TUBERCULOSIS IN HIV INFECTED PATIENTS

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Summary

The interaction between tuberculosis and HIV has implications for the public health approach to control tuberculosis among HIV-infected people. Untreated HIV infection leads to progressive immunodeficiency and increased susceptibility to infections, including tuberculosis. Tuberculosis in high HIV prevalence populations is a leading cause of morbidity and mortality, and HIV is driving the tuberculosis epidemic in many countries (especially in sub-Saharan Africa). Tuberculosis programmes and HIV programmes therefore share mutual concerns: prevention of HIV should be a priority for tuberculosis control; tuberculosis care and prevention should be priority concerns of HIV/AIDS programmes.

The public health approach to decrease the burden of TB/HIV requires more effective delivery of the available interventions by health service providers, with increased population coverage. The expanded scope of the new strategy for tuberculosis control in high HIV prevalence populations comprises interventions against tuberculosis (intensified case-finding and cure and tuberculosis preventive treatment) and interventions against HIV (and therefore indirectly against tuberculosis), e.g. condoms, STI treatment, safe injecting drug use (IDU) and highly active antiretroviral treatment (HAART). All co-infected patients should have individualized treatment including adherence-enhancing approaches such as staggering initiation of regimens, directly observed therapy, and patient counseling.

KEYWORDS*:* HIV:AIDS, Tuberculosis – HIV , Mixed drug resistance

Introduction

Tuberculosis (TB) is caused by the bacterium Mycobacterium *tuberculosis*. The bacterium can cause disease in any part of the body, but it normally enters the body though the lungs and resides there (1). Tuberculosis is a contagious disease that kills around 1.6 million people each year (2).

The human immunodeficiency virus (HIV) pandemic presents a massive challenge to the control of tuberculosis (TB) at all levels. Tuberculosis is also one of the most common causes of morbidity and one of the leading causes of mortality in people living with HIV/AIDS (3).

"*HIV/AIDS and TB are so closely connected that the term "co-epidemic" or "dual epidemic" is often used to describe their relationship. The intersecting epidemic is often denoted as TB/HIV or HIV/TB. TB is one of the leading causes of death in HIV-infected people* (4)."

Each disease speeds up the progress of the other. Many people infected with HIV in developing countries develop TB as the first manifestation of AIDS. The two diseases represent a deadly combination, since they are more destructive together than either disease alone.

It is estimated that one-third of the 40 million people living with HIV/AIDS worldwide are co-infected with TB. People with HIV are up to 50 times more likely to develop TB in a given year than HIV-negative people (1). HIV also promotes both the progression of latent TB infection to active disease and relapse of the disease in previously treated patients.

Another aspect of the resurgence of TB is the development of drug-resistant strains of *M.tuberculosis (MDR-TB)*. These strains can be created by inconsistent and inadequate treatment practices that encourage bacteria to become tougher. The MDRTB are much more difficult and costly to treat and MDR-TB is often fatal.

TUBERCULOSIS AND HIV POSITIVE PEOPLE:

People with advanced HIV infection are vulnerable to a wide range of infections and malignancies that are called 'opportunistic infections' because they take advantage of the opportunity offered by a weakened immune system. Tuberculosis is an HIV related opportunistic infection. A person who has both HIV and active TB has an AIDS-defining illness.

Because tuberculosis can spread through the air, the increase in active TB among people infected with both TB and HIV results in:

- increased transmission of the tuberculosis bacteria
- increase in number of people with latent TB
- increased incidence of TB disease in the whole population.

Latent TB increases the incidence of HIV infection, and increases the number of active TB patients as HIV weakens the immune system. Co infection of both HIV and latent TB increases 800 times greater risk for active TB disease development and makes the disease more infectious compared to people not infected with HIV (4).

The HIV/AIDS epidemic revived an old problem in well resourced countries and greatly worsened an existing problem in resource poor countries. There are several important associations between epidemics of HIV and tuberculosis:

- Tuberculosis is harder to diagnose in HIV positive people
- Tuberculosis progresses faster in HIV-infected people
- Tuberculosis in HIV positive people is more fatal if left untreated
- Tuberculosis occurs earlier in the course of HIV infection than other opportunistic infections (1).

TB occurs earlier than other opportunistic infections in HIV postive patients:

Mycobacterium bacilli infects the macrophages there by stimulating CD4 T lymphocytes an T-γδ lymphocytes to produce interferon gamma (IFN-γ), interleukin-2, tumor necrosis factor alpha (TNFα), and macrophage colony-stimulating factor, activating the macrophages and cytotoxic cells to inhibit their intracellular growth. IFN-γ plays a vital role in limiting the growth of mycobacteria (5). During HIV infection, the production of IFN- γ is decreased in parallel with the reduction of CD4+ T-lymphocytes and therefore leading to a marked increase in risk of developing reactivation or reinfection by M. tuberculosis in HIV positive patients(6,7).

Tuberculosis is the only major AIDS-related opportunistic infection that poses a risk to H9IV-negative people (8). A person infected with TB can have active or inactive tuberculosis. In active TB or TB disease, bacteria are active in the body and the immune system is unable to defend them from causing illness. People with active TB in their lungs transmit the bacteria to close associates. Active TB transmits through and causes infection. Each person with active TB will infects on an average between 10 to 15 people every year.

Inactive TB infection is also called latent TB as well as a disease which does not have symptoms and cannot spread tuberculosis. TB bacteria remains dormant for life time and gets activated depending on immune system of the body, for eg in HIV

"Tackling tuberculosis should include tackling HIV as the most potent force driving the tuberculosis epidemic; tackling HIV should include tackling tuberculosis as a leading killer of PLWH (People Living With HIV/AIDS) (9)."

SYMPTOMS:

Some of the symptoms include

- Cough hemoptysis, fever, night sweats, weight loss, shortness of breath, and chest pain.
- Other symptoms of TB disease include weakness or fatigue, lack of appetite, chills and night sweats (10,11,12,13).

DIAGNOSIS:

Patients suspected of having active disease are analysed for a chest X-ray and smears and cultures of sputum. The inability to demonstrate acid-fast bacilli (AFB) does not completely exclude TB.

Culture techniques detects mycobacterium in 10-14 days. The acid-fast bacilli smear of sputum detects mycobacterium within hours. Rapid diagnostic tests are used for patients with tuberculosis, HIV, AIDS positive AFB smear sputum.

Invasive tests such as a spinal tap or biopsy of lymph nodes, liver or bone marrow are needed for patients with extra-pulmonary disease (unexplained fevers and night sweats). Blood cultures for AFB are positive in up to 25-50% of patients with HIV disease and TB.

TB diagnosis in HIV positive people:

A major challenge in diagnosing Tb in HIV/AIDS patients is the fact that their sputa often contain few or no mycobacterium because they are less likely to have cavitary lung disease and more likely to have extra pulmonary disease then other types of TB patients. Diagnosis of TB by Mountoux test is not wholly reliable in detection of Tb infections among HIV positive people, their weakened immune systems are not strong enough to defend against the infectious proteins to cause induration**.**

Diagnosis of TB and determination of the disease site of TB disease

IF →	Then
Cough > 2 weeks or persistent fever, unexplained weight loss, severe under nutrition, suspicious lymph nodes (> 2 cm), or night sweats.	**• Send sputum samples. Refer to district doctor/medical officer if not producing sputum or if nodes are present.** **• If referral is not possible and the patient is HIV positive or if there is strong clinical evidence of HIV infection, it should be diagnosed with smear-negative pulmonary TB. In sputum negative patients it should be diagnosed with suspected extra pulmonary TB.** **• Recommend HIV test in all suspected TB patients.**

HIV-positive patients are more likely to be very ill when they present with possible TB disease. In patients with serious clinical conditions, patients are immediately referred to hospital without wasting time for sputum results.

Extra pulmonary TB, when referral is not possible prompt treatment is be initiated and every attempt is made to confirm the diagnosis and proper measures are ensured to manage patient's illness.

If additional diagnostic tests are unavailable and if referral to a higher level facility for confirmation of the diagnosis is not possible, TB treatment should be started and completed. Empirical treatment with incomplete regimens of anti-TB drugs should not be performed. Patient's treated with anti-TB drugs, should intiate therapy with first-line regimens, and therapy has to be standardised and completed. Bacteriological, histological, or strong clinical evidence of an alternative diagnosis is mandatory for cessation of therapy.

TB DIAGNOSIS BASED ON SPUTUM SMEAR MICROSCOPY EXAMINATION:

HIV-positive patients are more likely than HIV-negative patients to have extra pulmonary TB or smear-negative pulmonary TB.

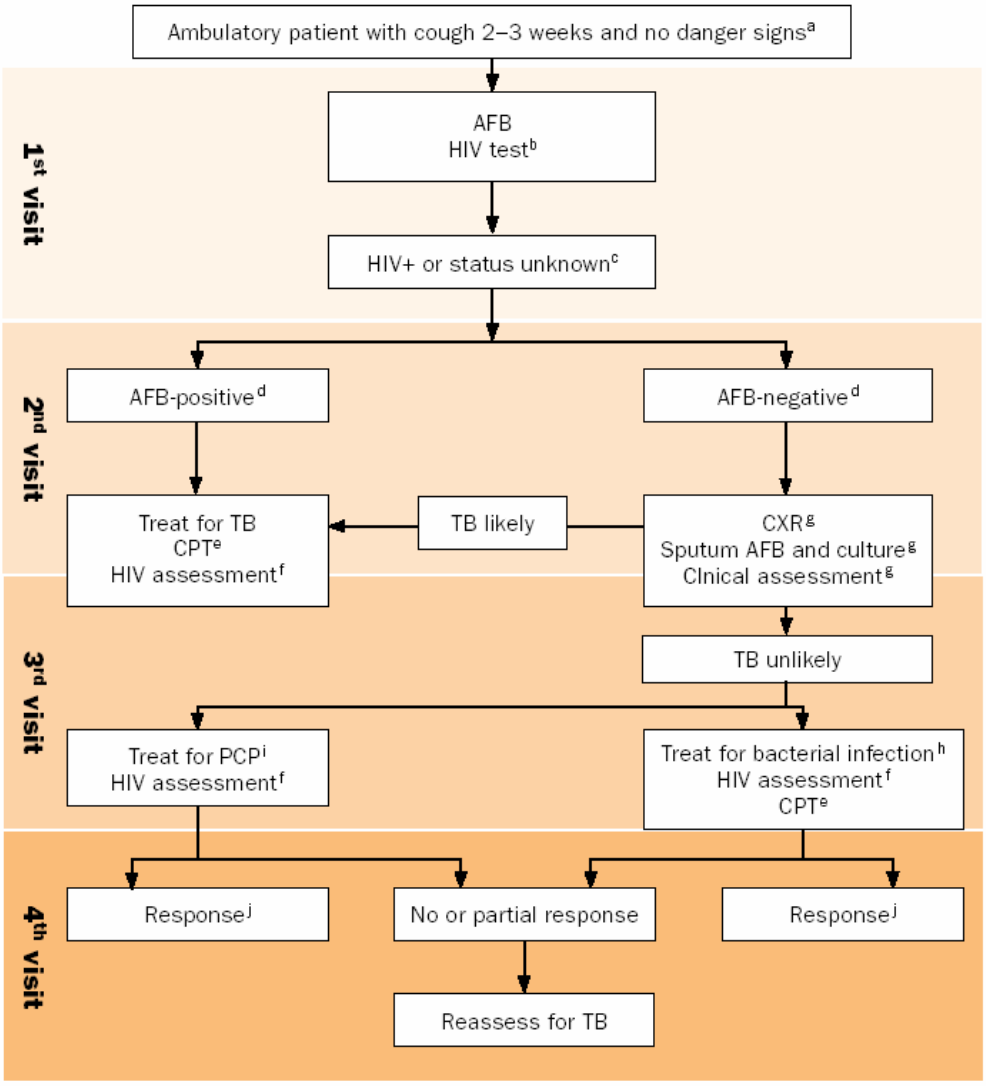
IF → Then

Two (or three) samples are Positive	Patient is **sputum smear-positive (has infectious pulmonary TB)**
Only one sample is positive in HIV-negative patient .	Diagnosis is **uncertain**. Refer patient to district doctor/ medical officer for further assessment
Only one sample is positive in HIV-positive patient	Patient is **sputum smear-positive (has infectious pulmonary TB)**
All samples are negative in HIV-negative patient	**Patient may or may not have pulmonary tuberculosis** • If patient does not have cough and has no other general complaints, no further investigation or treatment is needed. • If cough continues and/or having other general complaints (and not seriously ill), treat with a non-specific antibiotic such as cotrimoxazole or amoxicillin. • If cough persists and patient is not severely ill, repeat examination of three sputum smears. If sputum negative, refer patient to a doctor/medical officer.
All samples are negative in HIV-positive patient	**Patient may or may not have pulmonary tuberculosis:** • If cough persists, treat with non-specific antibiotic such as cotrimoxazole or amoxicillin and refer for evaluation for possible smear-negative pulmonary TB or other chronic lung/heart problem.

Extra pulmonary TB or smear-negative pulmonary TB incidence is more in HIV-positive patients than HIV-negative patients. Referring to a doctor/medical officer for further testing is necessary in HIV positive sputum negative patients. First-level facility clinician diagnosis when referral is not possible. S/he is treated as HIV positive if conformation of HIV status is not possible (13).

FIGURE 1

Algorithm for the diagnosis of tuberculosis in ambulatory patient in HIV-prevalent settings



[a] The danger signs include any one of: respiratory rate >30/minute, fever >39 °C, pulse rate >120/min and unable to walk unaided.
[b] For countries with adult HIV prevalence rate ≥1% or prevalence rate of HIV among tuberculosis patients ≥5%.
[c] In the absence of HIV testing, classifying HIV status unknown ias HIV-positive depends on clinical assessment or national and/or local policy.
[d] AFB-positive is defined at least one positive and AFB-negative as two or more negative smears.
[e] CPT = Co-trimoxazole preventive therapy.
[f] HIV assessment includes HIV clinical staging, determination of CD_4 count if available and referral for HIV care.
[g] 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 the diagnosis.
[h] Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.
[i] PCP: *Pneumocystis carinii* pneumonia, also known as *Pneumocystis jirovecii* pneumonia.
[j] Advise to return for reassessment if symptoms recur.

Reference no: 21

Treatment:

Treatment is initiated when disease is considered a reasonable possibility (positive sputum AFB smear)even when cultures reports are pending. Patient is suffering from persistent cough are to be isolated.

Multiple drug regimens are needed to treat active TB. Multiple drug therapy kills the bacteria and prevents the development of drug resistant strains. It is often recommended that the patient takes his or her pills in the presence of someone who can supervise the therapy, to ensure thorough treatment. This approach is called DOTS (directlyobserved treatment, short course). DOTS cure tuberculosis in 95% of cases, and a six-month supply of DOTS costs as little as $10 per person in some parts of the world (14). Now under TB eradication programme anti TB drugs under DOTS programme are supplied by WHO to all primary health care centres free of cost.

Initial drug regimen should consist isoniazid, rifampin, pyrazinamide and either ethambutol or streptomycin. In areas with multi-drug resistant strains, consideration should be given to using all five drugs and perhaps adding a quinolone.

The treatment regimen can be modified, depending upon the susceptibility results.

Four-drug Regimen
Isoniazid, 300 mg PO qd
Rifampin, 600 mg PO qd
Pyrazinamide, 25 mg/kg PO qd
Ethambutol, 15 mg/kg PO qd, max 2.5 g/d or Streptomycin 15 mg/kg IM qd.

Treatment is continued for at least three months after the last negative sputum culture. In case of non-compliance or a slow bacteriologic response, treatment is continued for a total of 9-12 months. DOT lowers rate of drug resistance, and is preferred for all patients (15).

If DOT is not available, combination tablets used. Eg: Rifamate is a combination tablet that contains rifampin 300 mg, isoniazid 150 mg; 2 cap qd. Rifater contains isoniazid 50 mg/rifampin 120 mg/pyrazinamide 300 mg; 6 tablets qd.

Clinical Follow-up: Response to therapy is signified by resolution of fever, cough, sputum production, and hemoptysis. Bacteriologic response is monitored by repeat sputum exams and cultures for AFB and more patients are culture-negative by 3 months. If sputum smears remain persistently positive, non-compliance is suspected and supervised daily therapy is considered. If non-compliance is unlikely, then drug resistance is considered. Active TB disease is cured with a combination of antibiotics. A proper combination of anti-TB drugs provides both prevention and cure.

Effective treatment quickly limits the contagious TB by converting it to non-contagious and therefore prevents further spread of TB. Achieving a cure takes about six to eight months of daily treatment (16,17).

TREATMENT OF PULMONARY AND EXTRA-PULMONARY TB

<table>
<tr><th>Disease Site</th><th>Laboratory results</th><th colspan="2">Type of Patient</th><th>Recommended treatment category</th></tr>
<tr><td rowspan="5">Pulmonary</td><td rowspan="4">Sputum smear-positive [a]</td><td colspan="2">New</td><td>CAT I</td></tr>
<tr><td rowspan="3">Previously treated</td><td>Relapse</td><td>CAT II</td></tr>
<tr><td>Treatment after failure</td><td>CAT II</td></tr>
<tr><td>Treatment after default</td><td>Usually CAT II</td></tr>
<tr><td>Sputum smear-negative[b]</td><td>Chronic or MDR-TB</td><td>CAT IV</td></tr>
<tr><td colspan="2">→</td><td>CAT I or III [c]</td></tr>
<tr><td>Extrapulmonary [b]</td><td colspan="3">→</td><td>CAT I or III [c]</td></tr>
</table>

a If only one sputum sample is positive, the HIV-positive patient is considered to be smear-positive. The HIV-negative patient should be referred to a clinician for diagnosis.

b Pulmonary sputum smear-negative cases and extrapulmonary cases may rarely be previously treated (treatment after failure, relapse, treatment after default, chronic). Diagnosis should be based on bacteriological and pathological evidence.

c As recommended by WHO, Category III treatment may be the same regimen as for Category I. Each country will decide whether Category I and III are different drug regimens or not. If they are different, the selection of a regimen for a particular patient will depend on the severity of disease.

A doctor/medical officer diagnoses and prescribes treatment for cases in the shaded boxes. Either a health worker or a doctor/medical officer selects the treatment category for the other cases (unshaded) and is based on the disease classification (site), laboratory results, type of patient, HIV status and recommendations in National Guidelines (13).

TB TREATMENT REGIMENS OF DIFFERENT CATEGORIES

TREATMENT CATEGORY	TUBERCULOSIS (TB) PATIENTS	ALTERNATIVE TREATMENT REGIMENS	
		INITIAL PHASE (DAILY OR 3 TIMES PER WEEK)	CONTINUATION PHASE
I	New smear-positive pulmonary TB; new smear-negative pulmonary TB with extensive parenchymal involvement; new cases of severe forms of extra-pulmonary TB.	2 EHRZ (SHRZ) 2 EHRZ (SHRZ) 2 EHRZ (SHRZ)	6 HE 4 HR 4 H_3R_3
II	Sputum smear-positive: Relapse; Treatment failure; Treatment after interruption.	2 SHRZE / 1 HRZE 2 SHRZE / 1 HRZE	5 $H_3R_3E_3$ 5HRE
III	New smear-negative pulmonary TB (other than in Category 1); new less severe forms of extra-pulmonary TB.	2 HRZ 2 HRZ 2 HRZ	6 HE 4 HR 4 H_3R_3
IV	Chronic case (still sputum-positive after supervised re-treatment)	Refer to WHO guidelines for use of second-line drugs in specialized centres[53]	

In the standard code for TB treatment regimens, each anti-TB drug has an abbreviation: streptomycin (S), isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E). A regimen consists of 2 phases. The number before a phase is the duration of that phase in months. A number in subscript (e.g. $_3$) after a letter is the number of doses of that drug per week. If there is no number in subscript after a letter, then treatment with that drug is daily. An alternative drug (or drugs) appears as a letter (or letters) in brackets.

Successfully treating HIV/TB treatment is complicated.Drug-to-drug interactions of HIV-TB drug regimens acts as limitations to therapy and paradoxically, HIV/AIDS leads to Immune Reconstitution Inflammatory Syndrome (IRIS), an over-reaction of the immune system that inflames TB. Successful TB treatment prolongs the lives of HIV patients by at least two years and probably longer , depending on the sucess of AIDS treatment as well(18,19).

In Inactive TB patient, active TB is prevented with a 6 to 9-month course of TB preventive therapy. Preventive therapy reduces the risk of development of active TB in HIV/TB patients by 60% (19,20).

"In the HIV-positive TB patient- TB-ART co-treatment plan"

The decision to initiate ART co-treatment in a TB patient is made by a TB-HIV trained doctor or medical officer. The recommendation for many TB-HIV patients is to start and complete TB treatment, and then initiate ART. However, if the patient's clinical status is poor (other signs of HIV clinical stage 3 or 4 or CD4 count less than 350/mm3), it is necessary to refer the patient for ART treatment sooner. If patient is not on ART, TB

treatment is started immediately, or if already started, TB treatment is continued.

COMMON TB-ART CO-TREATMENT REGIMENS:

A patient on TB-ART co-treatment will have higher pill burden and most likely to experience more side effects. Patient is educated to manage mild to moderate side effects and severe side effects are immediately reported to the health worker.

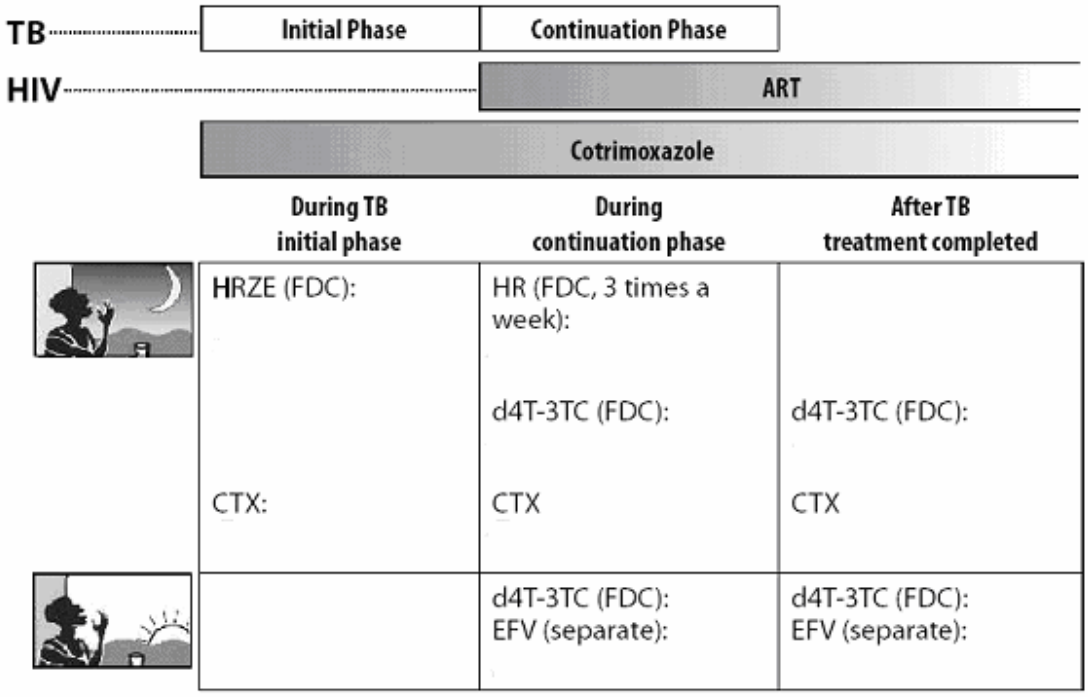
The following regimens include rifampin during the initial and continuation phases of TB treatment. The patient receives cotrimoxazole and an EFV-based ART regimen during TB treatment. There are many pills and several changes in the regimen, which requiring careful education of the patient and treatment supporter at each change.

Regimen 1 : Start ART as soon as TB treatment is tolerated

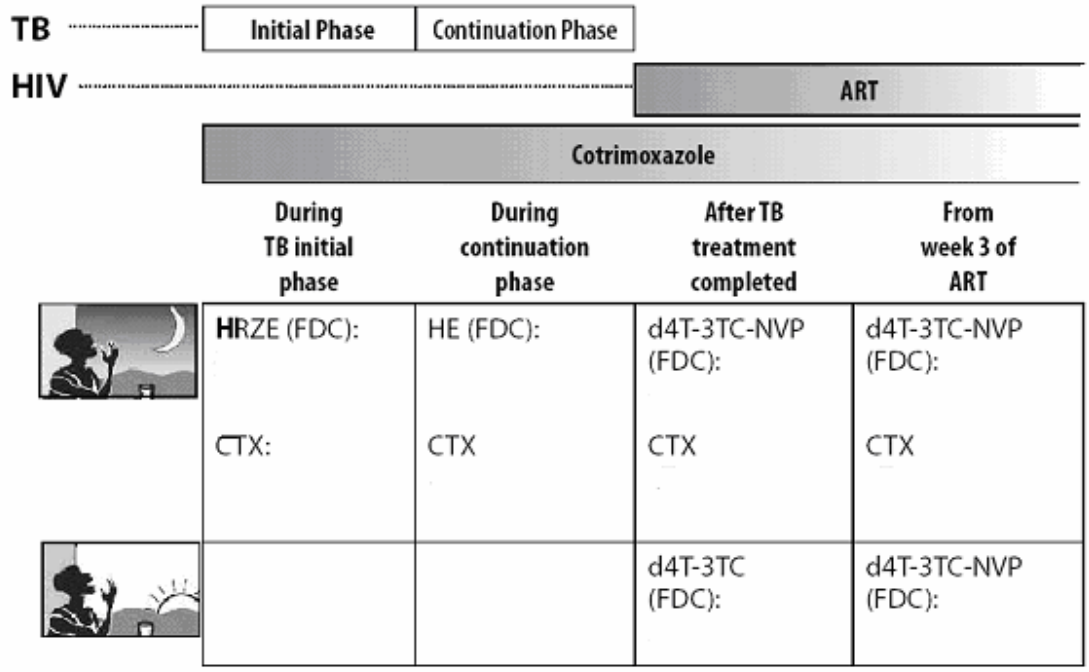
	TB initial phase- until tolerated	Until end of TB initial phase	During continuation phase	After TB treatment completed
	HRZE (FDC): CTX:	HRZE (FDC): d4T-3TC (FDC): CTX	HR (FDC, 3 times a week): d4T-3TC (FDC): CTX	 d4T-3TC (FDC): CTX
		d4T-3TC (FDC): EFV (separate):	d4T-3TC (FDC): EFV (separate):	d4T-3TC (FDC): EFV (separate):

H-isoniazid, R-rifampicin, Z-pyrazinamide, E-ethambutol,
CTX-cotrimoxazole, d4T-stavudine, 3TC-lamuvidine, NVP-nevirapine
EFV- efavirenz, FDC-fixed drug combination ART-Anti retroviral therapy.

Regimen 2 : Start ART after the initial phase of TB treatment



Regimen 3: Start ART after TB treatment is completed



Example: TB/HIV REFERRAL FORM

Patient name _____ Date: _____

Patient TB Register number _____

Referred from _____

(Name of TB treatment clinic/health facility)

Name of referral clinician: _____

Referred to _____

(Name of HIV care clinic/health facility, VCT, PMTCT)

Cotrimoxazole started: yes no Date started: _____

Current TB medications: (Check all that apply) Date TB treatment started:____/____/_____

__ isonaizid ___ pyrazinamide ___ streptomycin

__ rifampicin ___ ethambutol ___ other: _____

_____

Note from HIV Care Clinic/Facility to TB clinic/facility

(Name of clinic:_____)

Name of clinician:_____ Date: _____

Cotrimoxazole started: yes no Date started:_____

Antiretrovial medications prescribed:

___ zidovudine (AZT or ZDV) ___ didanosine (ddI) ___nelfinavir (NFV)

___ stavudine (d4T) ___ abacavir (ABC) ___saquinavir/ritonavir (SQV/r)

___ lamivudine (3TC) ___ tenofovir (TDF)

___ nevirapine (NVP) ___ Indinavir/ritonavir (IDV/r)

___ efavirenz (EFV) ___ lopinavir/ritonavir (LPV/r)

Notes to TB clinician:

Signed: _____

Patient's TB Treatment Card is prepared and, if HIV-positive, the HIV Care/ART Card which contains patient general information, clinical information like TB disease site and type of patient, sputum smear microscopy, HIV test treatment category, on the back of the card - HIV care, Pre ART Register Number, HIV care, CD4 result, X-ray report(13).

TREATMENT OF MDR-TB IN HIV INFECTED PATIENTS:

When a strain of tuberculosis bacteria is resistant to two or more 'first-line' antibiotic drugs it is called multi-drug resistant TB or MDR-TB and if it is resistant to three or more 'second-line' antibiotics as well, it is classed as extreme drug resistant TB, or XDR-TB. Drug resistance usually arises due to non-compliance of treatments and drug-resistant mutations of the bacteria replicates. People can also catch MDR- and XDR-TB from others.

MDR-TB is a serious problem and is very difficult to treat. First-line treatment of TB is isoniazid and rifampicin (the most effective tuberculosis drugs available) plus two or three, other first-line drugs for around six to eight months. Development of resistance to isoniazid and rifampicin however, confirm MDR-TB, and needs change in regime containing newer and often less widely-available 'second-line' drugs. Treatment with second-line drugs usually far more expensive than standard DOTS therapy and needs longer duration of treatment..

XDR-TB is even more serious, as they are not only resistant to isoniazid and rifampicin, but to three or more of the six available second-line drugs too. This makes it virtually impossible to formulate an effective treatment regimen for them. Many people with XDR-TB will die before it is even realised that they have the extreme resistant strain.

Although HIV infection does not by itself increase the chance of drug resistance, both MDR-TB and XDR-TB are very serious threats to HIV positive people, whose weakened immune systems render them unlikely to fight off tuberculosis naturally (often the only hope for those with a resistant strain) (16,17).

MEASURES TO REDUCE/ PREVENT THE RISK OF TB IN HIV CARE SETTINGS:

Infectious TB is found in HIV care settings and HIV co-infected persons will spread *M. tuberculosis* to other persons, including immunocompromised patients or staff. There are two main ways in which even HIV care settings with limited resources can reduce the chances of TB spread:

1. Work practice and administrative control measures
   - Infection control plan;
   - Administrative support for procedures in the plan, including quality assurance;
   - Training of staff;

- ❖ Education of patients and increasing community awareness; and
- ❖ Coordination and communication with the TB program.

2. Environmental control measures
   - Ventilation (natural and mechanical),
   - Filtration, and
   - Ultraviolet germicidal irradiation(16,17,23,24)

FIVE STEPS FOR PATEINT MANAGEMENT TO PREVENT TRANSMISSION OF TB IN HIV CARE SETTINGS

Step	Action	Description
1	**Screen**	Early **recognition** of patients with suspected or confirmed TB disease is the first step in the protocol. It can be achieved by assigning a staff member to screen patients for prolonged duration of cough immediately after they arrive at the facility. Patients with cough of more than two weeks duration, or who report being under investigation or treatment for TB*, should not be allowed to wait in the line with other patients to enter, register, or get a card. Instead, they should be managed as outlined below.
2	Educate	Instructing the above mentioned persons identified through screening in **cough hygiene**. This includes instructing them to cover their noses and mouths when coughing or sneezing, and when possible providing face masks or tissues to assist them in covering their mouths.
3	Separate	Patients who are identified as TB suspects or cases by the screening questions must be separated from other patients and requested to wait in a separate well-ventilated waiting area, and provided with a surgical mask or tissues to cover their mouths and noses while waiting.
4	Provide HIV services	Triaging symptomatic patients to the front of the line for the services they are seeking (e.g. voluntary HIV counseling and testing, medication refills), to quickly provide care and reduce the amount of time that others are exposed to them is recommended. In an integrated service delivery setting, if possible, the patient should receive the HIV services they are accessing before the TB investigation.

5	Invvestigate for TB or Refer	TB diagnostic tests should be done onsite or, if not available onsite, the facility should have an established link with a TB diagnostic center to which symptomatic patients can be referred**.** Also, each facility should have a linkage with a TB treatment center to which those who are diagnosed with TB can be **referred.**

Conclusion

The strategic goal is to reduce tuberculosis transmission, morbidity and mortality (while minimizing the risk drug resistance) as part of overall efforts to reduce HIV-related morbidity and mortality in high HIV prevalence populations. Achieving the goal requires scaling up of current efforts to implement interventions of proven effectiveness, and research to determine how to implement these interventions and monitor their impact, and to develop improved and new interventions, including specific tuberculosis control tools (e.g. a more effective vaccine, better diagnostic tests and preventive and therapeutic approaches).

The development of a new strategy to decrease the burden of TB/HIV, which frames tuberculosis as part of the overall HIV/AIDS epidemic, is a step towards a level of response which matches the enormity of the HIV/AIDS epidemic. The joint efforts of HIV/AIDS and tuberculosis programmes and other partners are necessary to implement the strategy, and deliver the interventions to reduce tuberculosis and HIV/AIDS-related morbidity and mortality.

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