing the GFATM proposal, granting the capacity to the prison to develop their laboratory and isolation wards for TB patients. NGOs and the Catholic Church also assist with HIV education and counseling activities.

Honduras
Prison directors in Honduran prisons have taken the initiative to seek donations from the private sector to support their TB IEC campaigns and to improve their health infrastructure. In the case of San Pedro Sula prison, the prison director established an agreement with a local soda company for the exclusive sale of its products inside the prison refreshment stands. The soda company, in turn, contributes to the printing of IEC materials for dissemination during the World TB Day celebration in the prison. Prison directors also use part of the revenue collected from the sale of produce grown on penal farms to fund prison educational activities and for other operational costs of their TB program (i.e. transportation of sputum and fixed smear slides to the local health center laboratory). To increase patients' adherence to TB therapy, a prison obtains milk from a local church; the patient receives the milk in the clinic with each dose of his medication. In another example, local merchants contributed lumber and nails for building a respiratory isolation area.

Indonesia
The public health and prison sector in Indonesia have actively collaborated to develop and implement a joint national strategy for TB control in prisons. This program is facilitated by a working group at the central and peripheral levels that includes multiple stakeholders, including the national AIDS program and NGOs working in prisons. These groups plan and oversee DOTS implementation in a more coordinated manner.

Endnotes for Chapter 19

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12. W. Mak, P. Mo, and R. Cheung. 2006. Comparative Stigma of HIV/AIDS, SARS, and Tuberculosis in Hong Kong. *Social Science and Medicine* 63(7): 1912–22.

Suggested Reading for Chapter 19

WHO. 2006. *Advocacy, Communication and Social Mobilization to Fight TB, A 10-year Framework for Action.* Geneva: WHO http://whqlibdoc.who.int/publications/2006/9241594276_eng.pdf

Today's date: _____ **Date of incarceration:** _____

Prison: _____

Registration Number: _____

Prisoner's Name: _____ **Sex:**

Female	
Male	

Age: _____

Date of imprisonment: _____

Prisoner's room number: _____ **Block:** _____

Screening due to: (please check)

Entry into prison	
Contact of TB case	
Symptomatic (passive)	
Referred from VCT	

Symptoms:	**Yes**	**No**
Cough with sputum > 2 weeks		
Hemoptysis		
Prolongued fever		
Unexplained weight loss (in last 3 months)		
Chest Pain		
Enalrged lymph nodes (>2cm)		

Duration of symptoms: _____

Previous anti-TB treatment: (in the last 5 years)

Yes	No

When (year): _____

Duration (months): _____

TB suspect?

Yes	No

If TB suspect , please register in TB Screening Register and evaluate for TB according to NTP/DOTS guidelines.

Memorandum of Understanding (MoU)
For Partnership in Implementation of the Tuberculosis Control Program in prisons

1. **Parties**
   The National Tuberculosis Control Program (NTP), Ministry of Health (MoH), … represented by the National Center for Tuberculosis Control (hereafter referred to as the…) and

   The Prison Department, general Administration Department of the Ministry of Interior, hereafter referred to as "Prison Department" agree to cooperate in the implementation of the NTP and DOTS activities in prisons in …..

2. **Background**
   The NTP is carrying out activities to expand the Directly Observed Therapy Short-course (DOTS) in sectors outside the MoH through its Public-Private/Public-Public Mix (PPM) strategy. This strategy encompasses prisons where TB morbidity is higher than in the general population and health services are generally substandard due to limited budgets and competing needs. Joint activities have been implemented by the Prison Department and … in the national penitentiaries in (name of country).

   The collaboration aims to strengthen these efforts and promote the integration of a TB control program in prisons that is closely linked to the civilian (NTP/MoH) program at the different levels of service throughout the country.

3. **Duration and Renewal**
   This MoU will be in force from the date of signing and it will remain valid until ____(day)_____(month)_____(year). This MoU can be extended for further periods with the consent of both parties in writing.

4. **Principles of Collaboration**
   Implementation of the Tuberculosis Control Program will be according to the NTP guidelines. Implementation of the program will eventually ensure availability and accessibility of quality TB services in prisons, specifically the implementation of sound and effective DOTS. Coordination between parties, mutual respect, trust, and recognition of mutual expertise will be ensured within the overall national development framework. Implementation of the program will be in the national penitentiaries and district prisons. It will strengthen the integration of DOTS into the current prison health services.

5. **Contribution of the NTP**
   A. Provide national guidelines for the Tuberculosis Control Program in prisons.
   B. Ensure coordination/cooperation of relevant authorities (MoI, MoH) with other partners (non-governmental organizations, donors)
   C. Supply guideline and operational manuals, and other relevant publications, TB drugs, laboratory reagents, other consumables, recording and reporting forms, and advocacy-communication-social mobilization materials on a regular basis.
   D. Ensure access to referral facilities for consultation and hospital care of cases.
   E. Ensure laboratory services and support quality control of laboratory services

through cross checking of slides.

F. Provide overall systematic supervision, monitoring and evaluation of the DOTS program in prisons
G. Provide feedback to the Prison Dept. authorities and prison health staff.
H. Provide training to the relevant prison personnel.

The Department of Prisons, subject to government policies, will:

6. Contribution of the Prisons Department

A. Implement the program according to the national guidelines in above mentioned areas
B. Assume financial responsibility for the training of own personnel and normal implementation of the program, i.e., all running costs except those mentioned in clause 5.
C. Work in coordination/cooperation with the relevant authorities, ensuring information and awareness of each other's work.
D. Implement the program as in the best of experience and capacity and in cooperation with the health referral network.
E. keeping adequate record on their consumption and submit timely indent for quarterly supply with consumption report.
F. Facilitate the monitoring and evaluation of DOTS implementation, jointly with local health authority at each level.
G. Support supervisory and other visits by the NTP whenever necessary.
H. Support and conduct DOTS activities and execution of special initiatives undertaken by providing human resources and other necessary input.

7. Guarantees

A. Either party can terminate this agreement at any time with 60 days notice in writing indicating reasons for same to the other party. In-kind, nonperishable goods will be returned to the NTP at the point of termination of this agreement.
B. In case of dispute, a final decision will be made by the _____.
C. Failure to implement the program as agreed upon in clauses 4, 5, or 6 may lead to termination of this agreement.

This memorandum of understanding is signed today, the
____(day)_____(month)_____(year).

For the Prison Dept. **For the NTP**

Prison: _____ District: _____ State: _____ Health Region No.: _____
Health Area No.: _____ Year: _____ Responsible person: _____

(1) No.	(2) Name	(3) Address	(4) Date of entry into prison (current episode)	(5) Previous incarceration (Y/N)	(6) Age / Sex	(7) Detection strategy (method)* (E, SR, CI. MS, VCT)	(8) TB suspect* (Y/N)	(9) Sputum smear(S)/ Culture (C) results / Dates			(10) Physician Review TB? (Y/N) / Date	(11) Radiography TB? (Y or N) / Date	(12) Date Treatment started	(13) Comments

- No. (7): Prison entry screening (**E**), self-referred TB suspect (**SR**), during contact investigation (**CI**), mass screening (**MS**), referred from VCT service (**VCT**)
- No. (8): **TB suspect**= patient with cough and sputum for 2-3 or more weeks of duration, and/or other symptoms in which TB is suspected.

(Filled by prison staff; 1 copy given to patient; 1 copy kept at prison clinic and; 1 copy sent to Local /District NTP Supervisor/Manager)

Name of referring prison:_____
Prison address:_____
District:_____ Province:_____
Telephone:_____Fax:_____
Name of health center or prison to which patient is being referred:_____
Address of health center of prison:_____
District:_____ Province:_____
Telephone:_____ Fax: _____

Name of the patient:_____
Sex:____Age:____(years)
Patient's address:_____
District:_____Province:_____
Telephone: _____
Name of patient relative/contact:_____
Telephone:_____

Reason of referring (please check applicable):

☐ Initiation of treatment

☐ Continuation of treatment (the TB treatment card should be attached)

Type of patient:

☐ New ☐ Transfer In

☐ Return after default

☐ Relapse ☐ Failure ☐ Other

Disease classification:

☐ Pulmonary ☐ Extrapulmonary

Site_____

Type of treatment:

☐ Cat I ☐ Cat II ☐ Cat III

Remarks: _____

Name (please print) and signature: _____

Date of Referral: _____

Initial Referral Feedback form

(Filled by staff at health center or prison where patient has been referred, upon receipt of patient)

Name of patient: _____ Patient TB No.: _____
Age:_____ Sex:_____
Date referred by prison:_____
Date reported to health center (or prison clinic):_____
Name of health center (prison): _____
District:_____ Province: _____
Name (please print) and signature of health center staff:_____
Date this form completed:_____

Keep one copy at unit; send 1 copy to prison as soon as the patient has reported and been registered at your unit and; send 1 copy to local local /District NTP supervisor/manager

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Final referral feedback form
Result of Treatment

[Filled by staff at health center (prison) upon completion of treatment of the referred patient]

Name of patient:_____ Patient TB No.: _____
Age:_____ Sex:_____
Date referred by prison:_____ Date reported to health center:_____
Name of health center: _____
District:_____ Province: _____

Treatment result of patient: (Please check appropriate box)

- ☐ Cured
- ☐ Completed treatment
- ☐ Died
- ☐ Default/drop-out
- ☐ Failed
- ☐ Transfer-out

Name (please print) and signature of health center staff:_____
Date this form completed:_____

Keep one copy at unit; and send 1 copy to prison and 1 copy to local/District NTP supervisor/manager as soon as the patient has completed TB treatment.

ANNEX 5. SAMPLE REFERRAL REGISTER

Month: _____ Year: _____

[Kept at Prison and/or by local/District TB Supervisor/Manager]

No.	MR No.	Name	Age		Address	P/EP	Result of sputum test (diagnosis)	Treatment category	Date starting treatment	Number of pills taken under DOT	
1			F	M						Intensive	Continuation
2											
3											
4											
5											
6											

...Continue

Number of pills was sent along patients		Referral		Date of				Treatment result	Notes
Intensive	Continuation	From	To	Referral form to health facility	Referral form to local/ District NTP supervisor	Receipt of Initial feedback form from health facility that received patient	Receipt of Final feedback form with treatment results from health facility that received patient		

How to fill in:

• **No.**	: According to order
• **PR No.**	: Prison medical record number
• **Name**	: Complete name, as written in ID card
• **Age/F/M**	: Age/ **F**emale/**M**ale
• **Address**	: as written in ID card
• **P/EP**	: Pulmonary/Extra pulmonary TB case
• **Result of sputum test**	: The result of diagnostic sputum test
• **Treatment category**	: Treatment category
• **Date of starting treatment**	: The date of starting treatment
• **Number of pills taken**	: The number of pills according to number of days patients has been treated before referring to other health facility
• **Number of pills brought by patient**	: The number of pills given to patients/sent along with the patient during the referral
• **Referral**	
o To	: Name of referred health facility, complete it with name of sub district, district/municipality, province
o From	: Name of referring health facility
• **Date**	
o Referral form to health facility	: Date when patient was given referral form for health center or prison (if transferred to another prison)
o Referral form to local/District TB supervisor	: Date when copy of referral form (TB09) was sent to Province/District NTP coord.
o Receipt of initial feedback form	:Date when initial referral feedback from (TB10 Part 1) was received at hospital
o Receipt of final feedback form	:Date when final referral feedback form (TB10 Part 2 –Treatment Result) was received at hospital
• **Treatment result**	: Result of treatment of referred patient (Cured, completed treatment, died, failed, defaulted, transferred-out)

ANNEX 6. SAMPLE BASELINE ASSESSMENT OF TB AND TB CONTROL IN PRISONS

Prison: _____ **Location:** _____
Date: _____
Respondent (name, position): _____

I. Structural and administrative aspects of detention:

-*Type of prison* (state, county jail, etc.): _____
_____
-*Type of prisoners* (sentenced, processes): _____
_____
-*Average daily prison population:* _____
-*Official inmate capacity:* _____
-*Number of rooms:* _____
-*Number of security staff per shift:* _____
-*Funding sources:* _____
_____
-*Prison resources and limitations:* (as viewed by respondent)
Salaries: _____
Infrastructure: _____
Provision of essential needs and supplies (food, medicines, health services and staff, medical supplies): _____
Other: _____
_____

-*Prison conditions:* (as observed by interviewer)
Overcrowding: _____
Nutrition status of detainees: _____
Hygiene: _____
Security: _____

-*Penal reform efforts* (amnesties) in the last 12 months: _____

II. Aspects of Health Care

-Treatment facilities: YES_____ NO_____
If YES, describe them:_____
_____
_____

-Diagnostic facilities (Laboratory): YES_____ NO_____
If YES, describe them:_____
_____
_____

-Referral facilities: YES_____ NO_____
If YES, describe:_____
_____
_____

-Transportation to referral facilities: YES_____ NO_____
If YES, describe:_____
_____
_____

-Health staff:
Number: _____
Training (doctor, professional nurse, auxiliary nurse, nurse assistant):_____
_____
_____
Salaries: _____

-Supplies:
Anti-TB drugs: YES_____ NO _____
Explain:_____
Lab material: YES_____ NO_____
Exlain:_____
Storage capacity: YES_____ NO_____
Explain:_____
Adequate stock management: YES_____ NO_____
Explain: _____

Sources:_____
_____
_____
_____

III. Demographic and TB related data

-Census (average daily pop.): _____
-Approximate number of admissions per year: _____
-Approximate number of discharges per year: _____

A. TB morbidity among inmates in the last year (Ask medical staff, check treatment cards)

Pulmonary Tuberculosis									New extra pulmonary		Total		
Smear positive							New Smear negative						
New			Relapse		Others								
M	F	Total	M	F	M	F	M	F	M	F	M	F	Total

-TB mortality in the current year: _____

-Number of prison staff with TB disease (and number of years working in prison):
_____

-Number of HIV-positives among TB patients (%): _____

B. TB case finding and diagnosis

a. *Screening upon entry:* YES_____ NO_____
Method for screening (physical, X-ray exam., etc.): _____
_____
_____
_____

b. *Passive case finding:* YES_____ NO_____
Method for finding cases (physical, X-ray, sputum analysis)
Explain: _____
_____
_____
_____
_____

c. *Other (active case finding):* YES_____ NO_____
Explain: _____
_____
_____

-Lab services in prison: YES_____ NO_____

-Radiology services in prison: YES_____ NO _____

-Referral facilities for TB services if used: _____

*-Average delay in days of diagnosis:*_____

-If screening activities performed, % and number of cases are found by active VRS passive case finding:_____

C. TB treatment

*-Average delay in days of treatment initiation:*_____
-Chemotherapy regimens in accordance with NTP/WHO: YES_____ NO _____
*-Methods of ensuring treatment adherence (DOTS, incentives):*_____
_____
_____
_____
*-Who provides anti-TB drugs?*_____

-Are they free of cost? YES_____ NO_____
If NO, explain: _____

-Has there been any drug interruption in the past 2 years? YES_____NO_____
If YES, when, why, how was it resolved? _____
_____
_____
_____

		Treatment Outcomes						
Total No. of smear-positive patients reported last year	Regimen	Cured	Treatment completed	Died	Failure	Defaulter	Transfer out	Total number evaluated
	Smear-positive new cases (1)							
	Smear-positive relapses (2)							
	Other smear-positive cases (3)							
	Total smear-positive retreatment cases (2+3)							

D. TB prevention and infection control policies

-Isolation wards for TB only: YES _____ NO _____

Explain:_____

_____

-Referral to another prison for TB treatment: YES _____ NO _____

If YES, where, explain:_____

_____

-Other infection control methods used (masks, etc.): YES _____ NO_____

If YES, explain:_____

_____

E. Registration, recording and reporting system

-Recording and reporting of cases done: YES _____ NO _____
If YES, by whom (NTP/MOH?): _____

-Registries are NTP/MOH formats? YES _____ NO _____
If NO, explain: _____

-Are cases reported (specified) as prison cases? YES _____ NO _____
-Are they included in civilian registries by the NTP? YES _____ NO _____
-Is a referral given every time when TB patients are transferred or released?
YES _____ NO _____

F. Education (to prisoners)

-Training of prison health staff: YES _____ NO _____
-Trainers: _____
-Type of training: _____
-Frequency of training: _____
-Date of last training: _____
-Training to administrative staff: _____
-Information, education to inmates: YES _____ NO _____
-Type of training: _____

G. Program management

-Supervision/evaluation of tuberculosis control program in prison:
YES _____ NO _____
-If YES, by whom? (NTP/MOH): _____
-Frequency supervision/evaluation: _____

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Seizures	**Cycloserine** Isoniazid Fluoroquinolones	1. Suspend the suspected agent pending resolution of seizures. 2. Initiate anticonvulsant therapy (e.g., phenytoin, valproic acid). 3. Increase pyridoxine to maximum daily dose (200 mg per day). 4. Restart the suspected agent or reinitiate the suspected agent at lower dose, if essential to the regimen. 5. Discontinue the suspected agent, if this can be done without comprising the regimen.	1. An anticonvulsant is generally continued until MDR-TB treatment is completed or suspected agent is discontinued. 2. History of previous seizure disorder is not a contraindication to the use of the agents listed here if a patient's seizures are well controlled, the patient is receiving anticonvulsant therapy, or both. 3. Patients with a history of previous seizures may be at increased risk for development of seizures during MDR-TB therapy.

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Peripheral neuropathy	**Cycloserine** **Isoniazid** Streptomycin Kanamycin Amikacin Capreomycin Ethionamide/ protionamide Fluoroquinolones	1. Increase pyridoxine to maximum daily dose (200 mg per day). 2. Change the injectable to capreomycin if the patient has documented susceptibility to capreomycin. 3. Initiate therapy with tricyclic antidepressants such as amitriptyline. Non-steroidal anti-inflammatory drugs or acetaminophen may help alleviate symptoms. 4. Lower the dose of the suspected agent, if this can be done without compromising the regimen. 5. Discontinue the suspected agent, if this can be done without compromising the regimen.	1. Patients with comorbid disease (e.g., diabetes, HIV, alcohol dependence) may be more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here. 2. Neuropathy may be irreversible; however, some patients may experience improvement when the offending agents are suspended.

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Hearing loss	**Streptomycin** **Kanamycin** **Amikacin** **Capreomycin** Clarithromycin	1. Document hearing loss and compare with a baseline audiometry, if available. 2. Change parenteral treatment to capreomycin if patient has documented susceptibility to capreomycin. 3. Increase the frequency or lower the dose of the suspected agent (or do both), if these measures can be taken without compromising the regimen. (Consider administration three times per week.) 4. Discontinue the suspected agent, if this can be done without compromising the regimen.	1. Patients with previous exposure to aminoglycosides may have baseline hearing loss. In such patients, audiometry may be helpful at the start of MDR-TB therapy. 2. Hearing loss is generally not reversible. 3. The risk of further hearing loss must be weighed against the risks of stopping the injectable in the treatment regimen.
Psychotic symptoms	**Cycloserine** **Isoniazid** Fluoroquinolones Ethionamide/ protionamide	1. Stop the suspected agent for a short period (1–4 weeks) while psychotic symptoms are brought under control. 2. Initiate antipsychotic therapy. 3. Lower the dose of the suspected agent, if this can be done without compromising the regimen. 4. Discontinue the suspected agent, if this can be done without compromising the regimen.	1. Some patients will need to continue antipsychotic treatment throughout MDR-TB therapy. 2. Previous history of psychiatric disease is not a contraindication to the use of the agents listed here but may increase the likelihood of psychotic symptoms developing during treatment. 3. Psychotic symptoms are generally reversible upon completion of MDR-TB treatment or cessation of the offending agent.

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Depression	If not due to socioeconomic circumstance and chronic disease **Cycloserine** Fluoroquinolones Isoniazid Ethionamide/ protionamide	1. Improve the socioeconomic conditions. 2. Provide group or individual counseling. 3. Initiate antidepressant therapy. 4. Lower the dose of the suspected agent, if this can be done without compromising the regimen. 5. Discontinue the suspected agent, if this can be done without compromising the regimen.	1. Socioeconomic conditions and chronic illness should not be underestimated as contributing factors to depression. 2. Depressive symptoms may fluctuate during therapy and may improve as the illness is successfully treated. 3. History of previous depression is not a contraindication to the use of the agents listed here but may increase the likelihood of depression developing during treatment.
Hypo-thyroidism	**Paraminosalicylic acid** **Ethionamide/ protionamide**	1. Initiate thyroxine therapy.	1. Condition is completely reversible upon discontinuation of P-aminosalicylic acid or ethionamide/protionamide. 2. The combination of ethionamide and protionamide with P-aminosalicylic acid is more frequently associated with hypothyroidism than the individual use of each medicine.

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Nausea and vomiting	**Ethionamide/ protionamide** **Paraminosalicylic acid** Isoniazid Ethambutol Pyrazinamide	1. Assess for dehydration; initiate rehydration if indicated. 2. Initiate antiemetic therapy. 3. Lower the dose of suspected agent, if this can be done without compromising the regimen. 4. Discontinue the suspected agent, if this can be done without compromising the regimen (rarely necessary).	1. Nausea and vomiting are universal in early weeks of therapy and usually abate with time on treatment and adjunctive therapy. 2. Electrolytes should be monitored and repleted if vomiting is severe. 3. Nausea and vomiting are reversible upon discontinuation of the suspected agent. 4. Severe abdominal distress and acute abdomen have been reported with the use of clofazimine. Although these reports are rare, if this effect occurs, clofazimine should be suspended.
Gastritis	**Paraminosalicylic acid** **Ethionamide/ protionamide**	1. Give H2-blockers, proton-pump inhibitors, or antacids. 2. Stop the suspected agent(s) for short periods (e.g., one to seven days). 3. Lower the dose of the suspected agent, if this can be done without compromising the regimen. 4. Discontinue the suspected agent, if this can be done without compromising the regimen.	1. Severe gastritis, as manifested by hematemesis, melena, or hematochezia, is rare. 2. Dosing of antacids should be carefully timed so as to not interfere with the absorption of anti-TB medicines (e.g., take two hours before or three hours after anti-TB medicines). 3. Gastritis is reversible upon discontinuation of the suspected agent(s).

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Hepatitis	**Pyrazinamide** **Isoniazid** **Rifampicin** Ethionamide/ protionamide Paraminosalicylic acid Ethambutol Fluoroquinolones	1. Stop all therapy pending the resolution of hepatitis. 2. Eliminate other potential causes of hepatitis. 3. Consider suspending the most likely agent permanently. Reintroduce the remaining medicines, one at a time with the most hepatotoxic agents first, while monitoring liver function.	1. History of previous hepatitis should be carefully analyzed to determine the most likely causative agent(s); these agents should be avoided in future regimens. 2. Generally, hepatitis is reversible upon discontinuation of the suspected agent.
Renal toxicity	**Streptomycin** **Kanamycin** **Amikacin** Capreomycin	1. Discontinue the suspected agent. 2. Considering using capreomycin if an aminoglycoside had been the prior injectable in regimen. 3. Consider dosing two to three times a week if the medicine is essential to the regimen and the patient can tolerate it. (Close monitoring of creatinine is required.) 4. Adjust all TB medications according to creatinine clearance.	1. History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these comorbidities may be at increased risk for developing renal failure. 2. Renal impairment may be permanent.

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Electrolyte disturbance (hypo-kalemia and hypo-magnesaemia)	**Capreomycin** Kanamycin Amikacin Streptomycin	1. Check potassium. 2. If potassium is low, also check magnesium (and calcium if hypocalcemia is suspected). 3. Replace electrolytes as needed.	1. If severe hypokalemia is present, consider hospitalization. 2. Amiloride (5–10 mg daily) or spironolactone (25 mg daily) may decrease potassium and magnesium wasting and is useful in refractory cases.
Optic neuritis	**Ethambutol**	1. Stop ethambutol. 2. Refer the patient to an ophthalmologist.	1. Condition usually reverses with cessation of ethambutol. 2. Rare case reports of optic neuritis have been attributed to streptomycin.

Adverse Effect	Suspected Agent(s)[a]	Suggested Management Strategies	Comments
Arthralgias	**Pyrazinamide** Fluoroquinolones	1. Initiate therapy with non-steroidal anti-inflammatory drugs. 2. Lower the dose of the suspected agent, if this can be done without compromising the regimen. 3. Discontinue the suspected agent, if this can be done without compromising the regimen.	1. Symptoms of arthralgia generally diminish over time, even without intervention. 2. Uric acid levels may be elevated in patients on pyrazinamide. Allopurinol appears not to correct the uric acid levels in such cases.

[a] Medicines in bold type are more strongly associated with the adverse effect than medicines not in bold.