TREATMENT OF TUBERCULOSIS

ABOUT TUBERCULOSIS

What is TB?
Tuberculosis (TB) is a disease caused by Mycobacterium tuberculosis. TB most often affects the lungs (pulmonary TB), but it can also affect other organs (extrapulmonary TB). When a person develops active TB, the symptoms (cough, fever, night sweats, weight loss etc.) may be mild and unspecific for many months.

How is TB spread?
TB is spread from person to person through the air. When people with active pulmonary TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected.

Latent TB
About one-third of the world's population has latent TB infection, which means people have been infected by TB bacteria but are not ill with disease and cannot transmit it. The only sign of TB infection is a positive reaction to the tuberculin skin test or TB blood test.

Active TB or TB disease
In some people, TB bacteria overcome the defenses of the immune system and begin to multiply, resulting in the progression from latent TB infection to TB disease.
A person with TB disease usually feels sick and has symptoms such as coughing, fever, and weight loss. A person with TB disease is considered infectious and may spread TB bacteria to others. If TB disease is suspected, the person should be referred for a complete medical evaluation. TB disease is a serious condition and can lead to death if not treated.

Diagnosis
It is very difficult to diagnose TB by a person's symptoms because some other diseases have the same symptoms. A combination of clinical and laboratory tests is usually needed. A TB diagnosis is usually only confirmed when there is definite evidence of TB bacteria.
Some of the TB tests used for diagnosis look directly for the bacteria. Others such as the chest X-ray look for the effect of the bacteria on the person suspected of having TB.
Tests for diagnosis include the TB skin test, sputum microscopy, the culture test as well as the GeneXpert MTB/RIF test.

Risk for TB in HIV-infected persons
People infected with TB bacteria have a lifetime risk of falling ill with TB of 10%. However, persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk of falling ill. According to WHO, people living with HIV are 20 to 30 times more likely to develop active TB disease than people without HIV.

Prevention of TB
A major part of the prevention of TB is to stop the spread of the bacteria from one adult to another. This is done by firstly finding the adults who have TB. Then providing them with effective treatment means that they are no longer infectious and they will also recover from being sick.

Treatment of TB
Tuberculosis is curable and preventable but without proper treatment up to two thirds of people ill with TB will die. TB can be either drug-susceptible or drug-resistant. In case of drug-resistant TB, treatment becomes more complicated.

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Treatment of new patients with drug-susceptible pulmonary TB [a, b]

Intensive phase treatment	Continuation phase
2 months: isoniazid + rifampicin + pyrazinamide + ethambutol	4 months: isoniazid + rifampicin
In populations with known or suspected high levels of isoniazid resistance:	
2 months: isoniazid + rifampicin + pyrazinamide + ethambutol	4 months: isoniazid + rifampicin + ethambutol

[a] The use of fixes dose formulation tablets is recommended over separate drug formulations in the treatment of patients with drug-susceptible TB
[b] In patients with drug-susceptible pulmonary TB, 4-month fluoroquinolone-containing regimens should not be used and the 6-month rifampicin-based regimen 2HRZE/4HR remains the recommended regimen

Recommended doses of first-line antituberculosis drugs for adults

Drug	Daily dose	
	Dose and range (mg/kg body weight)	Maximum (mg)
Isoniazid (H)	5 (4-6)	300
Rifampicin (R)	10 (8-12)	600
Pyrazinamide (Z)	25 (20-30)	–
Ethambutol (E)	15 (15-20)	
Streptomycin (S) [c]	15 (12-18)	–

[c] 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. Patients weighing less than 50 kg may not tolerate doses above 500-750 mg daily

Recommended dosing frequency for new TB patients

In all patients with drug-susceptible pulmonary TB, daily dosing is recommended dosing frequency in both the intensive and continuation phases of therapy. Thrice-weekly dosing should not be used.

Treatment of previously treated TB patients

- Specimens for culture and drug-susceptibility testing (DST) (for at least isoniazid and rifampicin) should be obtained from all previously treated TB patients at or before the start of treatment
- In settings where rapid molecular-based DST is available, the results should guide the choice of regimen
- In settings where rapid molecular-based DST results are not routinely available to guide the management of individual patients, TB patients whose treatment has failed or other patient groups with high likelihood of MDR-TB should be started on an empirical MDR regimen
- If MDR-TB is confirmed, so-called "second-line" drugs are used. Please see WHO treatment guidelines for drug-resistant tuberculosis for detailed information
- In patients who require TB retreatment, the 2HRZES/1HRZE/5HRE regimen should no longer be prescribed and DST should be conducted to inform the choice of treatment regimen

ESSENTIAL 1ST-LINE ANTITUBERCULOSIS DRUGS

Drug	Administration	Contraindications	Adverse effects
Isoniazid	Normally taken orally but may be administered intramuscularly or ntravenously to critically ill patients	- Known hypersensitivity - Active, unstable hepatic disease (with jaundice)	- Generally well tolerated at recommended doses - Systemic or cutaneous hypersensitivity reactions occasionally occur during the first weeks of treatment - Severe and sometimes fatal hepatitis associated with isoniazid therapy has been reported and may occur or may develop even after many months of treatment. The risk of developing hepatitis is age related. - Sleepiness or lethargy can be managed by reassurance or adjustment of the timing of administration
Rifampicin	Should preferably be given at least 30 minutes before meals. However, food can reduce intolerance to drugs. Should always be given in combination with other effective antimycobacterial agents. Available for intravenous administration in critically ill patients	- Known hypersensitivity to rifamycins - Active, unstable hepatic disease (with jaundice)	- Rifampin has been shown to produce liver dysfunction - May cause gastrointestinal reactions (abdominal pain, nausea, vomiting) and pruritus with or without rash - Other adverse effects (fever, influenza-like syndrome and thrombocytopenia) are more likely to occur with intermittent administration - Exfoliative dermatitis is more frequent in HIV-positive TB patients
Pyrazinamide	Administered orally	- Known hypersensitivity - Active, unstable hepatic disease (with jaundice) - Porphyria	- Pyrazinamide may cause gastrointestinal intolerance - Hypersensitivity reactions are rare, but some patients complain of slight flushing of the skin - Moderate rises in serum transaminase concentrations are common during the early phases of treatment
Streptomycin	Must be administered by deep intramuscular injection It is also available for intravenous administration	- Known hypersensitivity - Auditory nerve impairment - Myasthenia gravis - Pregnancy	- Vestibular ototoxicity (nausea, vomiting, and vertigo); paresthesia of face; rash; fever; urticaria; angioneurotic edema; and eosinophilia. - Injections are painful - Rash, induration, or sterile abscesses can form at injection sites - Numbness and tingling around the mouth occur immediately after injection - Cutaneous hypersensitivity reactions can occur
Ethambutol	Administered orally	- Known hypersensitivity - Pre-existing optic neuritis from any cause	- Dose-dependent optic neuritis can result in impairment of visual acuity and colour vision in one or both eyes. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly - Ocular toxicity is rare when ethambutol is used for 2–3 months at recommended doses - Signs of peripheral neuritis occasionally develop in the legs - Other rare adverse events include generalized cutaneous reaction, arthralgia and, very rarely, hepatitis

MEDICINES RECOMMENDED FOR THE TREATMENT OF RIFAMPICIN- AND MDR-TB:

Group A. Fluoroquinolones (levofloxacin, moxifloxacin, gatifloxacin)
Group B. Second-line injectable agents (amikacin, capreomycin, kanamycin, (streptomycin)
Group C. Other core second-line agents (ethionamide/prothionamide, cycloserine/terizidone, linezolid, clofazimine)
Group D. Add-on agents (not part of the core MDR-TB regimen): D1 (pyrazinamide, ethambutol, high-dose isoniazid), D2 (bedaquiline, delamanid), D3 (p-aminosalicylic acid, Imipenem-cilastatin, meropenem, amoxicillin-clavulanate, (thioacetazone)

HIV/TUBERCULOSIS CO-INFECTION

The first priority for HIV-positive TB patients is to initiate TB treatment, followed by co-trimoxazole and ART

Recommendations:
- The same regimens and the same duration of TB treatment as for HIV-negative TB patients
- Daily dosing is recommended in both the intensive and continuation phases of therapy
- Co-trimoxazole preventive therapy should be initiated in all HIV-positive TB patients as soon as possible and given throughout TB treatment

Antiretroviral treatment (ART)
- ART reduces TB rates by up to 90% at an individual level
- ART should be started in all TB patients living with HIV regardless of their CD4 cell count
- TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment
- HIV-positive patients with profound immunosuppression (e.g. CD4 cell counts less than 50 cells/mm^3) should receive ART within the first 2 weeks of initiating TB treatment
- In HIV-positive patients with drug-susceptible pulmonary TB who are receiving ART during TB treatment, a 6-month standard treatment regimen is recommended over an extended treatment for 8 months or more
- TB drugs can have drug-drug interactions with ARV-drugs, and this should be checked individually in every case. You can check it on http://www.hiv-druginteractions.org/

TB prevention for people with HIV in settings with a high prevalence of TB*
- People with HIV who are unlikely to have active TB should receive at least 6 months of isoniazid as a part of a comprehensive HIV care package irrespective of the immunosuppression degree
- People with HIV who are unlikely to have active TB should receive at least 36 months of isoniazid in settings with the highest rates of prevalence and transmission of TB among people with HIV
- Please refer to WHO Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings for detailed information

*Please refer to national TB prevention and treatment guidelines regarding the implementation of these recommendations in specific countries.

ITPC ru International Treatment Preparedness Coalition Eastern Europe and Central Asia

The poster has been developed and produced for informational purposes only. Please refer to national TB prevention and treatment guidelines regarding the implementation of these recommendations in specific countries.
The poster is designed based on the World Health Organization's Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 Update; Treatment of tuberculosis: guidelines, fourth edition, 2010, and Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings, 2010, CDC Factsheets about TB. Version: May 2017.