PHARM.D • YEAR 3

Medicinal Chemistry

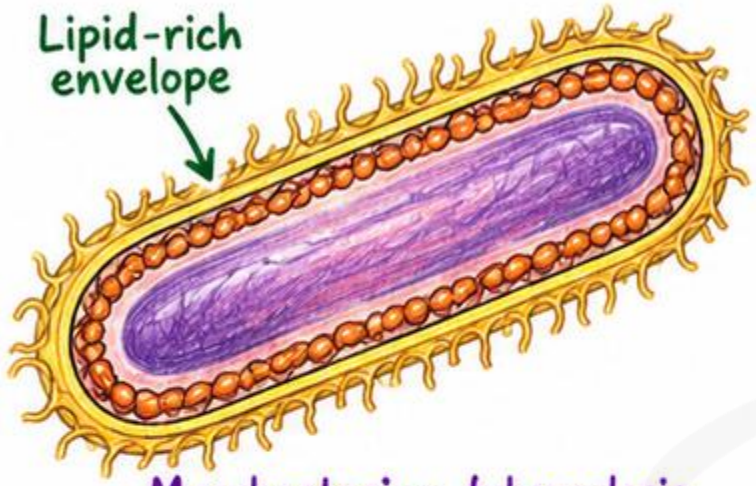
CHAPTER 2.5

Antitubercular Agents



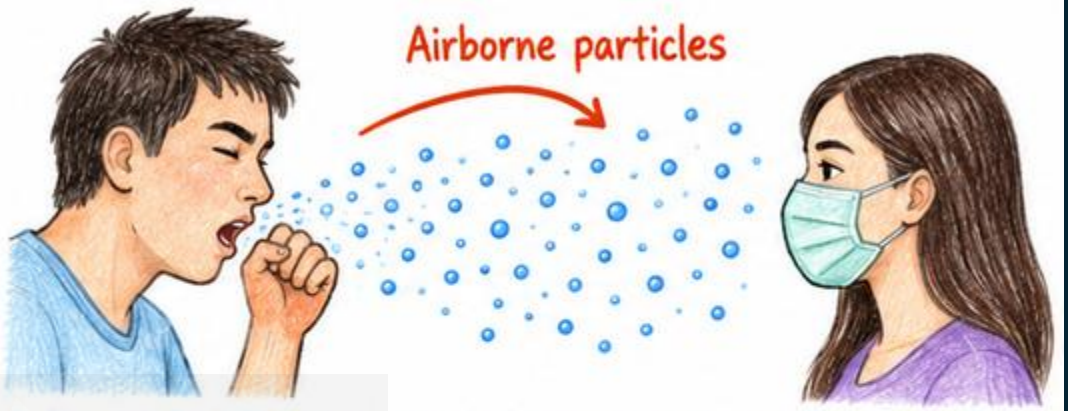
PPT CHAPTER COVER

Tuberculosis: organism and transmission



Mycobacterium tuberculosis

Tuberculosis is caused mainly by Mycobacterium tuberculosis. Its lipid-rich envelope and slowly growing or persistent populations complicate drug delivery and treatment.



Pulmonary TB can spread through airborne particles from a person with infectious disease. It is not normally transmitted by sharing utensils or by the routine needle/blood routes described in some notes.

Latent infection



Non-infectious

Active disease



Infectious

Latent infection and active disease are different states; latent infection does not spread TB.

Combination regimen

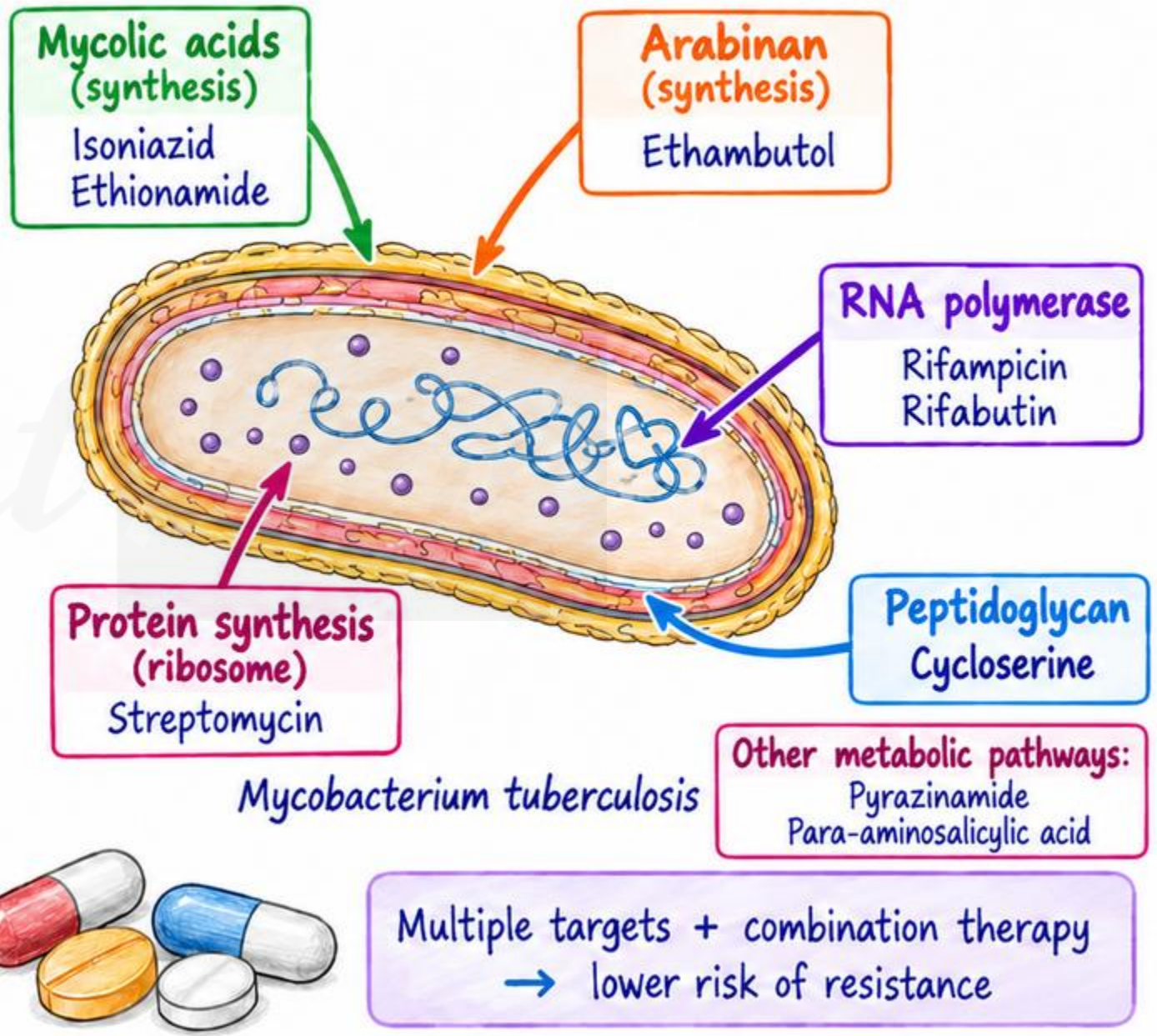


- ✔ Drug susceptibility
- ✔ Disease site
- ✔ Patient factors

Effective treatment uses an appropriate combination regimen. Drug susceptibility, disease site and patient factors determine the regimen and its duration.

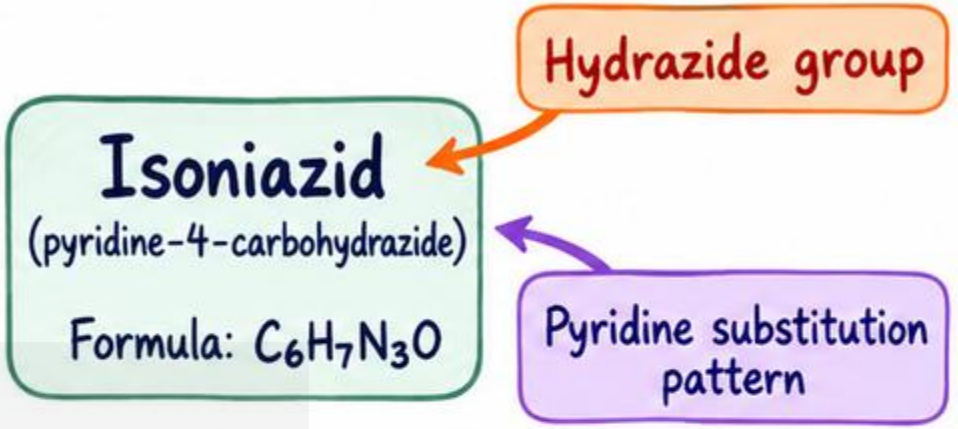
Antitubercular classification and targets

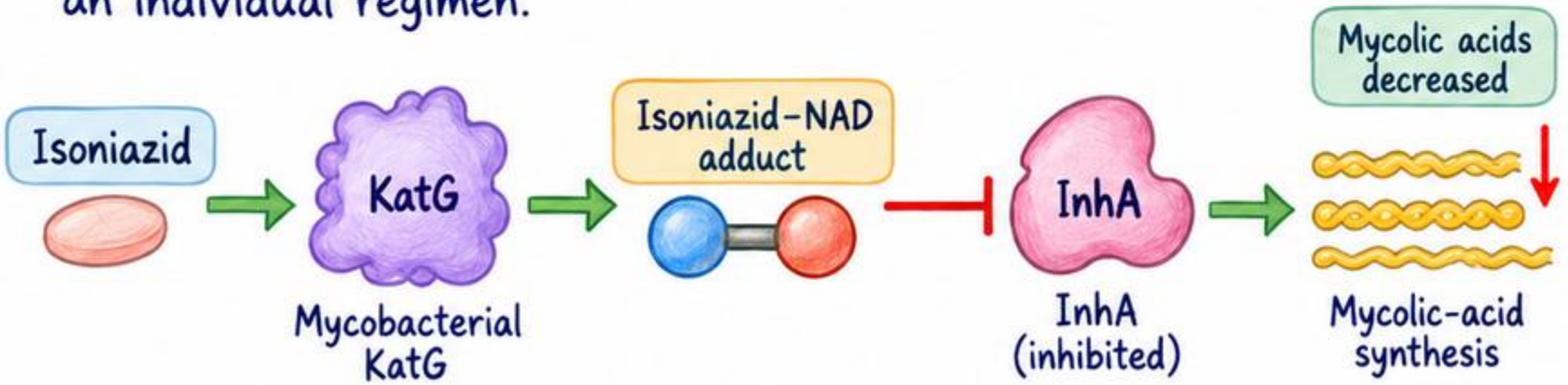
- The chapter groups synthetic agents such as isoniazid, ethionamide, ethambutol, pyrazinamide and para-aminosalicylic acid, alongside antibiotics such as rifampicin, rifabutin, streptomycin and cycloserine.
- Their targets differ: mycolic-acid synthesis, arabinan synthesis, RNA polymerase, protein synthesis and other metabolic pathways.
- Combining effective agents reduces the chance that resistant subpopulations survive. A single target diagram cannot explain an entire regimen.
- First-line and drug-resistant-TB roles change with evidence and guidance. Historical classification lists should not be converted into a current prescribing sequence.

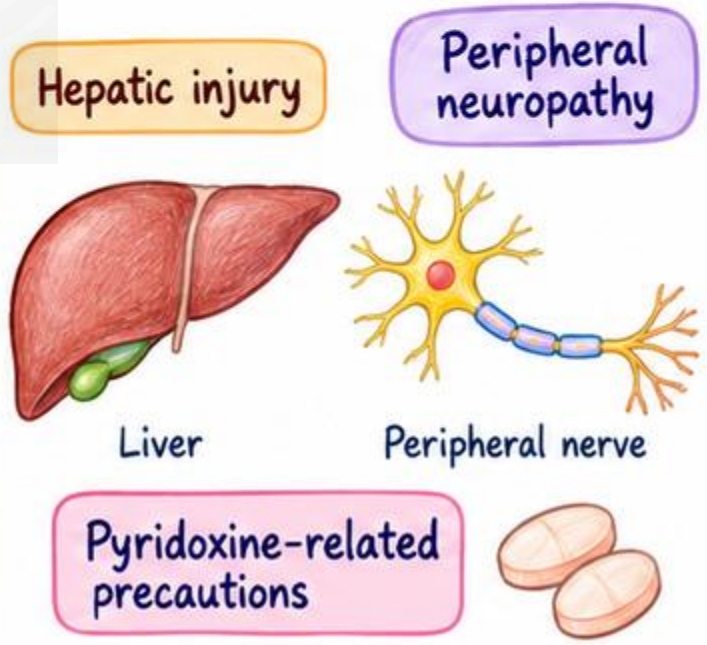


Isoniazid: activation and action

- Isoniazid is pyridine-4-carbohydrazide, formula $C_6H_7N_3O$. The hydrazide group and pyridine substitution pattern are central identity features.
- It is activated by mycobacterial KatG. An isoniazid–NAD adduct inhibits InhA and disrupts mycolic-acid synthesis.
- Changes in activation or target pathways can cause resistance. It should not be described as a simple universal direct inhibitor of all cell-wall enzymes.
- Hepatic injury and peripheral neuropathy are important adverse effects. Pyridoxine-related precautions depend on patient risk and clinical guidance; these notes do not specify an individual regimen.







Isoniazid synthesis and SAR

1. A representative synthesis reacts an isonicotinic-acid ester with hydrazine to form the carboxylic hydrazide, isoniazid.
2. The transformation is hydrazinolysis of an ester, not attachment of hydrazine directly to an unchanged nitrile structure.
3. The pyridine nitrogen and para carboxyhydrazide arrangement distinguish isoniazid from other pyridine derivatives. Hydrazide modification can change activation, stability and activity.
4. The source's abbreviated route must be interpreted carefully because incorrect intermediate identities change the claimed product.
5. A reaction name and correct product connectivity are more reliable than a memorized but inconsistent drawing.

Key structural features (SAR)

Pyridine nitrogen

Para carboxyhydrazide arrangement

Isoniazid

Distinguishes from other pyridine derivatives



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