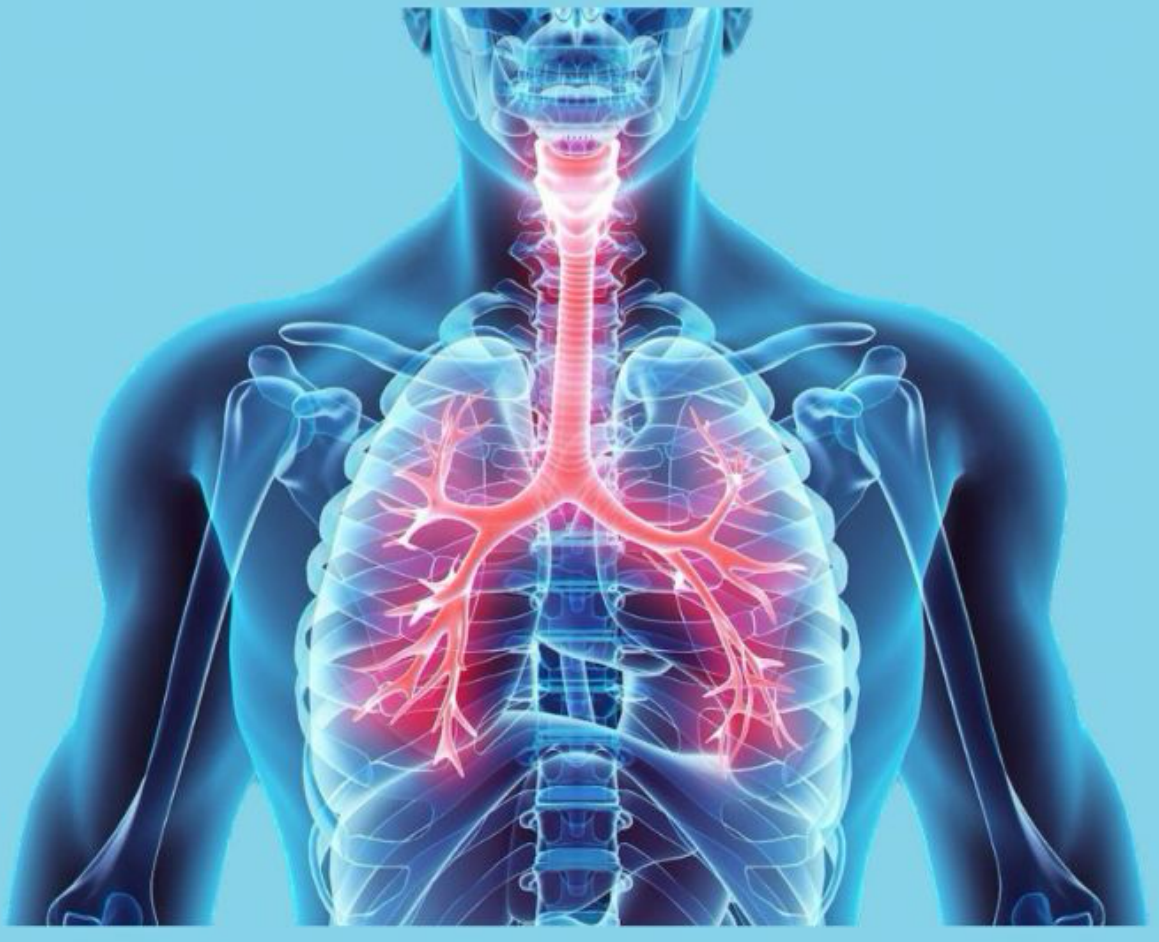
وَقُل رَّبِّ زِدْنِي عِلْمًا

النادي الطبي

RESPIRATORY SYSTEM

HAYAT BATCH



SUBJECT : _____

LEC NO. : Pharmacology L7

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Aspect	Details
Overview	- Caused by Mycobacterium tuberculosis (MTB) bacteria (infectious). - Affects the lungs primarily but can also affect other parts of the body. - Most infections are latent tuberculosis (LTB) with no symptoms.
Symptoms (Pulmonary)	- Chronic cough with blood-containing mucus - Night sweats - Poor appetite - Chest pain
Symptoms (Extrapulmonary)	- In 15–20% of active cases, the infection spreads outside the lungs, especially in the genitourinary system (GUS) or central nervous system (CNS). - More common in people with weakened immune systems and young children.
Diagnosis	- Active TB diagnosis: chest X-rays, microscopic examination, and culture of body fluids. - Skin test for latent TB.
Prevention	- Vaccination with the bacillus Calmette-Guérin (BCG) vaccine.
Treatment	- Multidrug therapy using first-line drugs: isoniazid, rifampin, ethambutol, and pyrazinamide. - Second-line drugs used for resistant TB cases or those intolerant to first-line drugs.
Treatment Regimens	- Traditional regimen (≥6 months): isoniazid, rifampin, pyrazinamide, and ethambutol. - Shortened, four-month regimen: isoniazid, rifapentine, pyrazinamide, and moxifloxacin
Drug Resistance	- Multidrug therapy to suppress resistant organisms. - Treatment continues for a longer duration to eradicate persistent organisms and prevent relapse.
MDR-TB Treatment	- Second-line regimens include at least four drugs: fluoroquinolone (levofloxacin or moxifloxacin), bedaquiline, Linezolid, and additional options such as clofazimine, Cycloserine, pyrazinamide, or ethambutol.
Note	- Tuberculosis is common in Jordan.

(2 months of isoniazid, rifapentine, pyrazinamide, moxifloxacin followed by 4 months of isoniazid, Rifampin
* Most of the clinical benefit from pyrazinamide and ethambutol occurs early in treatment. Therefore, this drug is usually discontinued after 2 months of a 6-month regimen.

Four are preferred because of their high efficacy and acceptable incidence of toxicity.

Both regimens have two treatment phases: 2 months then 4 and 8 weeks then 9 weeks

shortened

not traditional

Isoniazid (pro-drug) >> activated by a 1 mycobacterial catalase-peroxidase (KatG) >> enzymes acyl carrier protein reductase InhA & β-ketoacyl-ACP synthase (KasA) >> Inhibits mycolic acid >> disruption in the bacterial cell wall.

* inactivation of isoniazid is caused by chromosomal mutations of 1, 2 or 3

(The patient is infected with M. Tuberculosis without signs or symptoms of active Tb disease)

Air-borne (active NOT latent).
- Highly contagious
- Treated within the hospital

* Populations of M. tuberculosis contain small numbers of organisms that are naturally resistant to a particular drug. Multidrug therapy is employed to suppress these resistant organisms.

typically less effective, more toxic, and less extensively studied.

* Although clinical improvement can occur in the first several weeks of treatment

Capreomycin, kanamycin, macrolides: no longer recommended for inclusion in MDR-TB regimens

Drug	Mechanism of Action	Antibacterial Spectrum	Resistance Mechanisms	Pharmacokinetics	Adverse Effects
Isoniazid (INH)	- Activated by mycobacterial catalase–peroxidase (KatG) >> Inhibits mycolic acid >> disruption in the bacterial cell wall	Specific for treatment of M. tuberculosis	- Mutation or deletion of KatG - Mutations of acyl carrier proteins - Overexpression of the target enzyme InhA	- Readily absorbed after oral administration - Diffuses into all body fluids and cells and caseous material (necrotic tissue resembling cheese	- Hepatitis (Fatal.) - Peripheral neuropathy (can be avoided by daily supplementation of pyridoxine (vitamin B6). - CNS convulsions in patients prone to seizures
Rifampin Never given as a single agent Because resistant strains rapidly emerge during mono-therapy	- Blocks RNA transcription by interacting with the β subunit of mycobacterial DNA-dependent RNA polymerase.	Broader antimicrobial activity than isoniazid * Not specific to TB treatment.	- Mutations in the affinity of the bacterial DNA-dependent RNA polymerase gene for the drug	- Distribution to all body fluids and organs - Enterohepatic recycling	- Orange-red coloration of urine, feces, and other secretions (Tears may even stain soft contact lenses orange-red.) - Hepatitis - Flu-like syndrome with fever, chills, and myalgia, sometimes extending to acute renal failure, hemolytic anemia, and shock (When rifampin is dosed intermittently, especially with higher doses)
Rifabutin (derivative of rifampin)	- Similar to rifampin but preferred for TB-HIV co-infection	Broader antimicrobial activity than isoniazid	- Mutations in the affinity of the bacterial DNA-dependent RNA polymerase gene for the drug	- Distribution to all body fluids and organs	- Similar adverse effects to rifampin, with additional risks of uveitis, skin hyperpigmentation, and neutropenia

	Mechanism of drug	Antibacterial spectrum	Resistance mechanism	Pharmacokinetics	Adverse effects
Pyrazinamide ↳ orally	- Unclear Most of the clinical benefit from pyrazinamide occurs early in treatment. Therefore, this drug is usually discontinued after 2 months of a 6-month regimen.	Active against tuberculosis bacilli	- Not mentioned	- Not mentioned	- Liver toxicity
Ethambutol	- Inhibits arabinosyl transferase	Specific for mycobacteria	- Not mentioned	- Not mentioned	- Optic neuritis diminished visual acuity and loss of ability to discriminate between red and green.
Cycloserine	- Disrupts d-alanine incorporation into the bacterial cell wall	Not mentioned	- Not mentioned	- Primarily excreted unchanged in urine	- CNS disturbances - Seizures
Bedaquiline	- ATP synthase inhibitor	Not mentioned	- Not mentioned	- Black box warning for QT prolongation	- QT prolongation - Liver enzyme elevations - Contraindicated in patients with heart diseases
Linezolid	- Prevents the fusion of 30S and 50 ribosomal subunits ↳ 50 inhibits bacterial protein synthesis	Alternative to vancomycin in inpatient settings, particularly MRSA	- Not mentioned	- Not mentioned	- Myelosuppression neuropathy and hypoglycemia