Erythromycins(Macrolides)

- Same spectrum of penicillin, so substitutes in penicillin allergic patients.
- Widely distributed in the body, even the prostate gland.

Erythromycins(Macrolides)

- Safe drugs for children:
  - Can be given orally.
  - Can cause nausea, vomiting, and diarrhea.
  - Rarely can cause jaundice.
- Clarithromycin
- Azithromycin
  - Long acting, short courses.
  - Used to eradicate H*elicobacter pylori*.

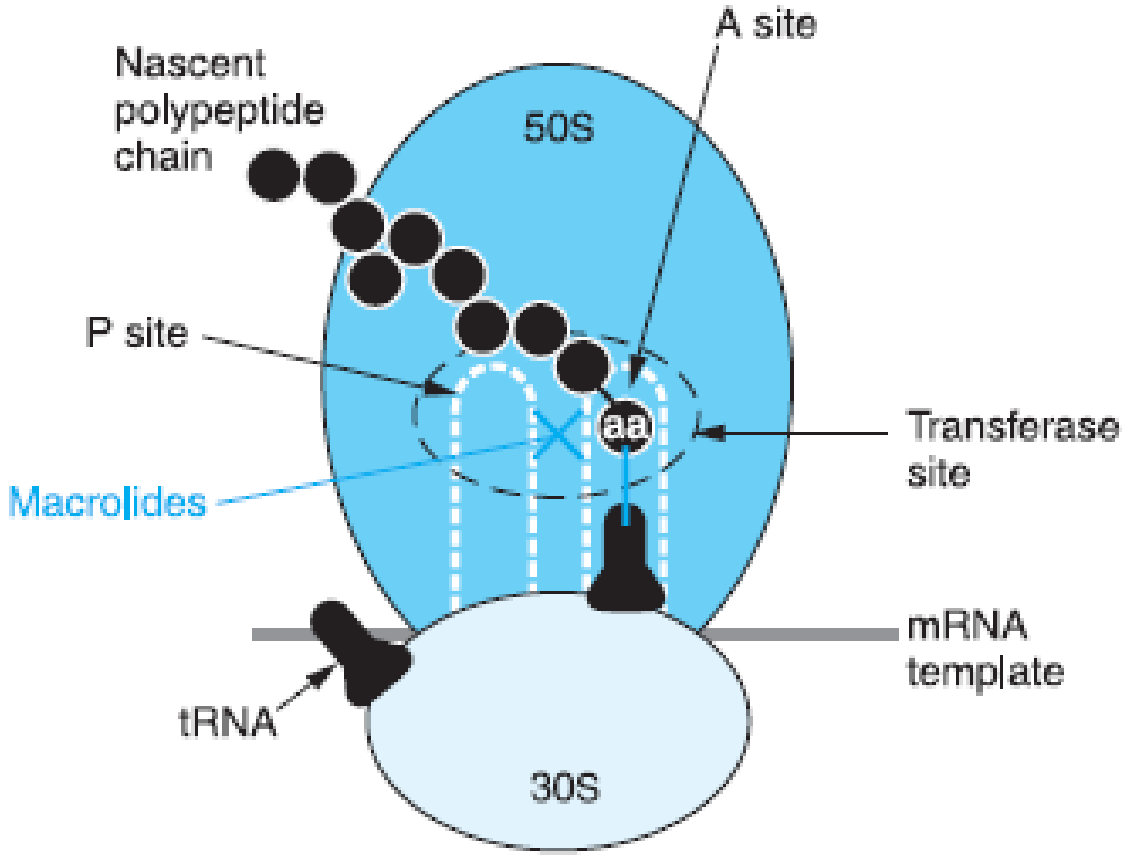

Figure 46–3. Inhibition of bacterial protein synthesis by the macrolide antibiotics erythromycin, clarithromycin, and azithromycin. Macrolide antibiotics are bacteriostatic agents that inhibit protein synthesis by binding reversibly to the 50S ribosomal subunits of sensitive organisms.

Lincomycin and Clindamycin

- Effective against Gram positive bacteria, like penicillins.
- Clindamycin binds exclusively to the 50S subunit of bacterial ribosomes and suppresses protein synthesis
- So misused by doctors in the treatment of simple sore throat or URTI.

Lincomycin and Clindamycin

- Should be reserved for deep seated infections like bone infection.
- Overuse of lincomycin caused many cases of Pseudomembraneous colitis caused by overgrowth of resistant intestinal flora

(*Clostridium difficilli*).

Vancomycin

- Very toxic agent: ototoxic and nephrotoxic.
- Reserved for severe Staphylococcal infection, given by slow IV infusion.

Vancomycin

- **Given orally for Pseudomembraneous colitis.**
- Vancomycin inhibits the synthesis of the cell wall in sensitive bacteria by binding with high affinity to the D-alanyl-D-alanine terminus of cell wall
- drug is bactericidal for dividing microorganisms

D-alanyl-D-alanine
A dipeptide comprising D-alanine with a D-alanyl residue attached to the α-nitrogen. It is a component of bacterial peptidoglycan and forms an important target for development of antibacterial drugs .

Tuberculosis

- The most important communicable disease in the world.
- Caused by *Mycobacterium tuberculosis*
- The ability of the tubercle bacillus to remain dormant but viable and capable of causing disease is a major therapeutic challenge.

Groups at high risk for tuberculosis infection

- HIV-infected persons,
- immigrants from countries with high rates of tuberculosis,
- the homeless,
- health care professionals,
- intravenous drug users,
- persons taking immunosuppressive agents,

The three basic concepts in tuberculosis treatment

(1) Regimens must contain multiple drugs to which the organism is susceptible.

(2) Drugs must be taken regularly.

(3) Drug therapy must continue for a sufficient time

first-line drugs

- isoniazid
- rifampin
- pyrazinamide
- ethambutol
- streptomycin

Antituberculous Drugs

Isoniazid(INH)

- primary action of isoniazid is to inhibit the biosynthesis of mycolic acids—long, branched lipids that are attached to polysaccharide, to form part of the mycobacterial cell wall.

Isoniazid(INH)

- First line drug.
- Rapidly absorbed after oral administration.
- Widely distributed and excreted by the kidneys.
- Diffuses widely in the body, enters infected cells.

Isoniazid(INH)

- Metabolized in the liver:
  - Fast metabolizers.
  - Slow metabolizers.
- Causes neuropathy, especially in slow metabolizers. Can be corrected by Vitamin B6.

If a drug is metabolized too quickly, it may decrease the drug's efficacy while if the drug is metabolized too slowly, toxicity may result

drugs that are metabolized by CYP2D6, certain individuals will eliminate these drugs quickly (ultrarapid metabolizers) while others slowly

Antituberculous Drugs

Rifampin

- Another first line drug.
- Broad spectrum antibiotic, so misused by doctors.
- Use in Jordan is restricted for TB and prophylaxis of meningitis contacts.
- Can cause red discoloration of secretions: tears, urine etc.

Rifampin

- inhibits RNA polymerase of mycobacteria and other microorganisms by forming a stable drug–enzyme complex, leading to suppression of initiation of chain formation in RNA synthesis.

RNA polymerase also known as DNA-dependent RNA polymerase, is an enzyme that produces primary transcript RNA

Antituberculous Drugs

Streptomycin

- An aminoglycoside, 1947.
- Was the first effective antituberculous drug.
- Should be given by injection, resulted in noncompliance of the patients.

Antituberculous Drugs

Streptomycin

- Ototoxic.
- Resistance developed very rapidly.
- Replaced by isoniazid.
- Still used in some cases.

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