Vancomycin

- **A bactericidal drug which acts by inhibiting cell wall synthesis.**
- **Active only against gram-positive bacteria, particularly staphylococci.**
- **Used IV in treating endocarditis caused by methicillin-resistant staphylococci and resistant enterococci.**
- **Also used orally in Pseudomembraneous Colitis caused by *Clostridium difficile* .**

Vancomycin

- **Valuable in severe staphylococcal infections in patients allergic to penicillins and cephalosporins.**

- **Resistance can be caused by changing the permeability to the drug and by decreasing the binding of Vancomycin to receptors.**

Vancomycin

- **Unwanted effects include fever, rashes and local phlebitis.**

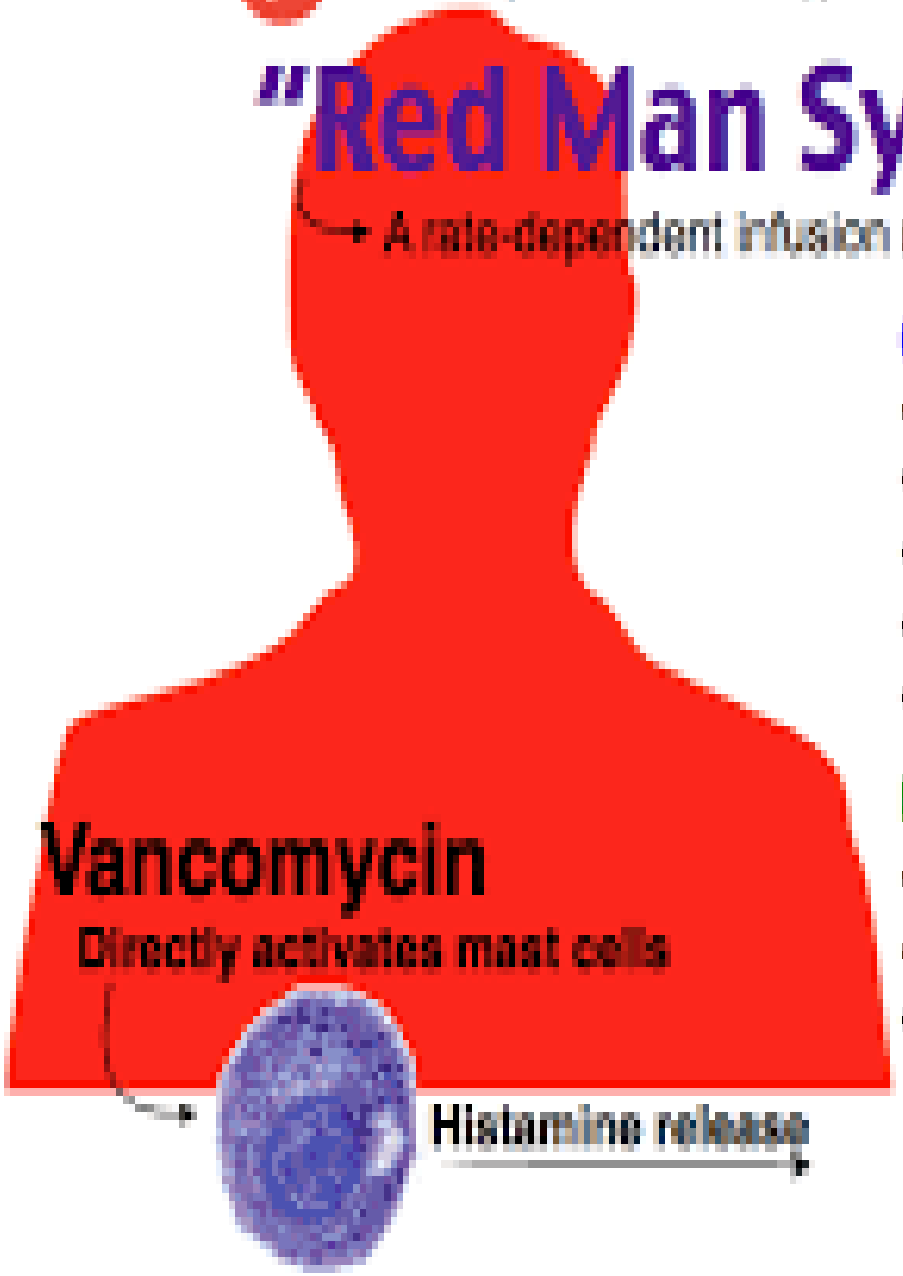
- **Ototoxicity and nephrotoxicity can occur and hypersensitivity reactions are occasionally encountered.**

- **Vancomycin must be administered in a dilute solution slowly, over at least 60 minutes to avoid an infusion reaction known as the Red Man Syndrome or Red Neck Syndrome.**

Immune system disorders/hypersensitivity

"Red Man Syndrome"

→ A rate-dependent infusion reaction (*not a true allergic reaction*)



Clinical

- Flushing
- Erythema
- Pruritus
- Affecting upper body, neck and face > lower body
- Myalgia, dyspnea, hypotension

Management

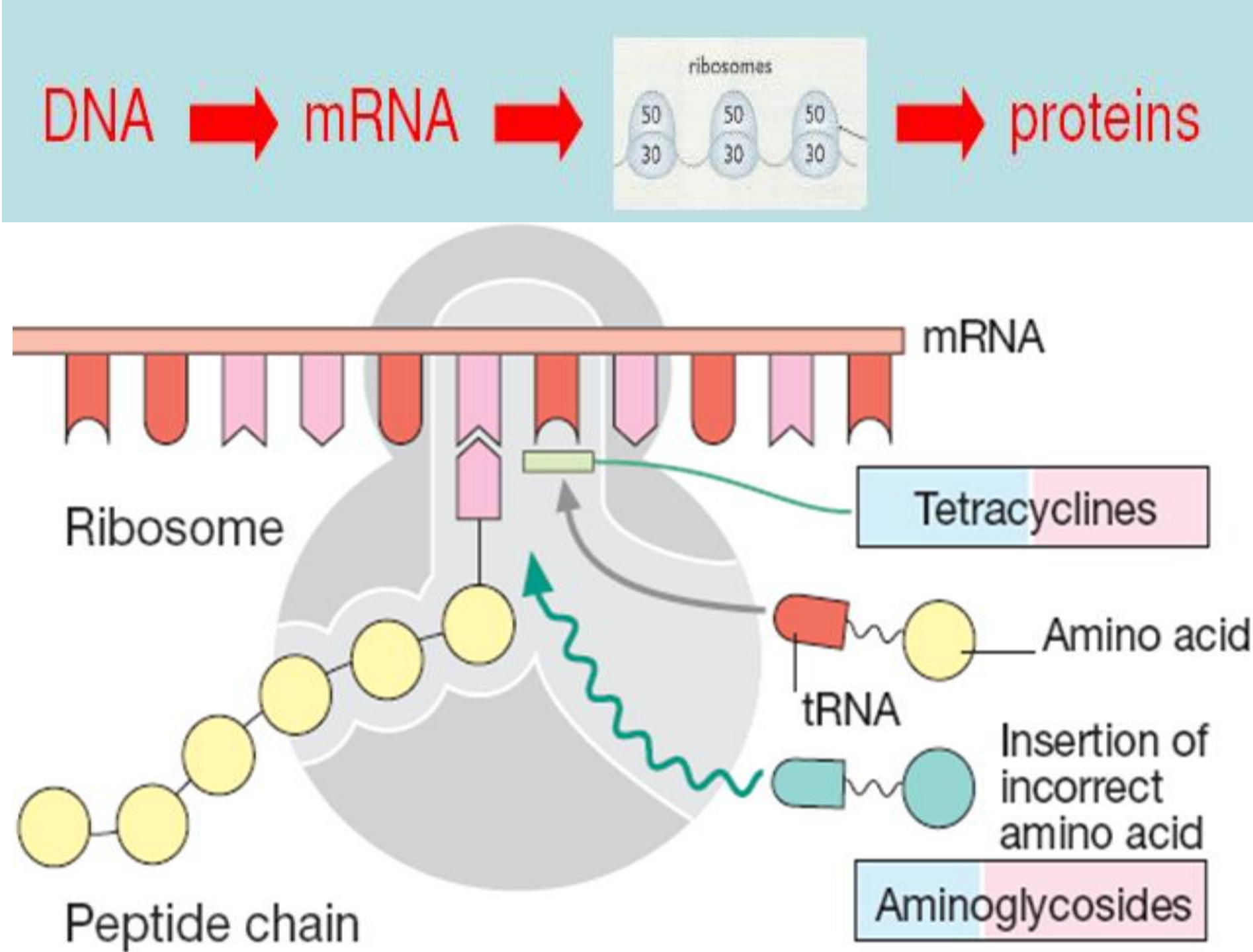
- Stop infusion
- Administer antihistamine (diphenhydramine)
- Can restart at slower rate once symptoms resolve

Protein Synthesis Inhibitors

- Active against a wide variety of organisms (broad spectrum).
- Most are bacteriostatic but a few are bactericidal against certain organisms.
- Because of overuse, resistance is common.

- Bacterial ribosomes differ in molecular detail from eukaryotic cells, enabling antibiotics to exhibit selective toxicity.

- Interfere with the main ribosomal processes:
  - Binding of aminoacyl-tRNA
  - Normal codon:anticodon recognition
  - Transpeptidation


DNA
mRNA
ribosomes
50
30
50
30
50
30
proteins
mRNA
Ribosome
Tetracyclines
Amino acid
tRNA
Insertion of incorrect amino acid
Aminoglycosides
Peptide chain

Tetracyclines

- Tetracycline, Methacycline, Moxycycline, doxycycline minocycline, and **Tigecycline**.
- Bind to both mRNA and the ribosomal 30S subunit where they prevent the binding of aminoacyl-tRNA.
- Bacteriostatic.
- Wide spectrum of activity and includes some spirochaetes and even some protozoa like amoebae.

CHLAMYDIAL INFECTIONS

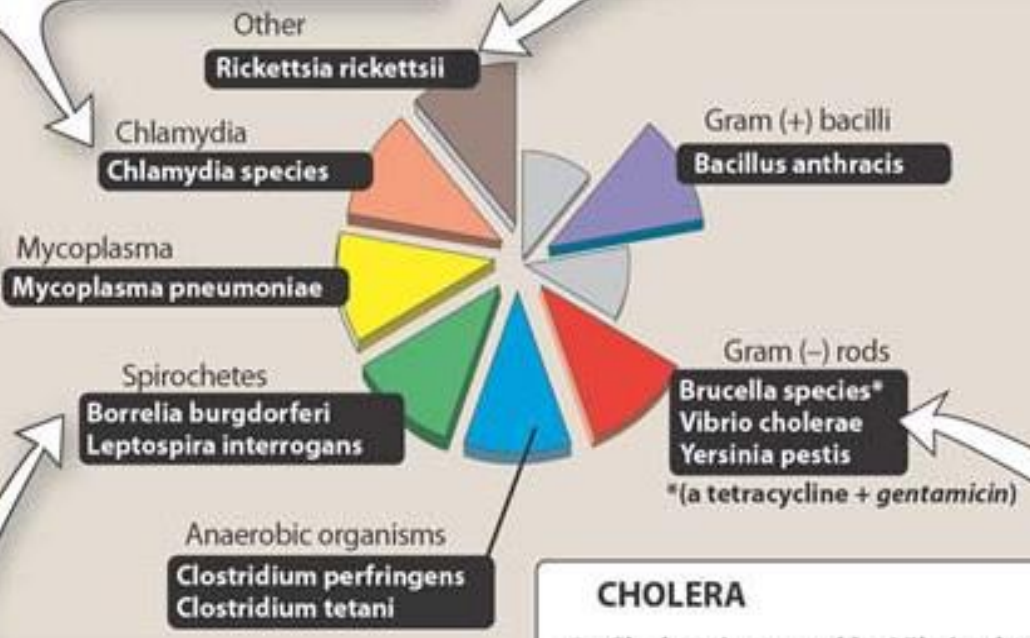
- Chlamydia trachomatis is the major cause of sexually transmitted disease in the United States. It causes nongonococcal urethritis, pelvic inflammatory disease, and lymphogranuloma venereum.
- Chlamydia psittaci causes psittacosis, which usually takes the form of pneumonia. Other clinical forms include hepatitis, myocarditis, and coma.
- *Doxycycline* or *azithromycin* is used to treat chlamydial infections.

ROCKY MOUNTAIN SPOTTED FEVER

- This disease, caused by Rickettsia rickettsii, is characterized by fever, chills, and aches in bones and joints.
- Response to tetracyclines is prompt if the drug is started early in the disease process.

MYCOPLASMA PNEUMONIA

- Mycooplasm pneumoniae is a common cause of pneumonia in young adults and in people who live in close confines, such as in military camps.
- Treatment leads to a shorter duration of fever, cough, and malaise.
- Treatment with marcrolides is also effective.



LYME DISEASE

- This is a spirochetal infection caused by Borrelia burgdorferi. The disease is transmitted by the bite of infected ticks.
- Infection results in skin lesions, headache, and fever, followed by meningoencephalitis and, eventually, arthritis.
- A single, 200–mg dose of *doxycycline*, given within 72 hours after a tick bite, can prevent development of the disease.

CHOLERA

- Cholera is caused by Vibrio cholerae ingested as part of fecally contaminated food or water.
- The organism multiplies in the gastrointestinal tract, where it secretes an enterotoxin that produces diarrhea.
- Treatment includes *doxycycline*, which reduces the number of intestinal vibrios, and fluid replacement.

Clinical Uses of Tetracyclines

Mycoplasma and chlamydia infections

Brucellosis: usually in combination with an aminoglycoside.

Acne

Occasionally used in dentistry to treat bacterial infections.

Syphilis

Tetracyclines

- **Resistance is common and mainly due to a plasmid-mediated energy-dependent efflux pump(typical of the multiple drug resistance type). Mutations in the tetracycline target site are also found.**

- **Usually administered orally but can be given parenterally.**

- **Absorption from the gut is irregular and better in the absence of food, but they are gastric irritants, so usually given after meals.**

- **Since Tetracyclines are chelated by di- and trivalent metal ions, forming insoluble complexes, absorption is decreased in the presence of milk, certain antacids and iron preparations.**

Tetracyclines

- **The most Common side-effects are GI disturbances, essentially due to direct irritation and later to modification of gut flora.**

- **Deposit in growing bones and teeth, so caused staining and dental hypoplasia and bone deformities in children.**

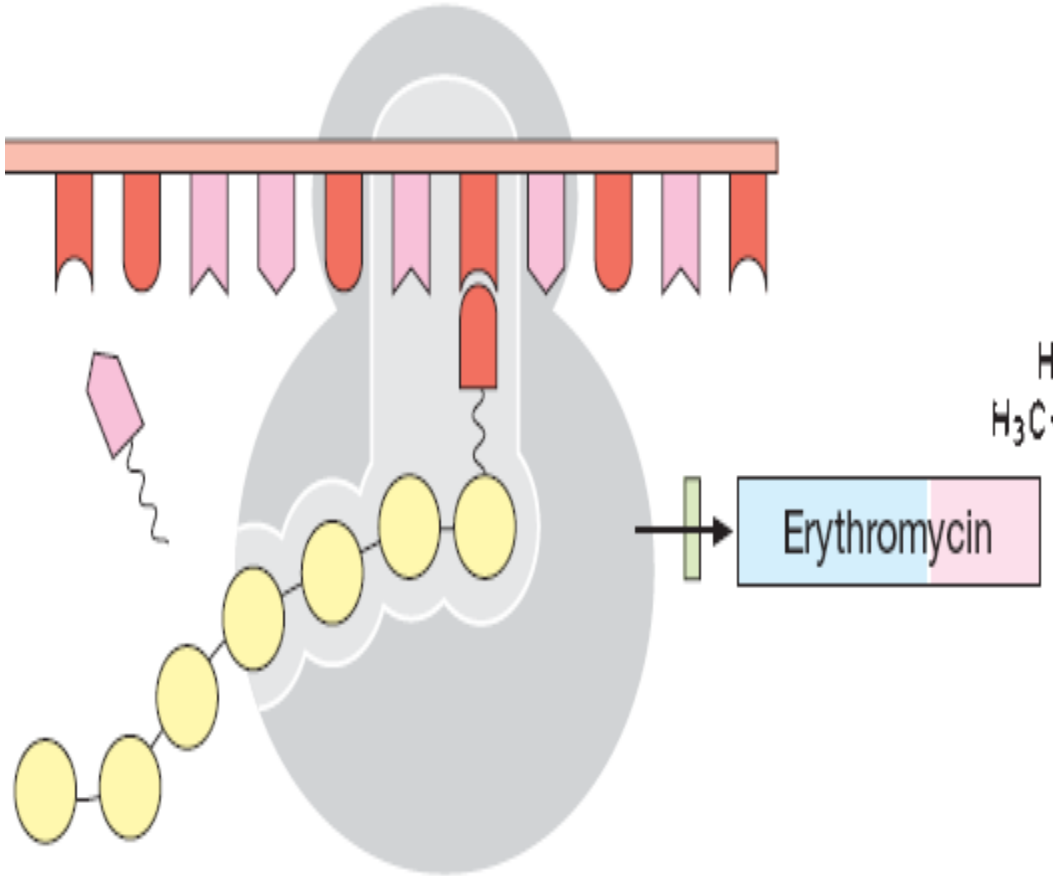
- **Phototoxicity: for example, severe sunburn, after exposure to sun or ultra-violet rays.**

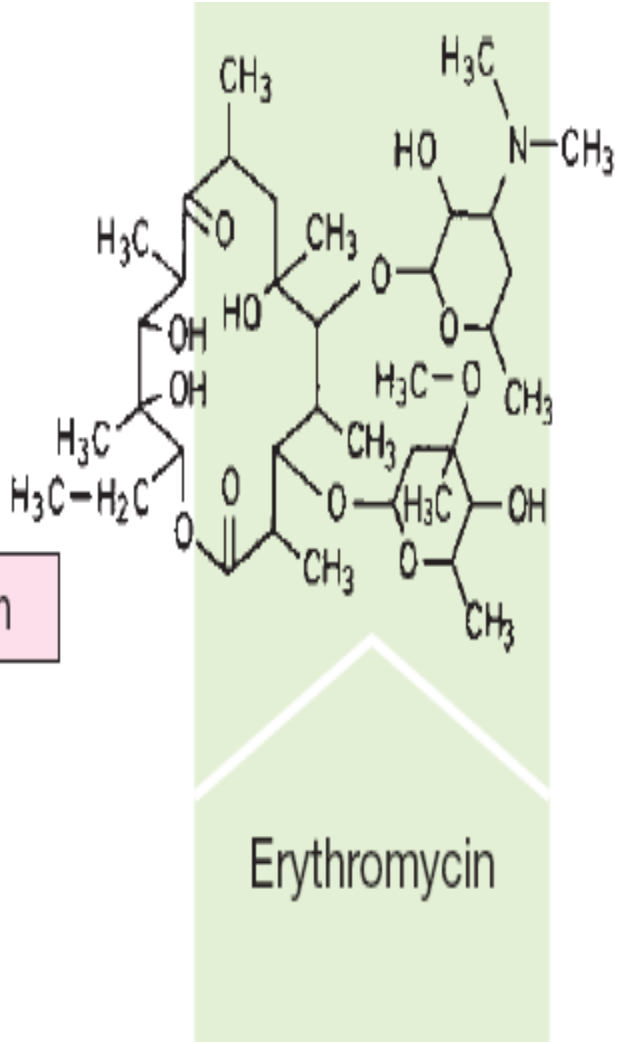
- **Contraindicated in children, nursing mothers and pregnant women (may causes hepatotoxicity in pregnant women).**

Macrolides

- **Erythromycin**
- **Clarithromycin(1 tablet for 14 days)**
- **Azithromycin(1 tablet for 5 days)**
- **Telithromycin.**

- These bind to the 50S ribosomal subunit and inhibit protein synthesis.
- Erythromycin is active against Gram-positive bacteria and spirochaetes but not against most Gram-negative organisms(the same spectrum of Penicillins).
- **Azithromycin is far more active against respiratory infections due to *Haemophilus influenzae* and *E.coli.***


Erythromycin

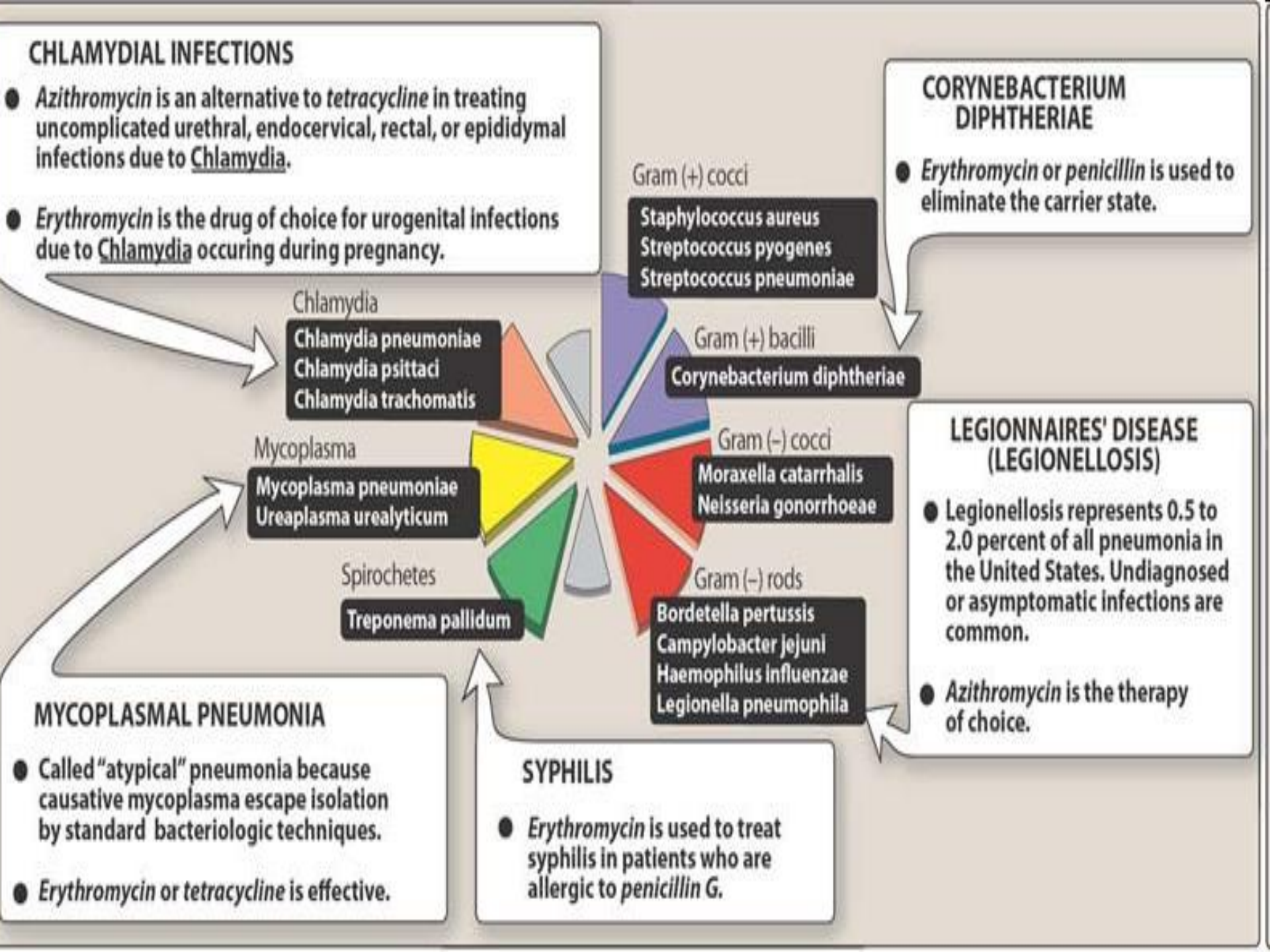

Erythromycin

CHLAMYDIAL INFECTIONS

- *Azithromycin* is an alternative to *tetracycline* in treating uncomplicated urethral, endocervical, rectal, or epididymal infections due to Chlamydia.
- *Erythromycin* is the drug of choice for urogenital infections due to Chlamydia occuring during pregnancy.

CORYNEBACTERIUM DIPHTHERIAE

- *Erythromycin* or *penicillin* is used to eliminate the carrier state.



LEGIONNAIRES' DISEASE (LEGIONELLOSIS)

- Legionellosis represents 0.5 to 2.0 percent of all pneumonia in the United States. Undiagnosed or asymptomatic infections are common.
- *Azithromycin* is the therapy of choice.

MYCOPLASMAL PNEUMONIA

- Called "atypical" pneumonia because causative mycoplasma escape isolation by standard bacteriologic techniques.
- *Erythromycin* or *tetracycline* is effective.

SYPHILIS

- *Erythromycin* is used to treat syphilis in patients who are allergic to *penicillin G.*

Clinical Uses of Macrolides

- **Because antibacterial spectrum is very similar to that of penicillins, they are considered as a very useful substitutes in penicillin-sensitive patients.**

- **Drugs of choice in corynebacterial infections (diphtheria, corynebacterial sepsis);**

Clarithromycin

- **Clarithromycin is effective against *Mycobacterium avium cellulare* which can cause chronic lung disease in elderly or immunologically compromised individuals.**

- **Clarithromycin is an aadjuvant in the treatment of peptic ulcer to eradicate *H. pylori* (1 tablet for 14 days).**

Azithromycin

- Penetrates well into most tissues (except cerebrospinal fluid), with tissue concentrations exceeding serum concentrations by 10- to 100-fold.
- Short treatment course, 1 tablet for 5 days.
- Slowly released from tissues (tissue half-life of 2–4 days) to produce an elimination half-life approaching 3 days.
- Azithromtcin is the drug of choice in respiratory(Community Aquired Pneumonia), neonatal, ocular, or genital chlamydial infections because the spectrum of activity includes pneumococcus, mycoplasma, and legionella.
- Azithromycin shows particularly good activity against chlamydial urethritis.

Side Effects of Macrolides

- **Macrolides are administered orally, although they can be given parenterally.**

- **Gastrointestinal disturbances are common side effects, but not serious. The newer agents seem to have less GI effects.**
- **Skin rashes, and fever.**
- **Transient hearing disturbances have been associated with erythromycin, especially at high dosages.**

- **Cholestatic jaundice especially with the estolate form of erythromycin**

DRUG INTERACTIONS

- Erythromycin, clarithromycin- inhibit CYP3A4. may increase concentrations of:

Theophylline	Digoxin, Disopyramide
Carbamazepine	Valproic acid
Cyclosporine	Terfenadine, Astemizole
Phenytoin	Cisapride
Warfarin	Ergot alkaloids

- Azithromycin - no drug interactions