



SHORT, ALL ORAL DR-TB REGIMEN

SESSION 2: TUBERCULOSIS 101

WHAT IS TUBERCULOSIS (TB)?

a. What causes TB?

TB is an infectious disease caused by a bacteria called **Mycobacterium Tuberculosis**.



b. How does TB spread?

TB is an airborne disease, anyone who inhales the bacteria can get infected with TB.



c. What are some of the risk factors for TB?

Poor nutrition, diabetes and HIV are some of the risk factors for TB, as they all lower a person's immunity

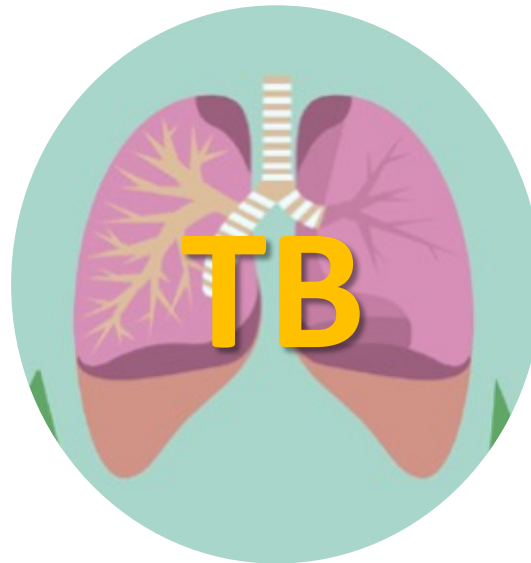


SYMPTOMS OF TB

d-f. Name a symptom of TB.



Persistent Cough



Loss of
Appetite



Blood in the
Sputum



Loss of
Weight



Fever



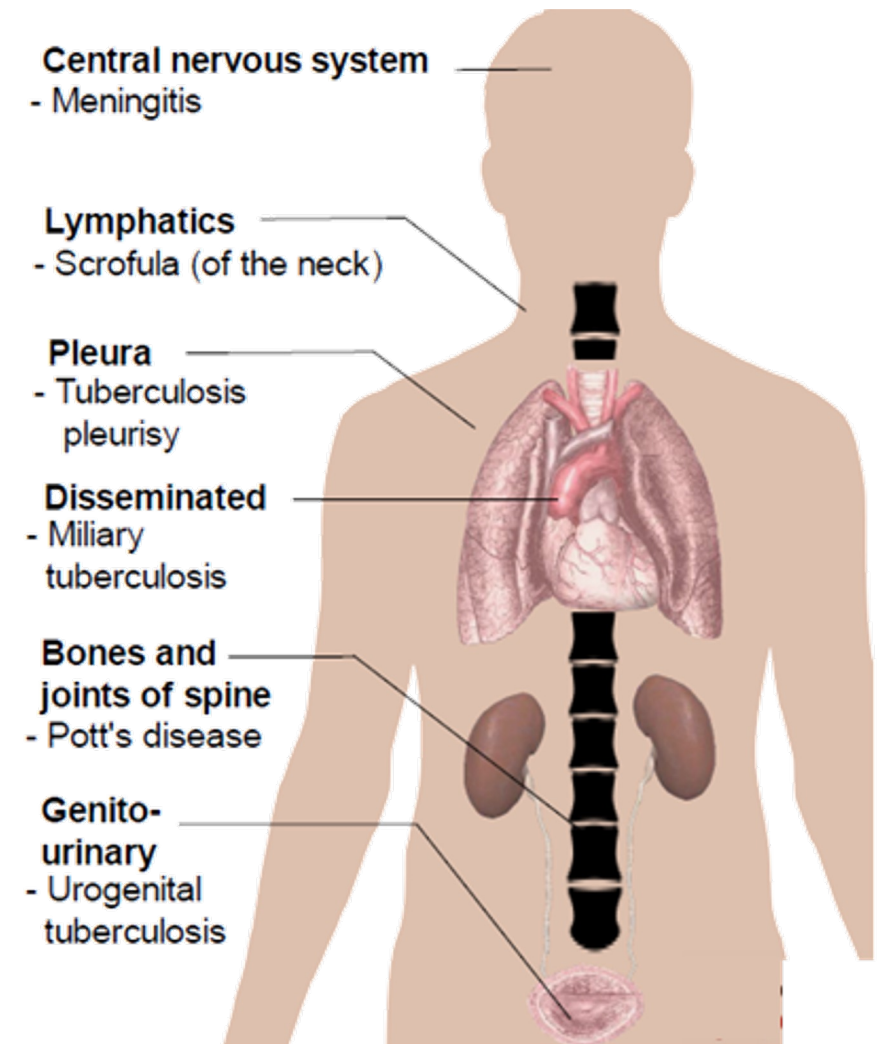
Chest Pain



Breathlessness

PULMONARY TB (PTB) AND EXTRA PULMONARY (EPTB)

- g. What is pulmonary TB?**
TB that affects the lungs
- h. What is extrapulmonary TB?**
TB that affects parts of the body other than lungs
- i. Name a part of the body TB cannot affect.**
 - Hair
 - Nails



GLOBAL TB BURDEN (2022)



7.9 billion
Population



10.6 million
Incidence



410,000
DR-TB Incidence



427,000
HIV+ TB Incidence



167,000
HIV+ TB Mortality



1.1 million
Mortality

TB PREVENTION

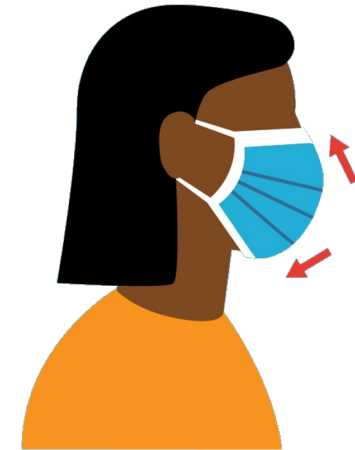
HOW CAN TB BE PREVENTED?



Cover your nose & mouth while coughing. Use a tissue or your arms



Wash your hands with soap or use alcohol-based hand sanitizer



Wear a mask if you have a cold and cough

TB PREVENTIVE TREATMENT (TPT)

- Everyone has a right to access the highest available standard of TB prevention.
- For TB preventive therapy, this means short-course regimens based on either rifapentine (3HP, 1HP) or rifampicin (3HR, 4R).
- These rifamycin-based TPT regimens are shorter than isoniazid preventive therapy (IPT), have better adherence, are easier to complete, and have less liver toxicity. They've been studied and used in a wide range of settings.
- The "IPT only" era is over! (But IPT is still important for certain populations e.g., kids with HIV on lopinavir-ritonavir).

- TB vaccination
 - BCG is a vaccine for TB
 - It is often given to infants and small children
 - Provides consistent protection (up to 80%) against severe forms of childhood TB
 - The protection from the BCG vaccine can last up to 15 years

DIAGNOSTICS

- **Sputum microscopy:** inexpensive, rapid (same day) but low sensitivity/specificity
- **Culture:** more sensitive than microscopy but only performed in specialized laboratories; takes longer
 - Solid: usually takes >30 days
 - Liquid (MGIT): highly sensitive, produces quicker results (usually 15 days), but relatively expensive



- Nucleic Acid Amplification Tests (NAAT)
 - GeneXpert/Xpert MTB/RIF
 - LPA: Line Probe Assay
 - TrueNat: TrueNat MTB is a portable molecular test developed by Molbio Diagnostics Pvt Ltd India for rapid detection of MTB

DRUG SUSCEPTIBLE TB (DS-TB)

- A bacteriologically confirmed or clinically diagnosed case of TB without evidence of infection with strains resistant to rifampicin and isoniazid.
- Diagnosis
 - **Genotypic:** based on DNA sequences, e.g., GeneXpert. These tests provide results in <3 days.
 - **Phenotypic:** based on growth/no growth of tubercle bacilli in the presence of the drug, e.g., MGIT DST. These tests take much longer, usually >3 weeks.
 - Not all tests can detect resistance to all drugs. At a minimum, the test should detect resistance to the key first-line drug rifampicin.

Treatment for drug-sensitive TB (DS-TB)

- The standard 6-month course of treatment consists of two phases:
 - The intensive phase (the first two months) - HRZE
 - The continuation phase (the last four months) - HR

First-line drugs:
isoniazid (H or INH)
rifampicin (R or RIF)
ethambutol (E or EMB)
pyrazinamide (Z or PZA)
rifabutin (RBT)
rifapentine (P or RPT)

DRUG-RESISTANT TUBERCULOSIS (DR-TB)

WHAT IS DRUG RESISTANT TUBERCULOSIS?

- Caused by TB bacteria **that are resistant to at least one of the first-line** TB medications.
- **DR-TB** results in fewer treatment options, higher treatment cost and increased mortality rate.
- **RR-TB:** TB bacteria that are resistant to rifampicin (R).
- **Multidrug-resistant TB (MDR-TB):** TB bacteria that are resistant to two of the most important TB drugs, **rifampicin (R) and isoniazid (INH)**.

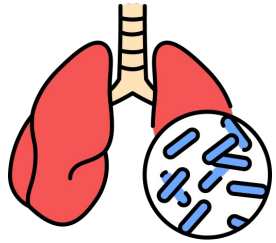
Mono-resistance: resistance to one first-line anti-TB drug only.

Poly-resistance: resistance to more than one first-line anti-TB drug, other than both isoniazid and rifampicin.

WHAT IS DRUG RESISTANT TUBERCULOSIS?

- **Pre-XDR-TB:** TB caused by Mycobacterium tuberculosis strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone*
*Fqs include **Lfx and Mfx** as they are the Fqs currently recommended by WHO for inclusion in longer regimens.
- **XDR-TB:** TB caused by Mycobacterium tuberculosis strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group A drug**
** The Group A drugs are: **Lfx, Mfx, Bdq, Lzd**. Therefore XDR-TB is MDR/RR-TB that is resistant to a fluoroquinolone and at least one of bedaquiline or linezolid (or both). The Group A is appropriate here and it will apply to any Group A drugs in the future.

CAUSES OF DRUG RESISTANCE



- Mechanistically, resistance is caused by a genetic mutation that makes a drug ineffective against the mutant bacilli at usual exposures
- Exposure to someone with DR-TB
- In clinical settings, an inadequate or poorly administered treatment regimen allows drug resistant mutants to become the dominant strain - e.g., interruptions or premature discontinuation of treatment, or poor patient adherence
- Clinical characteristics of patients have also been recognized where appropriately administered drugs have not achieved necessary drug levels to deal with all population of mycobacteria.
- From a programmatic perspective, weak TB services can lead to delay in detection and effective treatment of drug resistance.

DRUG RESISTANT TUBERCULOSIS: DIAGNOSIS

- GeneXpert | TrueNat
 - A molecular diagnostic test that can detect TB and resistance to Rifampicin in just two hours.
 - Detects Mycobacterium tuberculosis in high colony forming units (CFU)

GeneXpert

- Expensive
- Machine is not easily transported, test conducted in laboratory settings



TrueNat

- Affordable
- Portable machine, test can be conducted in clinical settings



Conventional Regimen

- At least 18 months long
- Individually designed based on a hierarchical grouping of second-line TB medicines, the drug-resistance profile and the patient's medical history

Second-line drugs:

Levofloxacin (Lfx)
Moxifloxacin (Mfx)
Bedaquiline (Bdq)
Linezolid (Lzd)
Clofazimine (Cfz)
Cycloserine (Cs)
Terizidone (Trd)
Ethambutol (E)
Delamanid (Dlm)
Pyrazinamide (Z)
Imipenem-cilastatin (Ipm-Cln)
Meropenemg (Mpm)
Amikacin (Am)
Streptomycin (S)
Ethionamide (Eto)
Prothionamide (Pto)
P-aminosalicylic acid (PAS)

DRUG RESISTANT TUBERCULOSIS: TREATMENT

Groups and Steps	Medicine	Abbreviation	Note
Group A Include all three medicines	Levofloxacin or Moxifloxacin	Lfx, Mfx	Medicines to be prioritized
	Bedaquiline	Bdq	
	Linezolid	Lzd	
Group B Add one or both medicines	Clofazimine	Cfz	Medicines to be added next
	Cycloserine or Terizidone	Cs, Trd	
Group C Add to complete the regimen and when medicines from Group A and Group B cannot be used	Ethambutol	E	Medicines to be included to complete the regimens and when agents from Groups A and B cannot be used
	Delamanid	Dlm	
	Pyrazinamide	Z	
	Imipenem–Cilastatin or Meropenemg	lpm–Cln, Mpm	
	Amikacin (or Streptomycin)	Am (S)	
	Ethionamide or Prothionamide	Eto, Pto	
	P-aminosalicylic acid	PAS	

WHO recommended novel regimen

- **BPaLM:** An all-oral regimen of Bedaquiline, Pretomanid, Linezolid and Moxifloxacin
 - 6-month regimen
- **BPaL:** An all-oral regimen of Bedaquiline, Pretomanid and Linezolid
 - 6-month regimen
 - Extendable to 9 months if culture is positive after 4-6 months of treatment

ADVERSE DRUG REACTION (ADR)

Adverse Drug Reaction: unwanted, uncomfortable, or dangerous effects that drugs (including medications) may have. Adverse drug reactions can be considered a form of toxicity.

- Development of side effects is one of the most common reason for people being irregular or not completing their anti TB treatment.

ADVERSE DRUG REACTIONS TO ANTI-TB DRUGS

Possible Adverse Drug Reactions (ADR) that need monitoring

Sl. No.	Adverse Drug Reaction	Early Signs and Symptoms	Usual Offending Agents
1	Gastro Intestinal Symptoms	Nausea, Vomiting, Gastritis Diarrhoea	Most drugs, especially Ethionamide / PAS / Pyrazinamide / Ethambuto
2	Balance	Giddiness, Oversleeping, Poor concentration	Amino glycosides Ethionamide Quinolones and / or Pyrazinamide
3	Vision	Blurring of vision, Disturbance in colour vision	Ethambutol
4	Movement	Joint pains	Pyrazinamide Quinolones
5	Skin Reactions	Itching, Localised Rash Generalized erythematous rash associated with fever and/or mucous membrane involvement	Any of the drugs may give rise to this

ADVERSE DRUG REACTIONS TO ANTI-TB DRUGS

Possible Adverse Drug Reactions (ADR) that need monitoring			
Sl. No.	Adverse Drug Reaction	Early Signs and Symptoms	Usual Offending Agents
6	Liver	Loss of appetite, Nausea/Vomiting Abdominal discomfort, Dark coloured urine, Jaundice	Ethionamide Pyrazinamide
7	Neural	Pain and/or tingling sensations in any part of the body especially feet and hands	Cycloserine Ethionamide Linezolid
8	Neural	Convulsions, Fits	Quinolones Cycloserine
9	Mental Health	Depressions Excessive chatting Unusual violent tendencies Suicidal tendencies	Cycloserine Quinolones Ethionamide

THANK YOU!