SMART PHARMACOLOGY

LESSON 10

Task 1

Give a definition to the concept of «*Antituberculous medicines (ATM)* ». Indicate the clinical significance of the drugs in this group at the present time.

Task 2

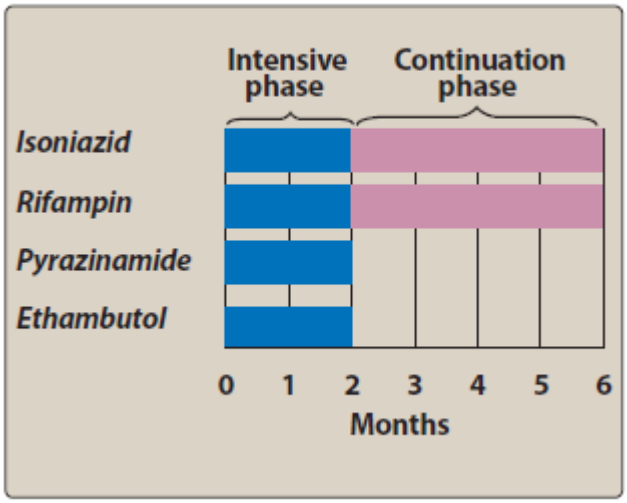
Give the classification of ATM. To do this, refer the following drugs to the appropriate group and fill in the table.

Classification	Drugs
Highly effective ATM	
Middle effective drugs ATM	
Low effective ATM	

Rifampicin
Thioacetazon
Prothionamide
Streptomycin, ,
Florimycine,
Para-aminosalicylic acid (PASA)
Canamycin
Isoniazid
Cycloserine
Ethambutol
Ethionamide
Pyrazinamide

Task 3

Please describe this picture which suggests one of of several recommended multidrug schedules for the treatment of tuberculosis.



Picture 1

Task 4

Discuss the features of first-line and second-line antibiotics for the treatment of tuberculosis.

First-line drugs	Second-line drugs

Task 6

Discuss the pharmacodynamics and side effects characteristics of first-line ATM. To do this, fill in the table all the necessary information.

IST LINE THERAPY (MAIN DRUGS)			
ISONICOTINIC ACID HYDRAZIDE DERIVATIVES	PARA-AMINO-SALICYLIC ACID (PASA) DERIVATIVES	ANTIBIOTICS	ISONICOTINIC ACID THIOAMIDE DERIVATIVES
Formation of complex compounds with heavy metals ions, which are components of respiratory enzymes → inhibition of mycobacteria breathing.	Competitive antagonism with PASA → inhibition of mycobacteria growth and reproduction.	Inhibition of protein synthesis at the ribosome level (7-9); inhibition of mycobacterial RNA synthesis (10).	Binding to ions of divalent metals, which are coenzymes → inhibition of mycobacteria growth.

DRUG	ADVERSE EFFECTS	COMMENTS
Ethambutol	Optic neuritis with blurred vision, red-green color blindness	Establish baseline visual acuity and color vision; test monthly.
Isoniazid	Hepatic enzyme elevation, hepatitis, peripheral neuropathy	Take baseline hepatic enzyme measurements; repeat if abnormal or patient is at risk or symptomatic. Clinically significant interaction with *phenytoin* and *carbamazepine*.
Pyrazinamide	Nausea, hepatitis, hyperuricemia, rash, joint ache, gout (rare)	Take baseline hepatic enzymes and uric acid measurements; repeat if abnormal or patient is at risk or symptomatic.
Rifampin	Hepatitis, GI upset, rash, flu-like syndrome, significant interaction with several drugs	Take baseline hepatic enzyme measurements and CBC; repeat if abnormal or patient is at risk or symptomatic. Warn patient that urine and tears may turn red-orange in color.

Figure 41.9
Some characteristics of first-line drugs used in treating tuberculosis. CBC = complete blood count. GI = gastrointestinal.

Task 7

Discuss the pharmacodynamics and side effects characteristics of second-line ATM. To do this, fill in the table all the necessary information.

IIND LINE THERAPY (RESERVE DRUGS)	
ANTIBIOTICS AND FLUOROQUINOLONES*	DRUGS FROM DIFFERENT GROUPS
Inhibition of synthesis of mycobacterial cell wall (13), proteins (14,15). Inhibition of the DNA-gyraze enzyme (16).	Inhibition of mycobacterial RNA synthesis.

DRUG	ADVERSE EFFECTS	COMMENTS
Fluoroquinolones	GI intolerance, tendonitis, CNS toxicity including caffeine-like effects	Monitor LFTs, serum creatinine / BUN, QT interval prolongation. Avoid concomitant ingestion with antacids, multivitamins or drugs containing di- or trivalent cations.
Aminoglycosides, Capreomycin	Nephrotoxicity, ototoxicity	Not available orally. Monitor for vestibular, auditory and renal toxicity.
Macrolides	GI intolerance, tinnitus	Monitor LFTs, serum creatinine / BUN, QT interval prolongation. Monitor for drug interactions due to CYP inhibition (except *azithromycin*).
Ethionamide	GI intolerance, hepatotoxicity, hypothyroidism	Monitor LFTs, TSH. A majority of patients experience GI intolerance. Cross-resistance with *isoniazid* is possible.
Para-aminosalicylic acid (PAS)	GI intolerance, hepatotoxicity, hypothyroidism	Monitor LFTs, TSH. Patients with glucose-6 phosphate dehydrogenase (G6PD) deficiency are at increased risk of hemolytic anemia.
Cycloserine	CNS toxicity	Close monitoring is needed for depression, anxiety, confusion, etc. Seizures may be exacerbated in patients with epilepsy. Monitor serum creatinine.

BUN = blood urea nitrogen; CNS = central nervous system; GI = gastrointestinal; LFTs = liver function tests; TSH = thyroid-stimulating hormone

Figure 41.10
Some characteristics of second-line drugs used in treating tuberculosis.

Task 8

Fill the table about fluoroquinolones derivatives. Specify the mechanism of action of this pharmacological group. Discuss the pharmacokinetic features of the combination of dietary calcium with first generation of flouroquinolnes.

Ist GENERATION	IInd GENERATION	IIIrd GENERATION

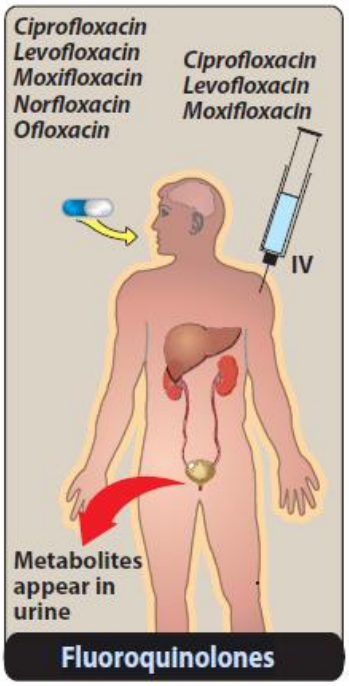


Figure 40.3
Administration and fate of the fluoroquinolones.

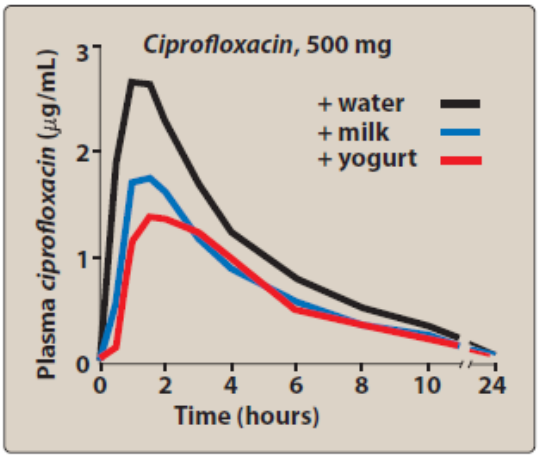


Figure 40.4
Effect of dietary calcium on the absorption of *ciprofloxacin*.