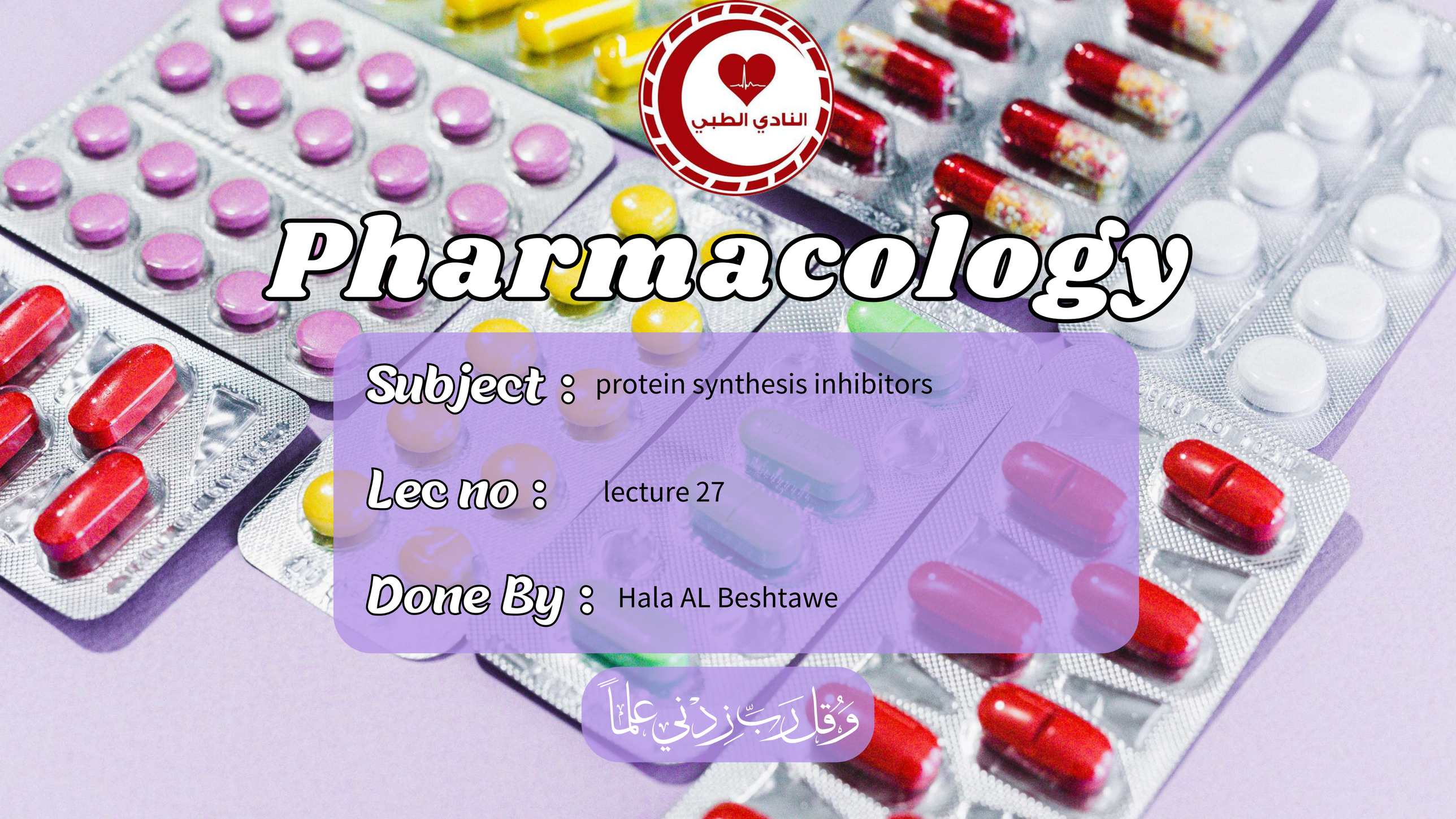


Pharmacology

Subject : protein synthesis inhibitors

Lec no : lecture 27

Done By : Hala AL Beshtawe

وَقُل رَّبِّ زِدْنِي عِلْمًا

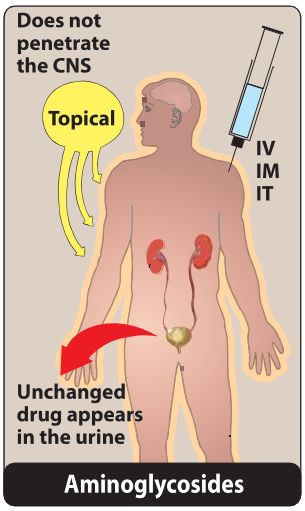


Figure 30.8
Administration and fate of aminoglycosides. CNS = central nervous system.

3. **Elimination:** More than 90% of the parenteral aminoglycosides are excreted unchanged in the urine (Figure 30.8). Accumulation occurs in patients with renal dysfunction; thus, dose adjustments are required. *Neomycin* is primarily excreted unchanged in the feces.

E. Adverse effects

Therapeutic drug monitoring of *gentamicin*, *tobramycin*, and *amikacin* plasma concentrations is imperative to ensure appropriateness of dosing and to minimize dose-related toxicities (Figure 30.9). The elderly are particularly susceptible to nephrotoxicity and ototoxicity.

1. **Ototoxicity:** Ototoxicity (vestibular and auditory) is directly related to high peak plasma concentrations and the duration of treatment. Aminoglycosides accumulate in the endolymph and perilymph of the inner ear. Deafness may be irreversible and has been known to affect developing fetuses. Patients simultaneously receiving concomitant ototoxic drugs, such as *cisplatin* or loop diuretics, are particularly at risk. Vertigo (especially in patients receiving *streptomycin*) may also occur.

2. **Nephrotoxicity:** Retention of the aminoglycosides by the proximal tubular cells disrupts calcium-mediated transport processes. This results in kidney damage ranging from mild, reversible renal impairment to severe, potentially irreversible acute tubular necrosis.

3. **Neuromuscular paralysis:** This adverse effect is associated with a rapid increase in concentration (for example, high doses infused over a short period) or concurrent administration with neuromuscular blockers. Patients with myasthenia gravis are particularly at risk. Prompt administration of *calcium gluconate* or *neostigmine* can reverse the block that causes neuromuscular paralysis.

4. **Allergic reactions:** Contact dermatitis is a common reaction to topically applied *neomycin*.

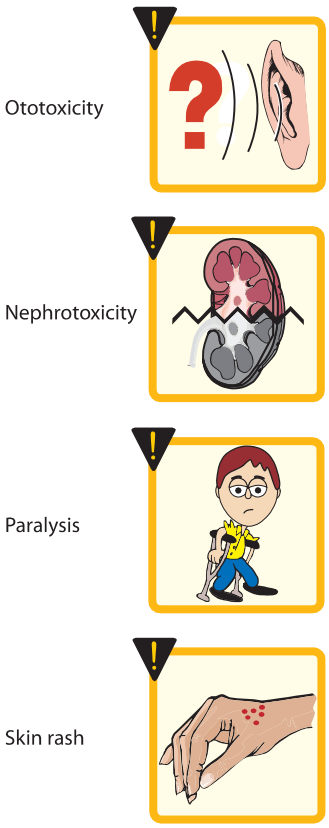
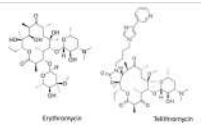


Figure 30.9
Some adverse effects of aminoglycosides.



V. MACROLIDES AND KETOLIDES

The macrolides are a group of antibiotics with a macrocyclic lactone structure to which one or more deoxy sugars are attached. *Erythromycin* [er-ith-roe-MYE-sin] was the first of these drugs to have clinical application, both as a drug of first choice and as an alternative to *penicillin* in individuals with an allergy to β-lactam antibiotics. *Clarithromycin* [kla-rith-roe-MYE-sin] (a methylated form of *erythromycin*) and *azithromycin* [a-zith-roe-MYE-sin] (having a larger lactone ring) have some features in common with, and others that improve upon, *erythromycin*. *Telithromycin* [tel-ith-roe-MYE-sin], a semisynthetic derivative of *erythromycin*, is a "ketolide" antimicrobial agent (no longer used in the United States).

A. Mechanism of action

The macrolides and ketolides bind irreversibly to a site on the 50S subunit of the bacterial ribosome, thus inhibiting translocation steps

MACROLIDES/KETOLIDES	
Azithromycin	ZITHROMAX
Clarithromycin	BIAXIN
Erythromycin	VARIOUS
Telithromycin	KETEK

of protein synthesis (Figure 30.2). They may also interfere with other steps, such as transpeptidation. Generally considered to be bacteriostatic, they may be bactericidal at higher doses. Their binding site is either identical to or in close proximity to that for *clindamycin* and *chloramphenicol*.

B. Antibacterial spectrum

1. **Erythromycin:** This drug is effective against many of the same organisms as *penicillin G* (Figure 30.10); therefore, it may be considered as an alternative in patients with *penicillin* allergy.

2. **Clarithromycin:** *Clarithromycin* has activity similar to *erythromycin,* but it is also effective against Haemophilus influenzae and has greater activity against intracellular pathogens such as Chlamydia, Legionella, Moraxella, Ureaplasma species, and Helicobacter pylori.

3. **Azithromycin:** Although less active than *erythromycin* against streptococci and staphylococci, *azithromycin* is far more active against respiratory pathogens such as H. influenzae and Moraxella catarrhalis. Extensive use of *azithromycin* has resulted in growing Streptococcus pneumoniae resistance.

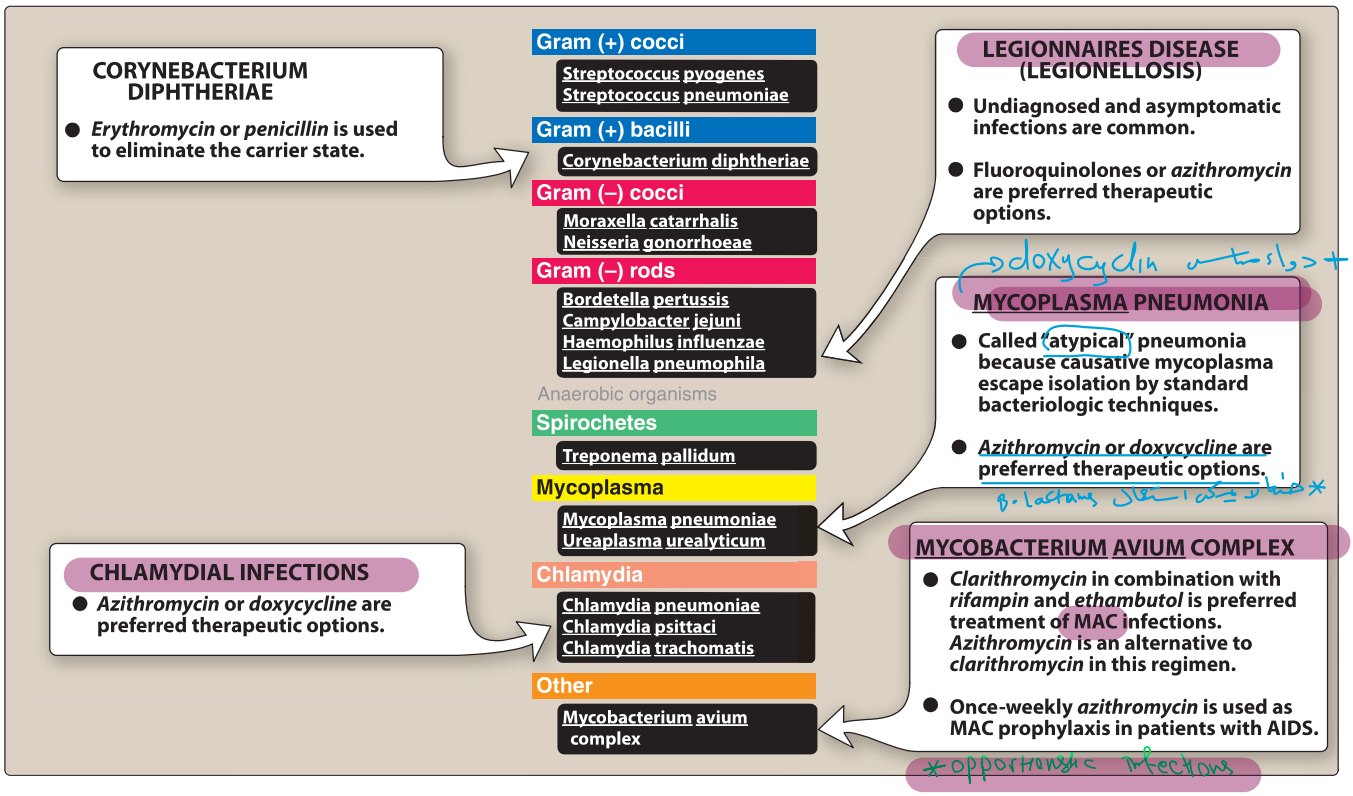


Figure 30.10
Typical therapeutic applications of macrolides.

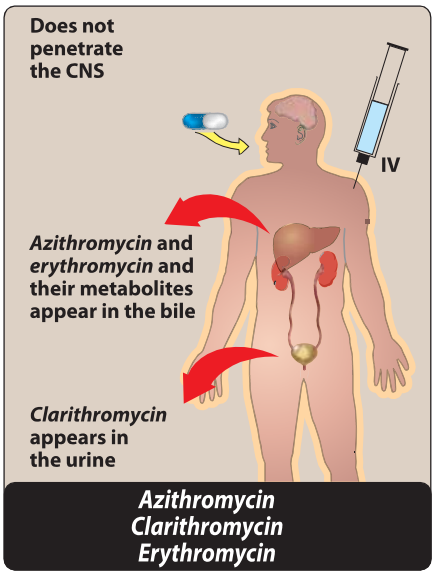


Figure 30.11
Administration and fate of the macrolide antibiotics. CNS = central nervous system.

	Erythro-mycin	*Clarithro-mycin*	*Azithro-mycin*	*Telithro-mycin*
Oral absorption	Yes	Yes	Yes	Yes
Half-life (hours)	2	3.5	68	10
Conversion to an active metabolite	No	Yes	No	Yes
Percent excretion in urine	< 15	30–50	< 10	13

Figure 30.12
Some properties of the macrolide antibiotics.

4. **Telithromycin:** *Telithromycin* has an antimicrobial spectrum similar to that of *azithromycin*. Moreover, the structural modification within ketolides neutralizes the most common resistance mechanisms that render *macrolides* ineffective.

C. Resistance

Resistance to macrolides is associated with: 1) the inability of the organism to take up the antibiotic, 2) the presence of efflux pumps, 3) a decreased affinity of the 50S ribosomal subunit for the antibiotic due to methylation of an adenine in the 23S bacterial ribosomal RNA in gram-positive organisms, and 4) the presence of plasmid- associated *erythromycin* esterases in gram-negative organisms such as the Enterobacteriaceae. *Erythromycin* has limited clinical use due to increasing resistance. Both *clarithromycin* and *azithromycin* share some cross-resistance with *erythromycin*. *Telithromycin* may be effective against macrolide-resistant organisms.

D. Pharmacokinetics

1. **Absorption:** The *erythromycin* base is destroyed by gastric acid; thus, either enteric-coated tablets or esterified forms of the antibiotic are administered and all have adequate oral absorption (Figure 30.11). *Clarithromycin*, *azithromycin*, and *telithromycin* are stable in stomach acid and are readily absorbed. Food interferes with the absorption of *erythromycin* and *azithromycin* but can increase that of *clarithromycin*. *Telithromycin* is administered orally without regard to meals. *Erythromycin* and *azithromycin* are available in IV formulations.

2. **Distribution:** *Erythromycin* distributes well to all body fluids except the CSF. It is one of the few antibiotics that diffuse into prostatic fluid, and it also accumulates in macrophages. All four drugs concentrate in the liver. *Clarithromycin*, *azithromycin*, and *telithromycin* are widely distributed in the tissues. *Azithromycin* concentrates in neutrophils, macrophages, and fibroblasts, and serum concentrations are low. It has the largest volume of distribution of the four drugs

3. **Elimination:** *Erythromycin* and *telithromycin* undergo hepatic metabolism. They inhibit the oxidation of a number of drugs through their interaction with the cytochrome P450 system. Interference with the metabolism of drugs such as *theophylline*, statins, and numerous antiepileptics has been reported for *clarithromycin*.

4. **Excretion:** *Azithromycin* is primarily concentrated and excreted in the bile as active drug. *Erythromycin* and its metabolites are also excreted in the bile (Figure 30.11). Partial reabsorption occurs through the enterohepatic circulation. In contrast, *clarithromycin* is hepatically metabolized, and the active drug and its metabolites are mainly excreted in the urine (Figure 30.12). The dosage of this drug should be adjusted in patients with renal impairment.

E. Adverse effects

1. **Gastric distress and motility:** Gastrointestinal upset is the most common adverse effect of the macrolides and may lead to poor

patient compliance (especially with *erythromycin*). The other macrolides seem to be better tolerated (Figure 30.13). Higher doses of *erythromycin* lead to smooth muscle contractions that result in the movement of gastric contents to the duodenum, an adverse effect sometimes employed for the treatment of gastroparesis or postoperative ileus.

2. **Cholestatic jaundice:** This adverse effect occurs most commonly with the estolate form of *erythromycin* (not used in the United States); however, it has been reported with other formulations and other agents in this class.

3. **Ototoxicity:** Transient deafness has been associated with *erythromycin,* especially at high dosages. *Azithromycin* has also been associated with irreversible sensorineural hearing loss.

4. **QT_c prolongation:** Macrolides and ketolides may prolong the QT_c interval and should be used with caution in those patients with proarrhythmic conditions or concomitant use of proarrhythmic agents.

5. **Contraindications:** Patients with hepatic dysfunction should be treated cautiously with *erythromycin*, *telithromycin*, or *azithromycin*, because these drugs accumulate in the liver. Severe hepatotoxicity with *telithromycin* has limited its use, given the availability of alternative therapies.

6. **Drug Interactions:** *Erythromycin*, *telithromycin*, and *clarithromycin* inhibit the hepatic metabolism of a number of drugs, which can lead to toxic accumulation of these compounds (Figure 30.14). An interaction with *digoxin* may occur. One theory to explain this interaction is that the antibiotic eliminates a species of intestinal flora that ordinarily inactivates *digoxin*, leading to greater reabsorption of *digoxin* from the enterohepatic circulation.

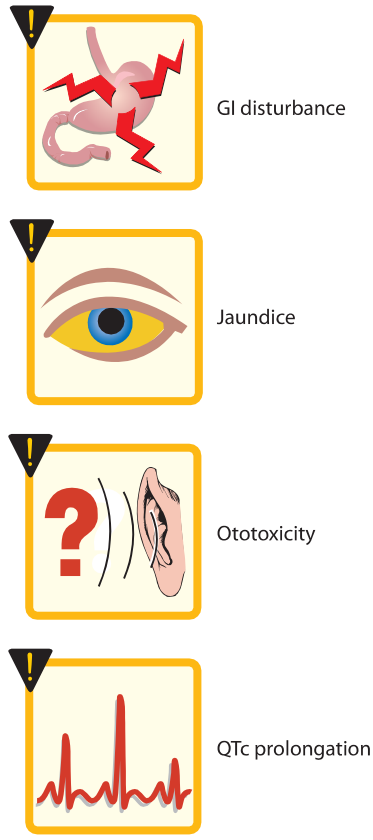


Figure 30.13
Some adverse effects of macrolide antibiotics.

VI. FIDAXOMICIN

Fidaxomicin [fye-DAX-oh-MYE-sin] is a macrocyclic antibiotic with a structure similar to the macrolides; however, it has a unique mechanism of action. *Fidaxomicin* acts on the sigma subunit of RNA polymerase, thereby disrupting bacterial transcription, terminating protein synthesis and resulting in cell death in susceptible organisms. *Fidaxomicin* has a very narrow spectrum of activity limited to gram-positive aerobes and anaerobes. While it possesses activity against staphylococci and enterococci, it is used primarily for its bactericidal activity against Clostridium difficile. Because of the unique target site, cross-resistance with other antibiotic classes has not been documented. Following oral administration, *fidaxomicin* has minimal systemic absorption and primarily remains within the gastrointestinal tract. This is ideal for the treatment of C. difficile infection, which occurs in the gut. The most common adverse effects include nausea, vomiting, and abdominal pain. Anemia and neutropenia have been observed infrequently. Hypersensitivity reactions including angioedema, dyspnea, and pruritus have occurred. *Fidaxomicin* should be used with caution in patients with a macrolide allergy, as they may be at increased risk for hypersensitivity.

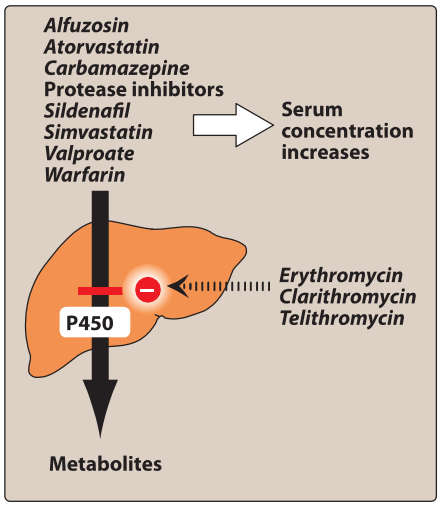


Figure 30.14
Inhibition of the cytochrome P450 system by *erythromycin*, *clarithromycin*, and *telithromycin*.

VII. CHLORAMPHENICOL

The use of *chloramphenicol* [klor-am-FEN-i-kole], a broad-spectrum antibiotic, is restricted to life-threatening infections for which no alternatives exist.

A. Mechanism of action

Chloramphenicol binds reversibly to the bacterial 50S ribosomal subunit and inhibits protein synthesis at the peptidyl transferase reaction (Figure 30.2). Because of some similarity of mammalian mitochondrial ribosomes to those of bacteria, protein and ATP synthesis in these organelles may be inhibited at high circulating *chloramphenicol* concentrations, producing bone marrow toxicity. [Note: The oral formulation of *chloramphenicol* was removed from the US market due to this toxicity.]

B. Antibacterial spectrum

Chloramphenicol is active against many types of microorganisms including chlamydiae, rickettsiae, spirochetes, and anaerobes. The drug is primarily bacteriostatic, but it may exert bactericidal activity depending on the dose and organism.

C. Resistance

Resistance is conferred by the presence of enzymes that inactivate *chloramphenicol*. Other mechanisms include decreased ability to penetrate the organism and ribosomal binding site alterations.

Critical Thinking Question

?

Since chloramphenicol is toxic due to its targeting of the mammalian protein synthesis ... which type of ribosomes in mammalian cells will be most susceptible to inhibition by chloramphenicol? And why?

D. Pharmacokinetics

Chloramphenicol is administered intravenously and is widely distributed throughout the body. It reaches therapeutic concentrations in the CSF. *Chloramphenicol* primarily undergoes hepatic metabolism to an inactive glucuronide, which is secreted by the renal tubule and eliminated in the urine. Dose reductions are necessary in patients with liver dysfunction or cirrhosis. *Chloramphenicol* is also secreted into breast milk and should be avoided in breastfeeding mothers.

E. Adverse effects

1. **Anemias:** Patients may experience dose-related anemia, hemolytic anemia (observed in patients with glucose-6-phosphate dehydrogenase deficiency), and aplastic anemia. [Note: Aplastic anemia is independent of dose and may occur after therapy has ceased.]

2. **Gray baby syndrome:** Neonates have a low capacity to glucuronidate the antibiotic, and they have underdeveloped renal function, which decreases their ability to excrete the drug. This leads to drug accumulation to concentrations that interfere with the function of mitochondrial ribosomes, causing poor feeding, depressed breathing, cardiovascular collapse, cyanosis (hence the term "gray baby"), and death. Adults who have received very high doses of *chloramphenicol* may also exhibit this toxicity.

3. **Drug interactions:** *Chloramphenicol* inhibits some of the hepatic mixed-function oxidases, preventing the metabolism of drugs such as *warfarin* and *phenytoin*, which may potentiate their effects.

VIII. CLINDAMYCIN

Clindamycin [klin-da-MYE-sin] has a mechanism of action that is similar to that of the macrolides. *Clindamycin* is used primarily in the treatment of infections caused by gram-positive organisms, including MRSA and streptococcus, and anaerobic bacteria. Resistance mechanisms are the same as those for *erythromycin,* and cross-resistance has been described. C. difficile is resistant to *clindamycin*, and the utility of *clindamycin* for gram-negative anaerobes (for example, Bacteroides sp.) is decreasing due to increasing resistance. *Clindamycin* is available in both IV and oral formulations, but use of oral *clindamycin* is limited by gastrointestinal intolerance. It distributes well into all body fluids but exhibits poor entry into the CSF. *Clindamycin* undergoes extensive oxidative metabolism to active and inactive products and is excreted into bile and urine. Low urinary excretion of active drug limits its clinical utility for urinary tract infections (Figure 30.15). Accumulation has been reported in patients with either severe renal impairment or hepatic failure. In addition to skin rash, the most common adverse effect is diarrhea, which may represent a serious pseudomembranous colitis caused by overgrowth of C. difficile. Oral administration of either *metronidazole* or *vancomycin* is usually effective in the treatment of C. difficile infection.

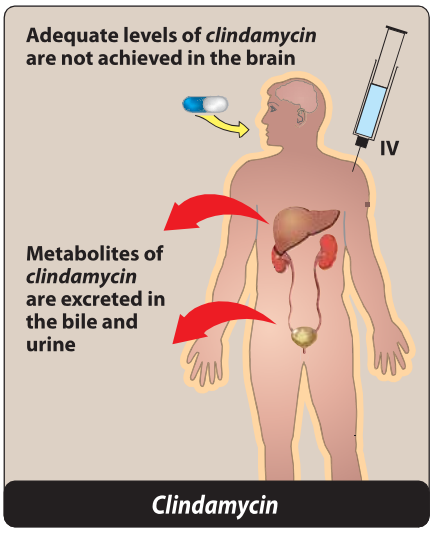


Figure 30.15
Administration and fate of *clindamycin*.

IX. QUINUPRISTIN/DALFOPRISTIN

Quinupristin/dalfopristin [KWIN-yoo-pris-tin/DAL-foh-pris-tin] is a mixture of two streptogramins in a ratio of 30 to 70, respectively. Due to significant adverse effects, this combination drug is normally reserved for the treatment of severe infections caused by *vancomycin*-resistant Enterococcus faecium (VRE) in the absence of other therapeutic options.

A. Mechanism of action

Each component of this combination drug binds to a separate site on the 50S bacterial ribosome. *Dalfopristin* disrupts elongation by interfering with the addition of new amino acids to the peptide chain. *Quinupristin* prevents elongation similar to the macrolides and causes release of incomplete peptide chains. Thus, they synergistically interrupt protein synthesis. The combination drug has bactericidal activity against most susceptible organisms and has a long PAE.

B. Antibacterial spectrum

Quinupristin/dalfopristin is active primarily against gram-positive cocci, including those resistant to other antibiotics. Its primary use is for the treatment of E. faecium infections, including VRE strains, against which it is bacteriostatic. The drug is not effective against E. faecalis.

C. Resistance

Enzymatic processes commonly account for resistance to these agents. For example, the presence of a ribosomal enzyme that methylates the target bacterial 23S ribosomal RNA site can interfere in *quinupristin* binding. In some cases, the enzymatic modification can change the action from bactericidal to bacteriostatic. Plasmid-associated acetyltransferase inactivates *dalfopristin.* An active efflux pump can also decrease levels of the antibiotics in bacteria.

D. Pharmacokinetics

Quinupristin/dalfopristin is available intravenously. It does not achieve therapeutic concentrations in CSF. Both compounds undergo hepatic metabolism, with excretion mainly in the feces.

E. Adverse effects

Venous irritation commonly occurs when *quinupristin/dalfopristin* is administered through a peripheral rather than a central line. Hyperbilirubinemia occurs in about 25% of patients, resulting from a competition with the antibiotic for excretion. Arthralgia and myalgia have been reported when higher doses are administered. *Quinupristin/dalfopristin* inhibits the cytochrome P450 CYP3A4 isoenzyme, and concomitant administration with drugs that are metabolized by this pathway may lead to toxicities.

X. OXAZOLIDINONES

Linezolid [lih-NEH-zo-lid] and *tedizolid* [ted-eye-ZOE-lid] are synthetic oxazolidinones developed to combat gram-positive organisms, including resistant isolates such as *methicillin*-resistant Staphylococcus aureus, VRE, and *penicillin*-resistant streptococci.

A. Mechanism of action

Linezolid and *tedizolid* bind to the bacterial 23S ribosomal RNA of the 50S subunit, thereby inhibiting the formation of the 70S initiation complex (Figure 30.2) and translation of bacterial proteins.

B. Antibacterial spectrum

The antibacterial action of the oxazolidinones is directed primarily against gram-positive organisms such as staphylococci, streptococci, and enterococci, Corynebacterium species and Listeria monocytogenes. It is also moderately active against Mycobacterium tuberculosis (Figure 30.16). The main clinical use of *linezolid* and *tedizolid* is to treat infections caused by drug-resistant gram-positive organisms. Like other agents that interfere with bacterial protein synthesis, *linezolid* and *tedizolid* are bacteriostatic; however, *linezolid* has bactericidal activity against streptococci. *Linezolid* is an alternative to *daptomycin* for infections caused by VRE. Because they are bacteriostatic, the oxazolidinones are not recommended as first-line treatment for MRSA bacteremia.

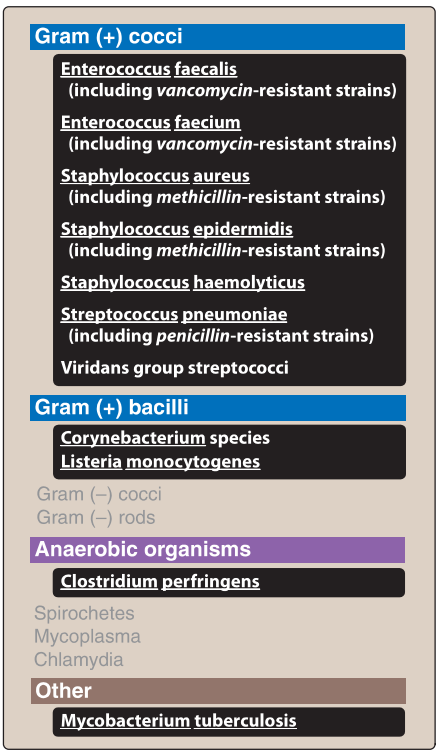


Figure 30.16
Antimicrobial spectrum of oxazolidinones.

C. Resistance

Resistance primarily occurs via reduced binding at the target site. Reduced susceptibility and resistance have been reported in S. aureus and Enterococcus sp. Cross-resistance with other protein synthesis inhibitors does not occur.

D. Pharmacokinetics

Linezolid and *tedizolid* are well absorbed after oral administration. IV formulations are also available. These drugs distribute widely

throughout the body. Although the metabolic pathway of *linezolid* has not been fully determined, it is known that it is metabolized via oxidation to two inactive metabolites. The drug is excreted both by renal and nonrenal routes. *Tedizolid* is metabolized by sulfation, and the majority of elimination occurs via the liver, and drug is mainly excreted in the feces. No dose adjustments are required for either agent for renal or hepatic dysfunction.

E. Adverse effects

The most common adverse effects are gastrointestinal upset, nausea, diarrhea, headache, and rash. Thrombocytopenia has been reported, usually in patients taking the drug for longer than 10 days. *Linezolid* and *tedizolid* possess nonselective monoamine oxidase activity and may lead to serotonin syndrome if given concomitantly with large quantities of tyramine-containing foods, selective serotonin reuptake inhibitors, or monoamine oxidase inhibitors. The condition is reversible when the drug is discontinued. Irreversible peripheral neuropathies and optic neuritis causing blindness have been associated with greater than 28 days of use, limiting utility for extended-duration treatments.

Study Questions

Choose the ONE best answer.

30.1 Which of the following adverse effects is often employed as a therapeutic use for erythromycin?

A. QTc prolongation
B. Increased gastrointestinal motility
C. Photosensitivity
D. Deposition in bone

Correct answer = B. Macrolides, but especially erythromycin, cause GI distress and increase motility of the GI tract, which is often used to treat gastroparesis and/or postoperative ileus. QTc prolongation is an adverse effect of erythromycin but not one employed therapeutically. Photosensitivity and deposition in bone are adverse effects of tetracyclines.

30.2 Which of the following describes the mechanism of action of tetracycline antibiotics?

A. Bind the 30S subunit of the bacterial ribosome, preventing binding of tRNA to the mRNA–ribosome complex.
B. Bind the 30S ribosomal subunit, interfering with assembly of the functional ribosomal apparatus.
C. Bind irreversibly to a site on the 50S subunit of the bacterial ribosome, inhibiting translocation steps of protein synthesis.
D. Bind the bacterial 23S ribosomal RNA of the 50S subunit, inhibiting the formation of the 70S initiation complex.

Correct answer = A. Tetracyclines enter susceptible organisms via passive diffusion and also by an energy-dependent transport protein mechanism unique to the bacterial inner cytoplasmic membrane. The drugs bind reversibly to the 30S subunit of the bacterial ribosome. This action prevents binding of tRNA to the mRNA–ribosome complex, thereby inhibiting bacterial protein synthesis. B is the mechanism for aminoglycosides, C is the mechanism for macrolides, and D is the mechanism for oxazolidinones.

30.3 Linezolid would be a good choice for antibiotic treatment in which of the following patient scenarios?

A. Bacteremia caused by Staphylococcus aureus
B. Urinary tract infection caused by Escherichia coli
C. Pneumonia caused by drug-resistant Streptococcus pneumoniae
D. Diabetic foot infection caused by Pseudomonas aeruginosa

Correct answer = C. Linezolid does have coverage against resistant S. pneumoniae. It is not an optimal choice for treatment of bacteremia. Linezolid also does not have gram-negative coverage against E. coli and P. aeruginosa.

30.4 After 5 days of clindamycin treatment for a skin infection, a patient develops diarrhea (10 watery stools/day), severe abdominal pain, and fever. Which of the following organisms would you be concerned about as the causative pathogen of diarrhea?

A. Escherichia coli
B. Bacteroides fragilis
C. Staphylococcus aureus
D. Clostridium difficile

Correct answer = D. Clindamycin use has been associated with Clostridium difficile–associated diarrhea. This infection should be considered in a patient who presents with diarrhea while on clindamycin.

30.5 Which of the following statements accurately describes the difference in spectrum of activity between erythromycin and azithromycin?

A. Azithromycin has better activity against respiratory pathogens such as Haemophilus influenzae and Moraxella catarrhalis but less potent activity against staphylococci and streptococci.
B. Erythromycin has the same activity as azithromycin against gram-positives and gram-negatives.
C. Azithromycin has better activity against staphylococci and streptococci compared to erythromycin.
D. Erythromycin has better activity against gram-negatives such as H. influenza.

Correct answer = A. Erythromycin has better activity against gram-positive organisms, so B and C are incorrect. D is incorrect as azithromycin has better activity against H. influenza.

30.6 Which of the following antibiotic agents should not be given to children less than 8 years of age due to its deposition in bone and teeth?

A. Azithromycin
B. Doxycycline
C. Linezolid
D. Quinupristin/dalfopristin

Correct answer = B. Tetracyclines are contraindicated in this age group because they are deposited in tissues undergoing calcification, such as teeth and bone, and can stunt growth.

30.7 A 77-year-old woman was started on antibiotics for pneumonia treatment. After 3 days of antibiotic therapy, the serum creatinine doubled. Which of the following antibiotics is most likely responsible for this increase in serum creatinine?

A. Doxycycline
B. Clarithromycin
C. Tobramycin
D. Linezolid

Correct answer = C. Aminoglycosides such as tobramycin accumulate in the proximal tubular cells of the kidney and disrupt calcium-mediated transport processes. This results in kidney damage ranging from mild, reversible renal impairment to severe, potentially irreversible acute tubular necrosis. Nephrotoxicity is not commonly associated with tetracyclines, macrolides or oxazolidinones.

30.8 A 24-year-old pregnant woman was diagnosed with community-acquired pneumonia and will be managed in the outpatient setting. Which antibiotic is a safe option for this patient to treat her pneumonia?

A. Azithromycin
B. Doxycycline
C. Fidaxomicin
D. Gentamicin

Correct answer = A. Azithromycin is available orally and considered safe in pregnancy. Doxycycline should not be used in pregnancy due to its ability to cross the placenta and affect bone and skeletal development in the fetus. Fidaxomicin does not reach therapeutic concentrations in serum or at this site of infection. It concentrates in the gut. Gentamicin crosses the placental barrier and may accumulate in fetal plasma and amniotic fluid. It would also not be used clinically in this outpatient scenario.

30.9 Parents of a 1-month-old baby are told their child has developed "gray baby syndrome." Which of the following antibiotics did the baby likely receive?

A. Tobramycin
B. Linezolid
C. Erythromycin
D. Chloramphenicol

Correct answer = D. Gray baby syndrome is an adverse effect caused by chloramphenicol in neonates due to their underdeveloped renal function and low capacity to glucuronidate the antibiotic. The other agents do not undergo this glucuronidation.

30.10 Aminoglycosides are commonly used for their concentration-dependent bactericidal activity against which group of organisms?

A. Gram-positive aerobes
B. Gram-negative aerobes
C. Gram-positive anaerobes
D. Gram-negative anaerobes

Correct answer = B. Although aminoglycosides (such as gentamicin) are sometimes used synergistically against gram-positive aerobes, this is not their most common use. They are typically used for their activity against gram-negative aerobes. Aminoglycosides do not have good anaerobic activity.