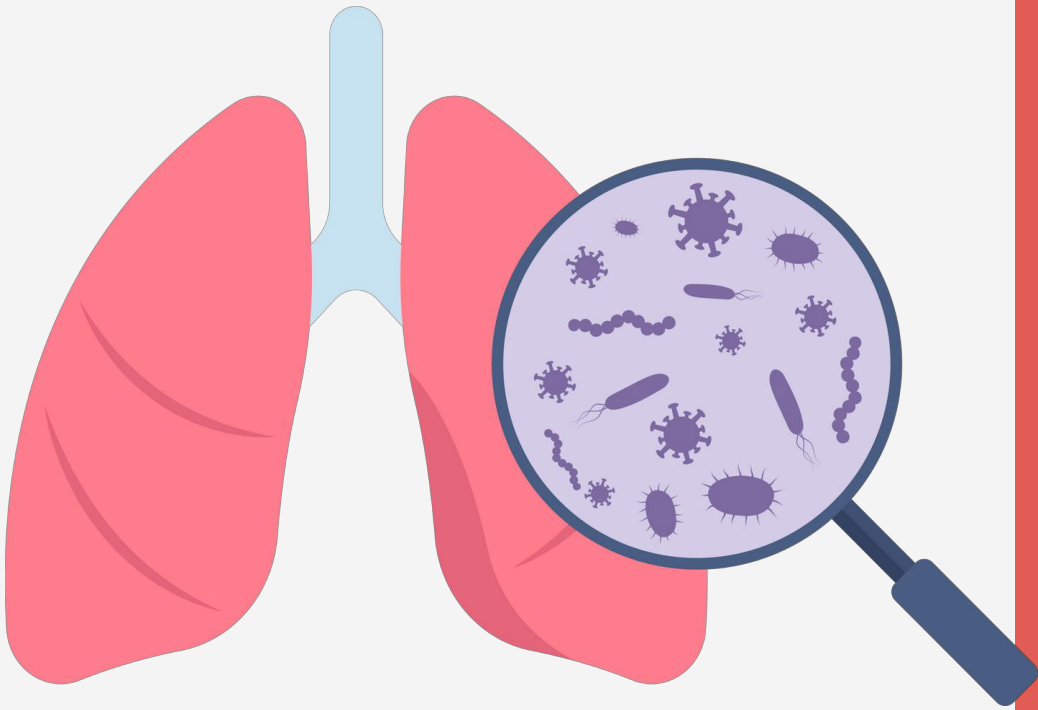
PHARMACOLOGY 201 | DR. MORA

Pulmonary System

Pulmonary Infections Antibiosis



Learning Objectives

By the end of this lecture, students should be able to:

1. Classify the major drug classes used to treat pulmonary infections, including beta-lactams, macrolides, fluoroquinolones, aminoglycosides, antifungals, antivirals, and anti-TB agents.
2. Describe the mechanism of action of each drug class and its effect on bacterial, viral, or fungal pathogens.
3. Identify the first-line treatments for community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), tuberculosis (TB), and opportunistic infections in immunocompromised patients.
4. Compare and contrast the spectrum of activity for major antimicrobial agents, including their efficacy against Gram-positive, Gram-negative, atypical, and anaerobic pathogens.
5. Explain the indications for each drug class, including patient populations, disease severity, and resistance considerations.

Learning Objectives

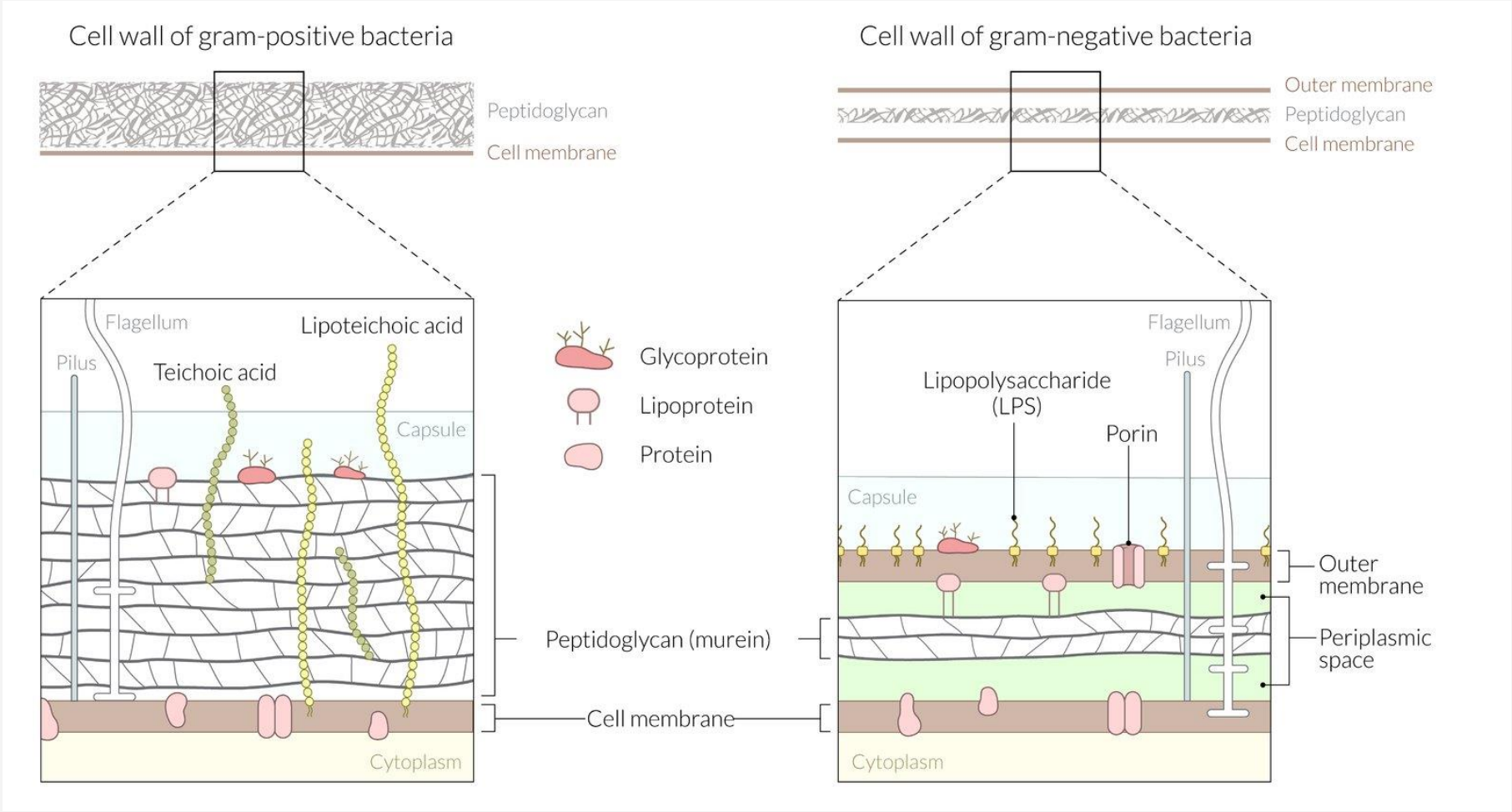
By the end of this lecture, students should be able to:

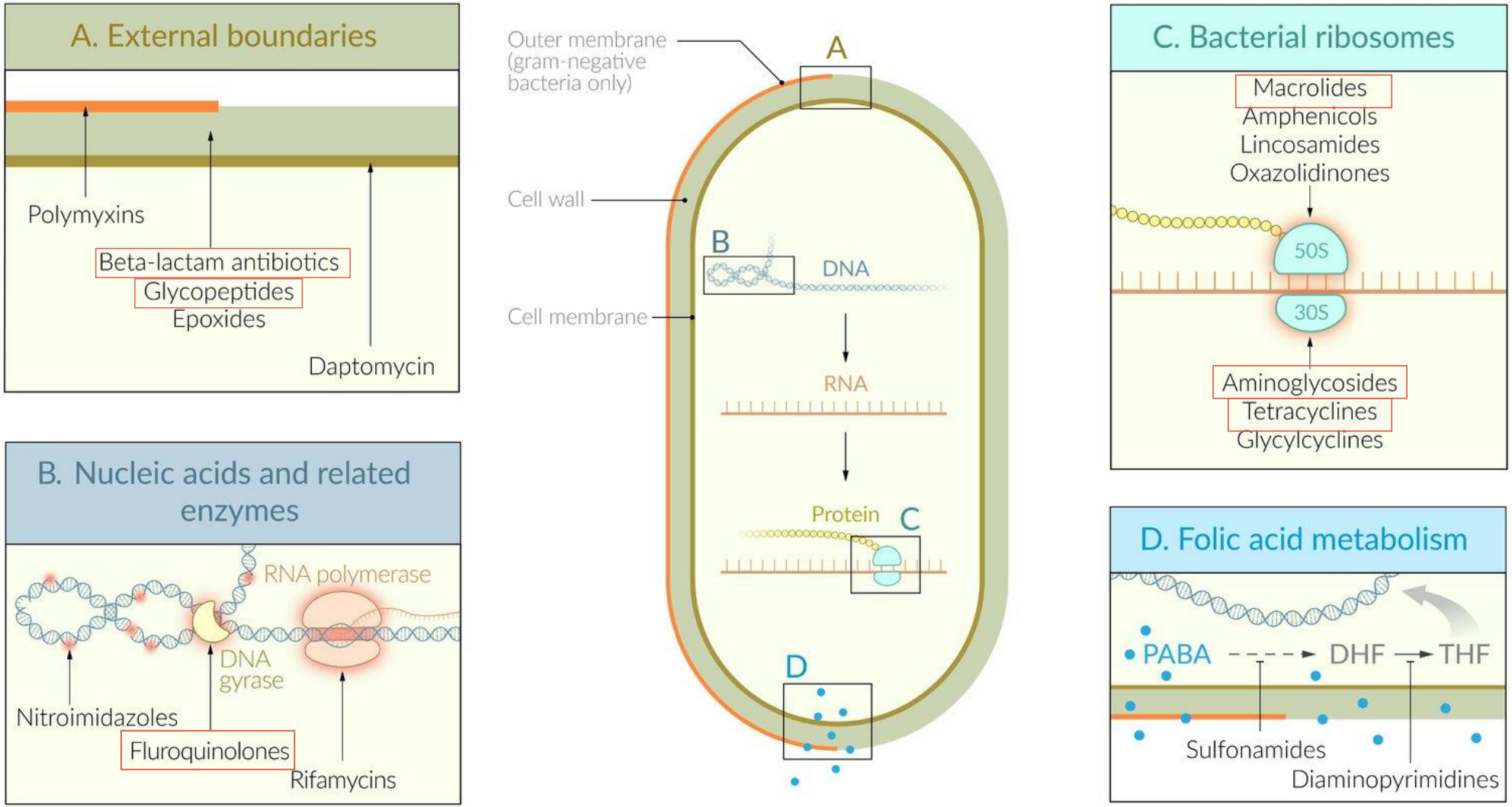
6. Recognize the most common adverse effects associated with pulmonary infection treatments, such as QT prolongation (macrolides, fluoroquinolones), nephrotoxicity (aminoglycosides), and hepatotoxicity (TB medications, antifungals).
7. Evaluate potential contraindications and drug interactions, including renal and hepatic impairment, pregnancy considerations, and QT-prolonging agents.
8. Apply knowledge of empiric and targeted therapy selection in clinical scenarios, ensuring appropriate use of narrow vs. broad-spectrum antibiotics.
9. Discuss the rationale for antimicrobial stewardship, including strategies to minimize resistance, avoid unnecessary antibiotic use, and optimize patient outcomes.
10. Interpret case-based scenarios to select appropriate pharmacologic treatment based on clinical presentation, risk factors, and local resistance patterns.

Overview

- **Drug Classes**: Antibiotics, antifungals, antivirals, and anti-TB agents.
- **MoA**: How these drugs work at the molecular and cellular levels.
- **Indications**: When & why specific drugs are used for PNA & resp infxn
- **Adverse Effects & CI**: Key side effects and safety considerations.
- **Empiric vs. Targeted Therapy**: Broad-spectrum v. pathogen-specific tx

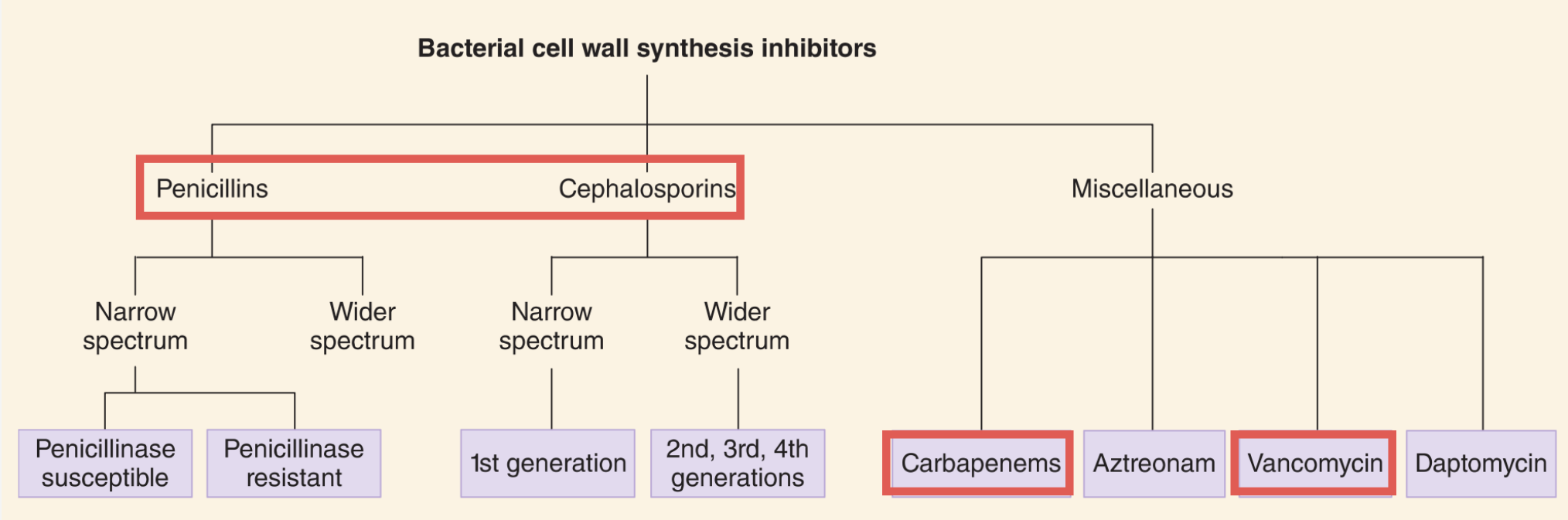
Overview


Cell wall of gram-positive bacteria
Peptidoglycan
Cell membrane
Flagellum
Pilus
Teichoic acid
Lipoteichoic acid
Capsule
Cytoplasm
Glycoprotein
Lipoprotein
Protein
Peptidoglycan (murein)
Cell membrane
Cell wall of gram-negative bacteria
Outer membrane
Peptidoglycan
Cell membrane
Flagellum
Pilus
Lipopolysaccharide (LPS)
Porin
Capsule
Outer membrane
Periplasmic space
Cytoplasm


A. External boundaries
Polymyxins
Beta-lactam antibiotics
Glycopeptides
Epoxides
Daptomycin
B. Nucleic acids and related enzymes
RNA polymerase
DNA gyrase
Nitroimidazoles
Fluroquinolones
Rifamycins
Outer membrane (gram-negative bacteria only)
Cell wall
Cell membrane
A
B
DNA
RNA
Protein
C
D
C. Bacterial ribosomes
Macrolides
Amphenicols
Lincosamides
Oxazolidinones
50S
30S
Aminoglycosides
Tetracyclines
Glycylcyclines
D. Folic acid metabolism
PABA
DHF
THF
Sulfonamides
Diaminopyrimidines

Cell Wall Inhibitors

Cell Wall Inhibitors



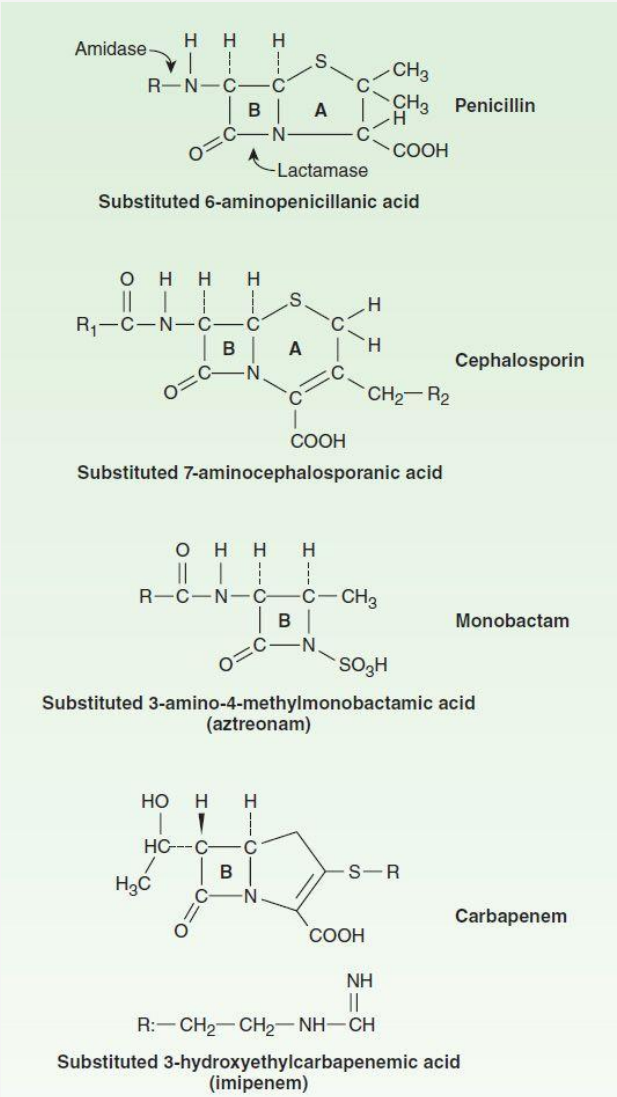
Beta-Lactams (Penicillins)

Beta-Lactams (Penicillins)

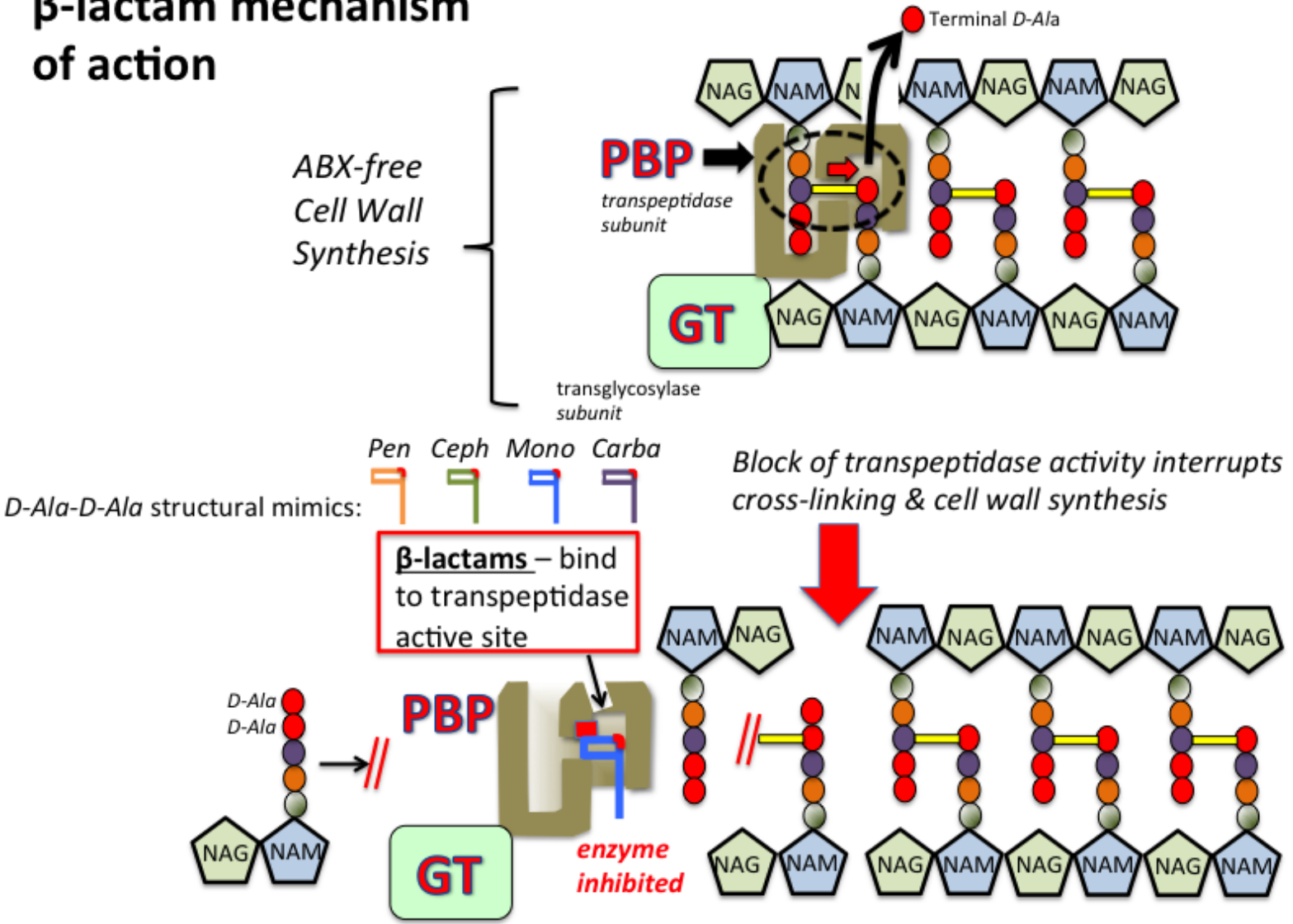
Examples: Penicillin, Nafcillin, Ampicillin, Piperacillin

Mechanism of Action

- Inhibits bacterial cell wall synthesis
    1. **Bind to PBPs** (penicillin-binding proteins) in bacterial membrane
    2. **Inhibit transpeptidation**, preventing cross-linking of peptidoglycan
- Bactericidal



β-lactam mechanism of action



Beta-Lactams (Penicillins)

Examples: Penicillin, Nafcillin, Ampicillin, Piperacillin

Indications

- Penicillin – Pen G (IM, IV), Pen VK (PO)
  - Treponema pallidum (syphilis), clostridium perfringens, Neisseria, Pasteurella
  - Strep infections (Group A Strep, S. pneumoniae*)
  - Avoid in staph*
- Anti-staphylococcal penicillin – Nafcillin (IV), dicloxacillin (PO), methicillin (PO), oxacillin (PO)
  - Methicillin sensitive staph aureus (MSSA), coagulase negative staph (CoNS*)
  - Strep species

* May have resistance

Beta-Lactams (Penicillins)

Examples: Penicillin, Nafcillin, Ampicillin, Piperacillin

Indications

- Aminopenicillins – Ampicillin (IV) and amoxicillin (PO)
  - Listeria monocytogenes
  - Beta-lactamase added to expand Staph activity
    - Clavulanic acid (Amoxicillin-Clavulanic acid)
    - Sulbactam (Ampicillin-Sulbactam)
  - Gram negative rods (E. coli, H. flu, M. catarrhalis), gut anaerobes
- Antipseudomonal – Piperacillin (IV)
  - Given with beta-lactamase inhibitor (Piperacillin-Tazobactam)
  - Broadest spectrum penicillin
  - Broad coverage against GPs, enteric GNRs, gut anaerobes, and Pseudomonas

Beta-Lactams (Penicillins)

Examples: Penicillin, Nafcillin, Ampicillin, Piperacillin

Adverse Effects

- Hypersensitivity reactions
- Jarisch–Herxheimer reaction (syphilis treatment)

Contraindications

- Penicillin allergy
- Severe renal impairment (particularly methicillin)

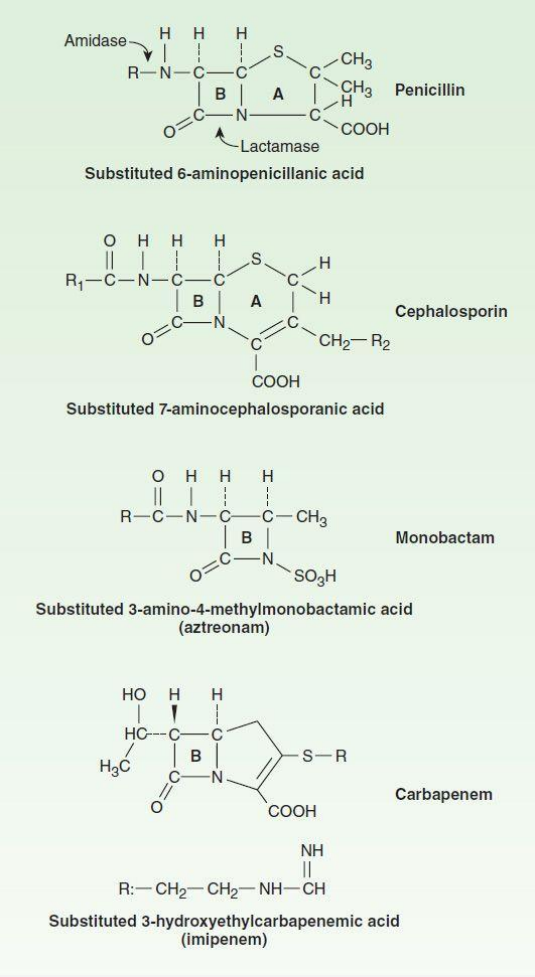
Beta-Lactams (Cephalosporins)

Beta-Lactams (Cephalosporins)

Examples: Cefazolin, Cefpodoxime, Ceftriaxone, Cefepime, Ceftazidim

Mechanism of Action

- Inhibits bacterial cell wall synthesis
- Disrupts peptidoglycan cross-linking
- Bactericidal



Beta-Lactams (Cephalosporins)

Examples: Cefazolin, Cefpodoxime, Ceftriaxone, Cefepime, Ceftazidime

Indications

- 1st generation – cefazolin (IV) and cephalexin (PO)
  - Good GP coverage (MSSA, some CoNS species, Strep species)
  - Avoid empiric staph coverage given prevalence or resistance
  - Limited GN coverage
- 2nd generation – cefuroxime (PO, IV), cefaclor (PO), cefofetan (IV), cefoxitin (IV)
  - GN coverage (H. flu, Klebsiella, Moraxella)
  - GP coverage as above

Beta-Lactams (Cephalosporins)

Examples: Cefazolin, Cefpodoxime, Ceftriaxone, Cefepime, Ceftazidime

Indications

- 3rd generation – Ceftriaxone (IV), cefotaxime (IV), cefdinir (PO) , cefpodoxime (PO)
  - Good Strep and GNR coverage
  - No anaerobic coverage
- 3rd generation – Ceftazidime (IV)
  - Limited GP coverage (no Staph)
  - Activity against PsA
- 4th generation – cefepime (IV)
  - PsA

Beta-Lactams (Cephalosporins)

Examples: Cefazolin, Cefpodoxime, Ceftriaxone, Cefepime, Ceftazidime

Adverse Effects

- Hypersensitivity

Contraindications

- Cephalosporin allergy

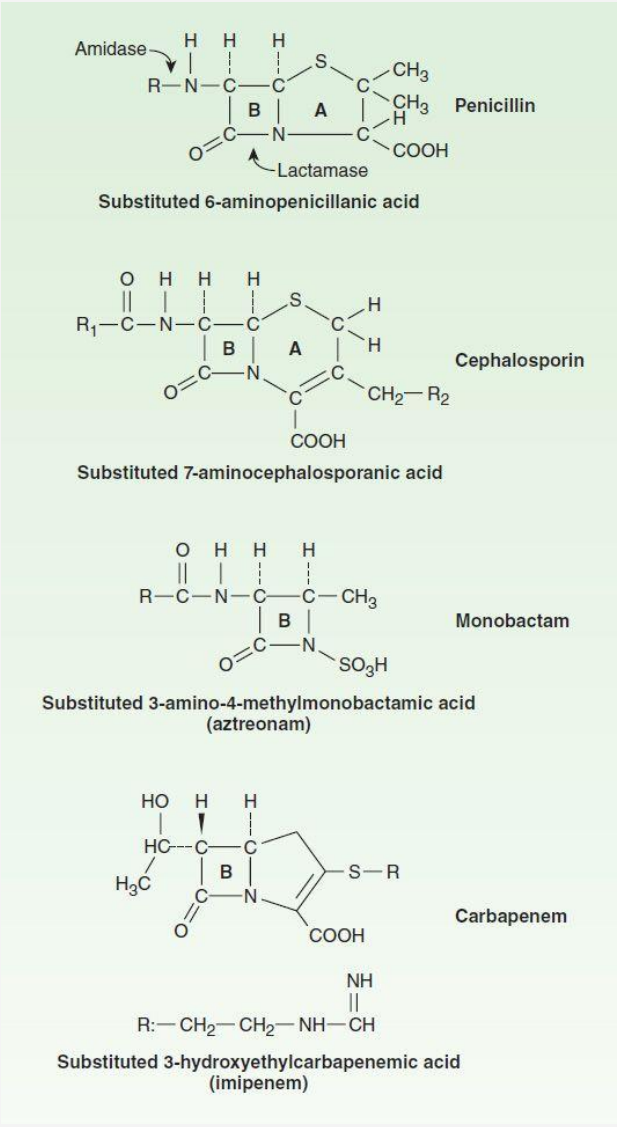
Carbapenems

Carbapenems

Examples: Meropenem, Imipenem, Ertapenem

Mechanism of Action

- Inhibits bacterial cell wall synthesis
- Broad-spectrum beta-lactam activity
- Bactericidal



Carbapenems

Examples: Meropenem, Imipenem, Ertapenem

Indications

- Broadest antibiotic class with GP, GN, and anaerobic coverage
- Ertapenem – No PsA coverage
  - First line agent for ESBL E. coli infection
- Meropenem/ imipenem/ doripenem –Similar spectrum as ertapenem
  - Additional PsA coverage

Carbapenems

Examples: Meropenem, Imipenem, Ertapenem

Adverse Effects

- Seizures
- Hypersensitivity reactions

Contraindications

- Seizure disorders

Glycopeptide

Vancomycin

Mechanism of Action

- Binds peptidoglycan precursors, disrupting polymerization and cross-linking required for maintenance of cell wall integrity
- Bactericidal

Glycopeptide

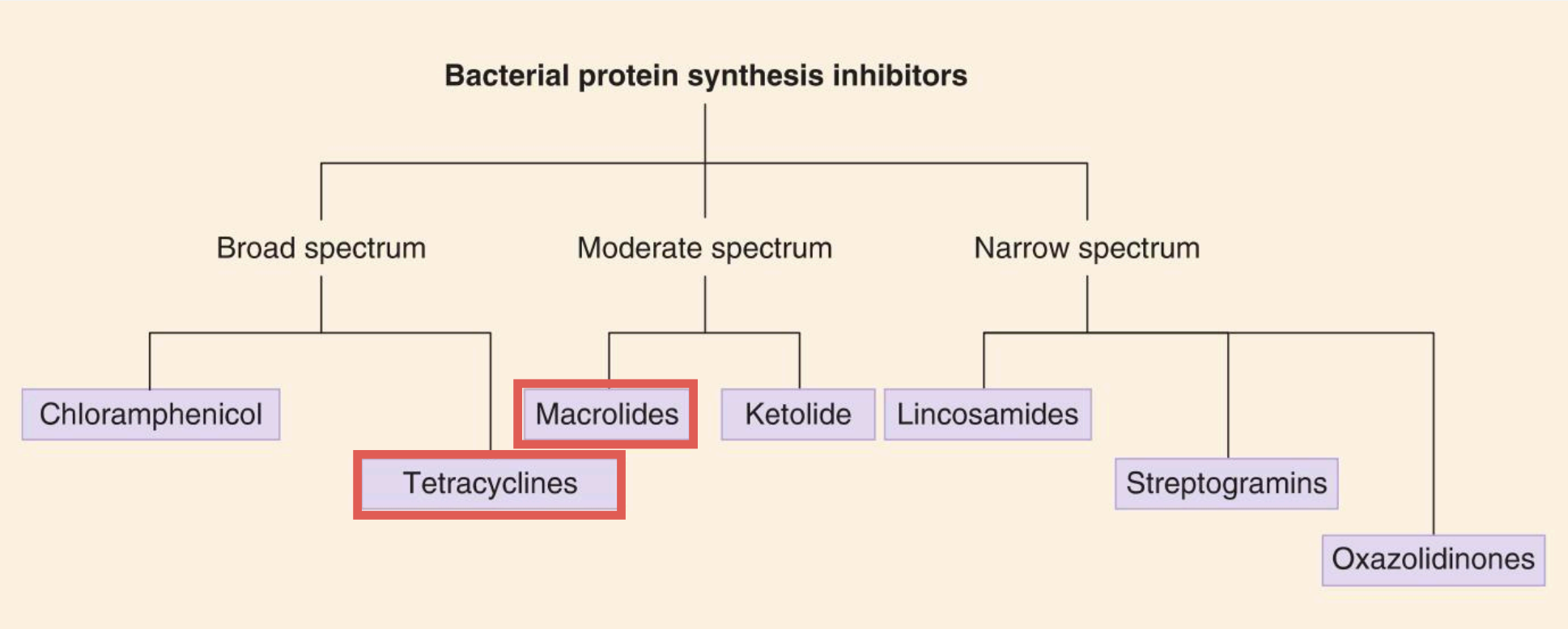
Vancomycin

Indications

- Activity against aerobic and anaerobic GP (MRSA, MSSA), Enterococcus spp., C difficile

Protein Synthesis Inhibitors

Protein Synthesis Inhibitors



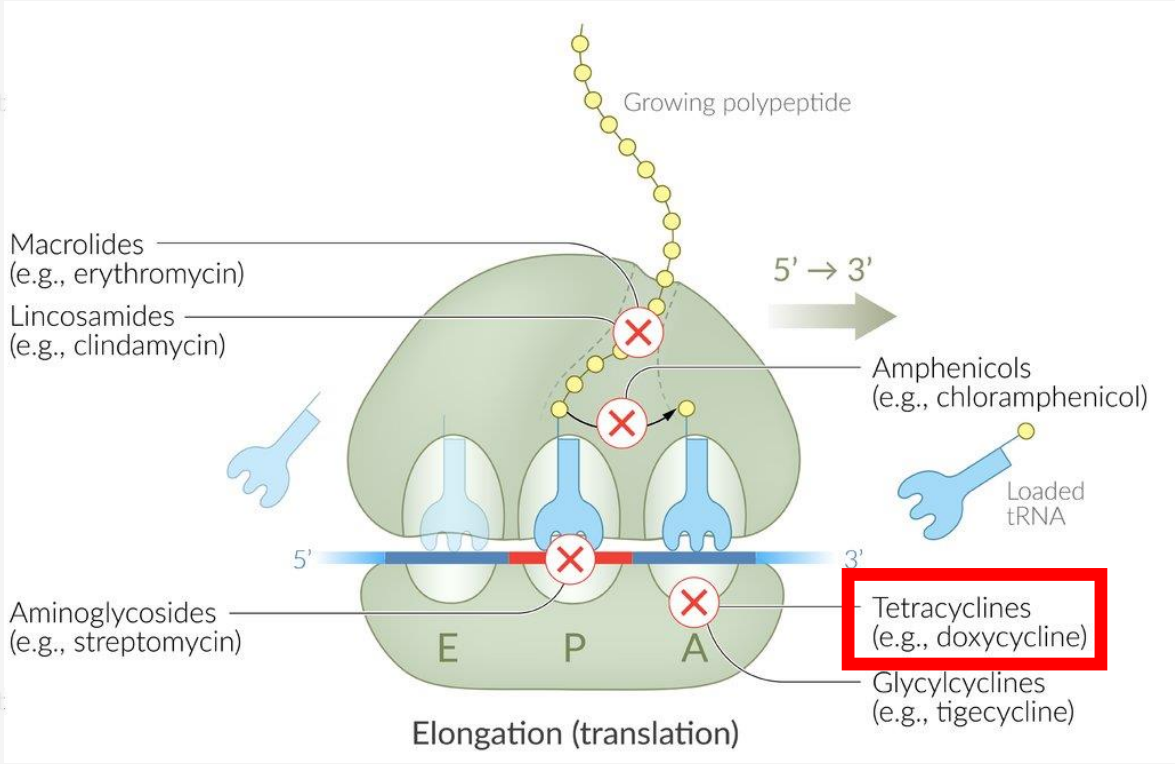
Tetracyclines

Tetracyclines

Examples: Doxycycline , Minocycline

Mechanism of Action

- Binds 30S ribosomal subunit
- Prevent tRNA-AA binding to acceptor site on ribosome mRNA complex
- Inhibits bacterial protein synthesis
- Bacteriostatic



Tetracyclines

Examples: Doxycycline , Minocycline

Indications

- Gram-positive
- Gram-negative
- Protozoa, spirochetes, mycobacteria, atypical species
- Atypical pneumonia
- COPD exacerbations
- Lyme disease

Tetracyclines

Examples: Doxycycline , Minocycline

Adverse Effects

- Photosensitivity
- Esophageal irritation
- Tooth discoloration

Contraindications

- Pregnancy (contraindicated in children <8 years)

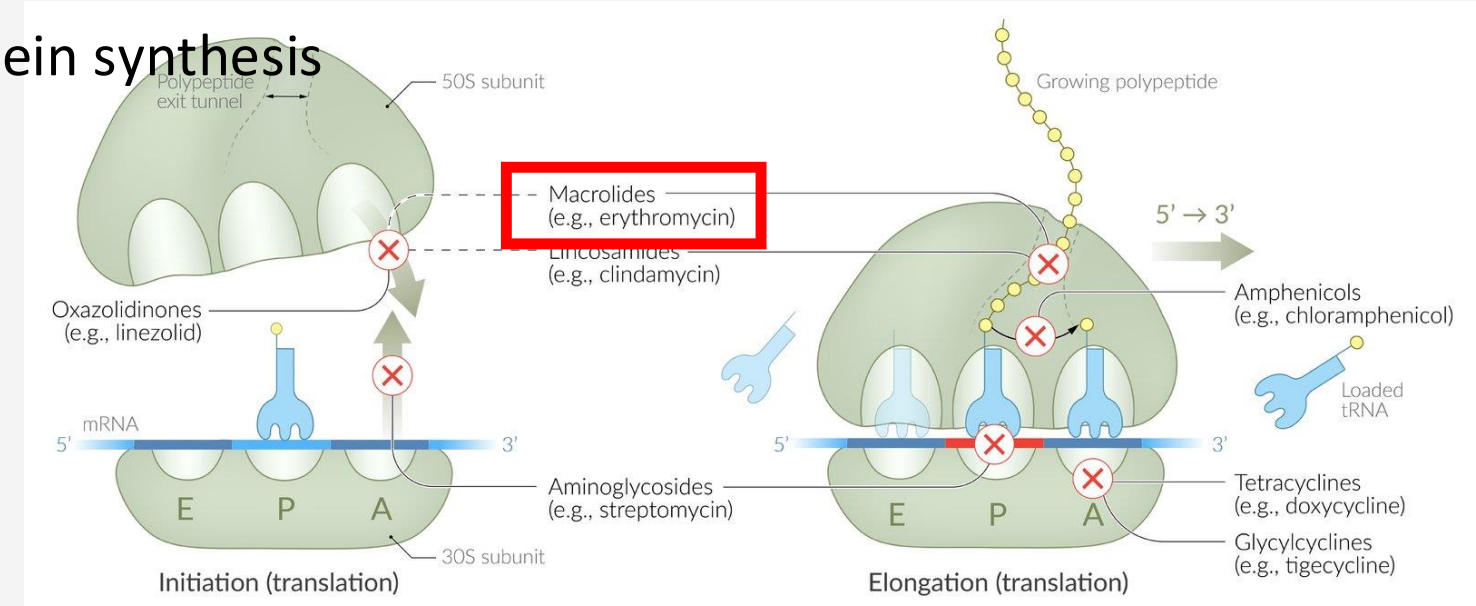
Macrolides

Macrolides

Examples: Azithromycin , Clarithromycin , Erythromycin

Mechanism of Action

- Bind 50S ribosomal subunit
- Block transpeptidation
- Inhibit bacterial protein synthesis
- Bacteriostatic



Macrolides

Examples: Azithromycin , Clarithromycin , Erythromycin

Indications

- Atypical pneumonia (Mycoplasma, Legionella, Chlamydia, Haemophilus influenzae)
- Pertussis

Macrolides

Examples: Azithromycin , Clarithromycin , Erythromycin

Adverse Effects

- QT prolongation
- GI upset
- Cholestatic hepatitis

Contraindications

- QT prolongation
- Hepatic dysfunction

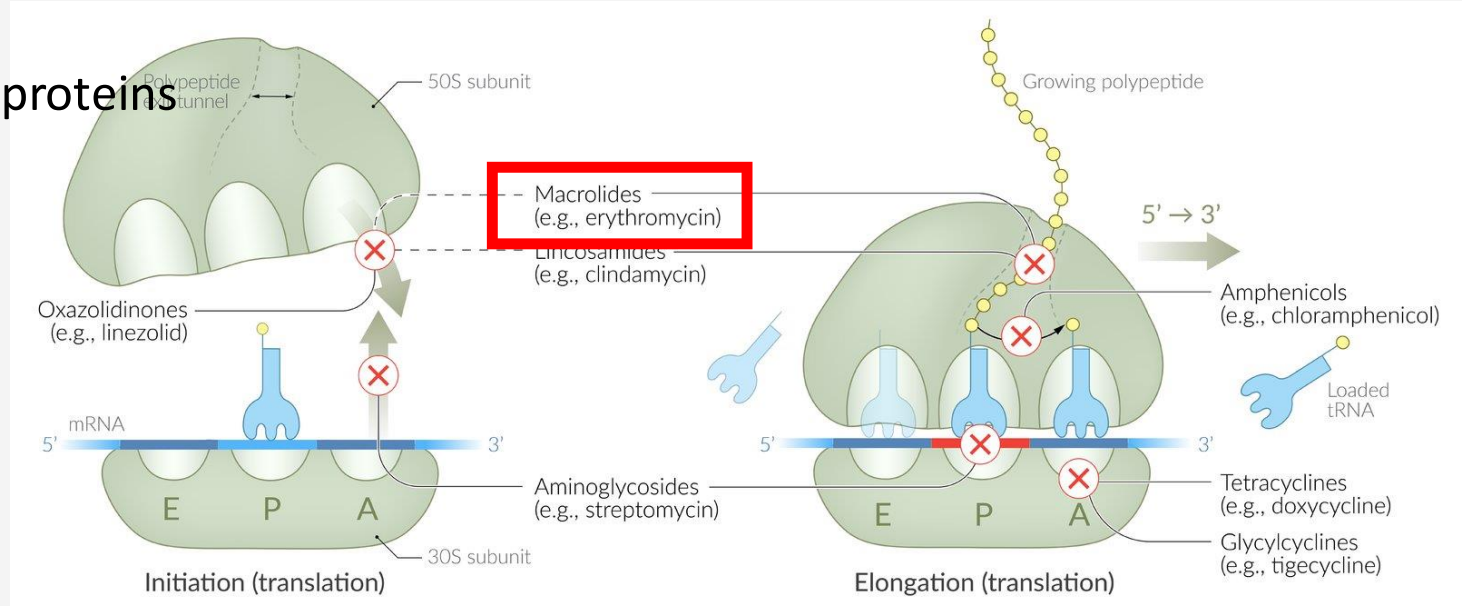
Aminoglycosides

Aminoglycosides

Examples: Gentamicin , Tobramycin , Amikacin

Mechanism of Action

- Binds 30S ribosomal subunit
- Misreading of mRNA & incorporate incorrect amino acids
- Results in nonfunctional proteins
- Inhibit translocation
- Bactericidal



Aminoglycosides

Examples: Gentamicin, Tobramycin, Amikacin

Indications

- Majority of aerobic GNR (Pseudomonas, Klebsiella pneumoniae, Enterobacter sp.)
- Severe Gram-negative pneumonia
- Pseudomonas infections

Aminoglycosides

Examples: Gentamicin, Tobramycin, Amikacin

Adverse Effects

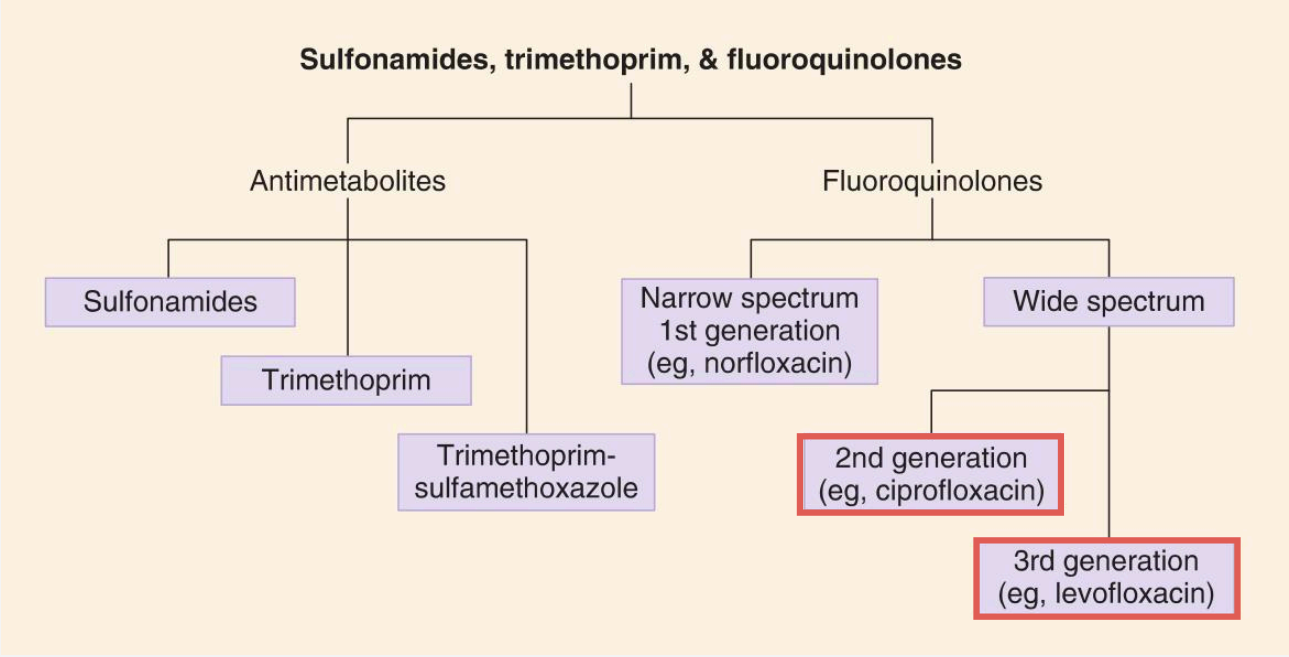
- Nephrotoxicity
- Ototoxicity
- Neuromuscular blockade

Contraindications

- Renal failure
- Myasthenia gravis

Fluoroquinolones

Fluoroquinolones



Fluoroquinolones

Examples: Levofloxacin , Moxifloxacin , Ciprofloxacin

Mechanism of Action

- Inhibits DNA Gyrase (Topo II) → Blocks supercoil relaxation (GN)
- Inhibits Topoisomerase IV → Blocks chromosomal DNA separation during cell division (GP)
- Bactericidal and bacteriostatic

Fluoroquinolones

Examples: Levofloxacin , Moxifloxacin , Ciprofloxacin

Indications

- Ciprofloxacin (urinary) –
  - Good GNR coverage in GU and GI tract
  - However, increasing E. coli resistance
  - No Staph coverage, poor Strep coverage -> no empiric coverage
- Levofloxacin (urinary/respiratory) –
  - Improved GP coverage (notably, MSSA, some CoNS species, and S. pneumoniae, S. viridans, and E. faecalis)
  - Good empiric coverage for low risk respiratory and GU infections.
  - It also covers some oral anaerobes such as Peptostreptococcus.
- Moxifloxacin (respiratory) –
  - Limited anti-PsA activity and poor renal penetration.
  - FQ with broadest anaerobic coverage (most reliable FQ for GI infections or aspiration pneumonia)

Fluoroquinolones

Examples: Levofloxacin , Moxifloxacin , Ciprofloxacin

Adverse Effects

- QT prolongation
- Tendon rupture
- CNS toxicity

Contraindications

- QT prolongation
- Tendon disorders
- Myasthenia gravis

Anti-MRSA Agents

Anti-MRSA Agents

Examples: Vancomycin , Linezolid, Daptomycin* (not for PNA)

Mechanism of Action

- Inhibits bacterial cell wall synthesis (Vancomycin)
- Inhibits protein synthesis (Linezolid)

Anti-MRSA Agents

Examples: Vancomycin , Linezolid, Daptomycin* (not for PNA)

Indications

- MRSA pneumonia
- HAP
- VAP

Anti-MRSA Agents

Examples: Vancomycin , Linezolid, Daptomycin* (not for PNA)

Adverse Effects

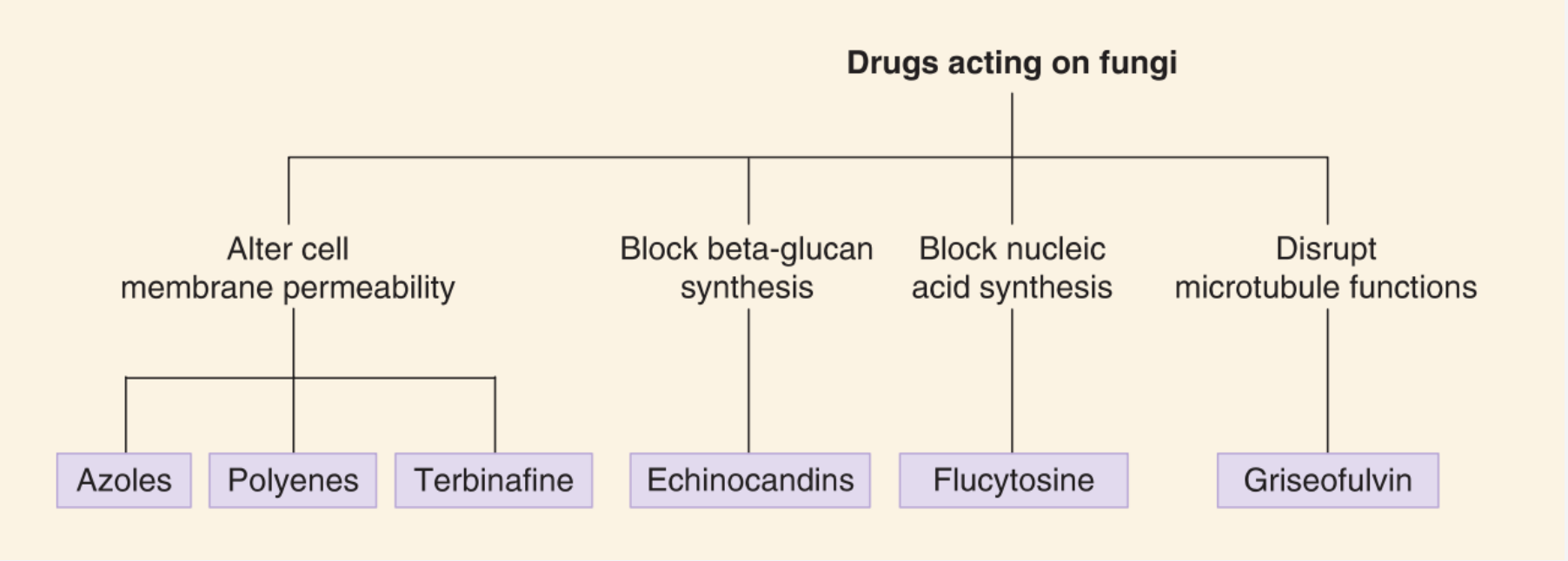
- Nephrotoxicity (Vancomycin)
- Red man syndrome (Vancomycin)
- Bone marrow suppression (Linezolid)

Contraindications

- Vancomycin allergy
- Severe renal failure

Antifungals

Antifungal


Drugs acting on fungi
Alter cell membrane permeability
Block beta-glucan synthesis
Block nucleic acid synthesis
Disrupt microtubule functions
Azoles
Polyenes
Terbinafine
Echinocandins
Flucytosine
Griseofulvin

Antifungals

Examples: Fluconazole, Voriconazole , Amphotericin B

Mechanism of Action

- Inhibits fungal ergosterol synthesis (Azoles)
- Binds ergosterol (Amphotericin B)
- Fungal cell membrane disruption

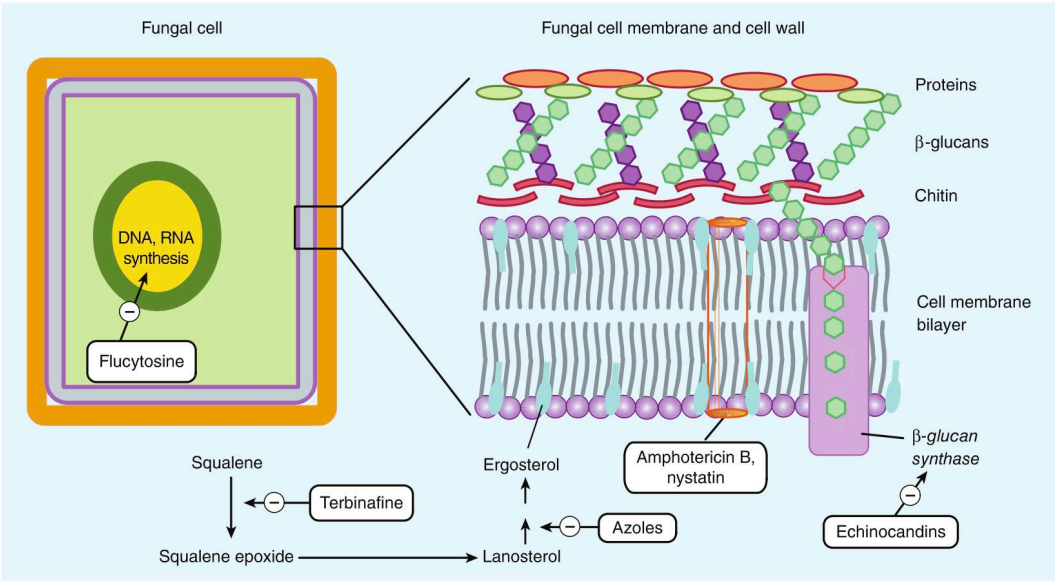


FIGURE 48–1 Targets of antifungal drugs. Except for flucytosine (and griseofulvin, not shown), all available antifungal drugs target the fungal cell membrane or cell wall. (Reproduced with permission from Katzung BG, Vanderah TW: *Basic & Clinical Pharmacology,* 15th ed. New York, NY: McGraw Hill; 2021.)

Antifungals

Examples: Fluconazole, Voriconazole , Amphotericin B

Indications

- Fungal pneumonia
- (Aspergillus, Histoplasma, PCP)

Antifungals

Examples: Fluconazole, Voriconazole , Amphotericin B

Adverse Effects

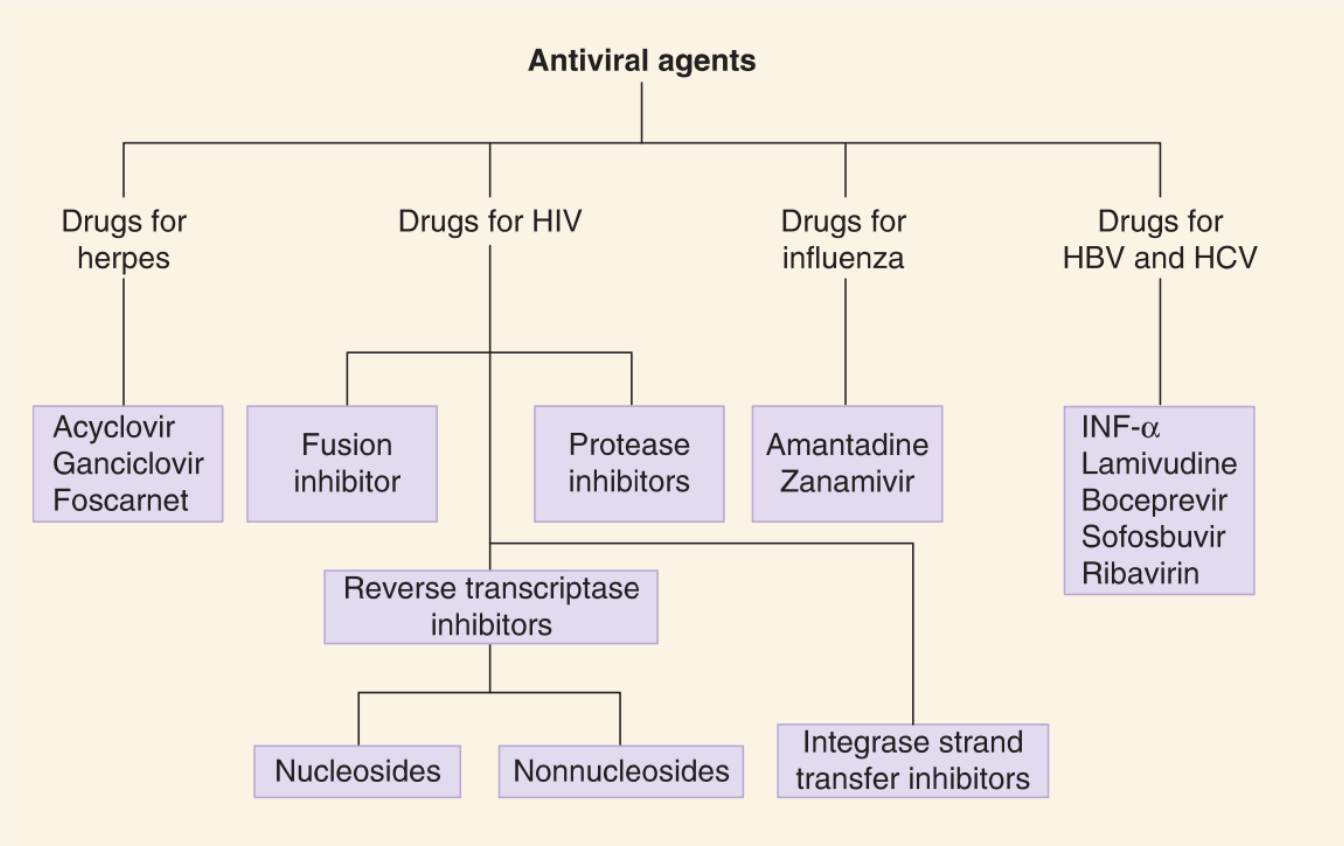
- Hepatotoxicity (Azoles)
- Nephrotoxicity (Amphotericin B)
- Electrolyte disturbances

Contraindications

- Liver failure (Azoles)
- Renal impairment (Amphotericin B)

Anti-Virals

Anti-Virals


Antiviral agents
Drugs for herpes
Drugs for HIV
Drugs for influenza
Drugs for HBV and HCV
Acyclovir
Ganciclovir
Foscarnet
Fusion inhibitor
Protease inhibitors
Amantadine
Zanamivir
INF-α
Lamivudine
Boceprevir
Sofosbuvir
Ribavirin
Reverse transcriptase inhibitors
Nucleosides
Nonnucleosides
Integrase strand transfer inhibitors

Antiviral Agents

Examples: Oseltamivir , Zanamivir , Remdesivir

Mechanism of Action

- Inhibits viral neuraminidase (Oseltamivir, Zanamivir)
- Inhibits viral RNA-dependent RNA polymerase (Remdesivir)

Antiviral Agents

Examples: Oseltamivir , Zanamivir , Remdesivir

Indications

- Influenza
- COVID-19 pneumonia

Antiviral Agents

Examples: Oseltamivir , Zanamivir , Remdesivir

Adverse Effects

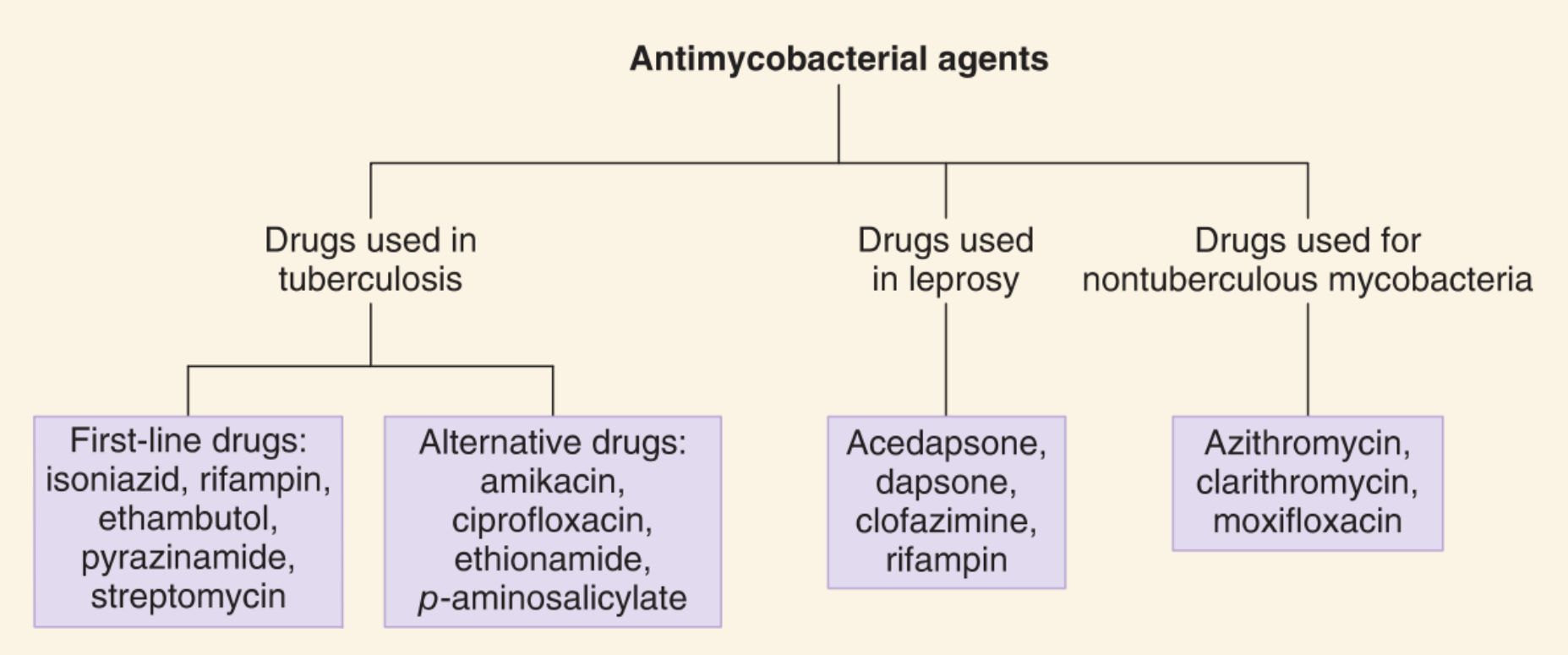
- Bronchospasm (Zanamivir)
- GI upset, Headache

Contraindications

- Severe asthma (Zanamivir)
- Hepatic impairment

Tuberculosis Medications

Antimycobacterial

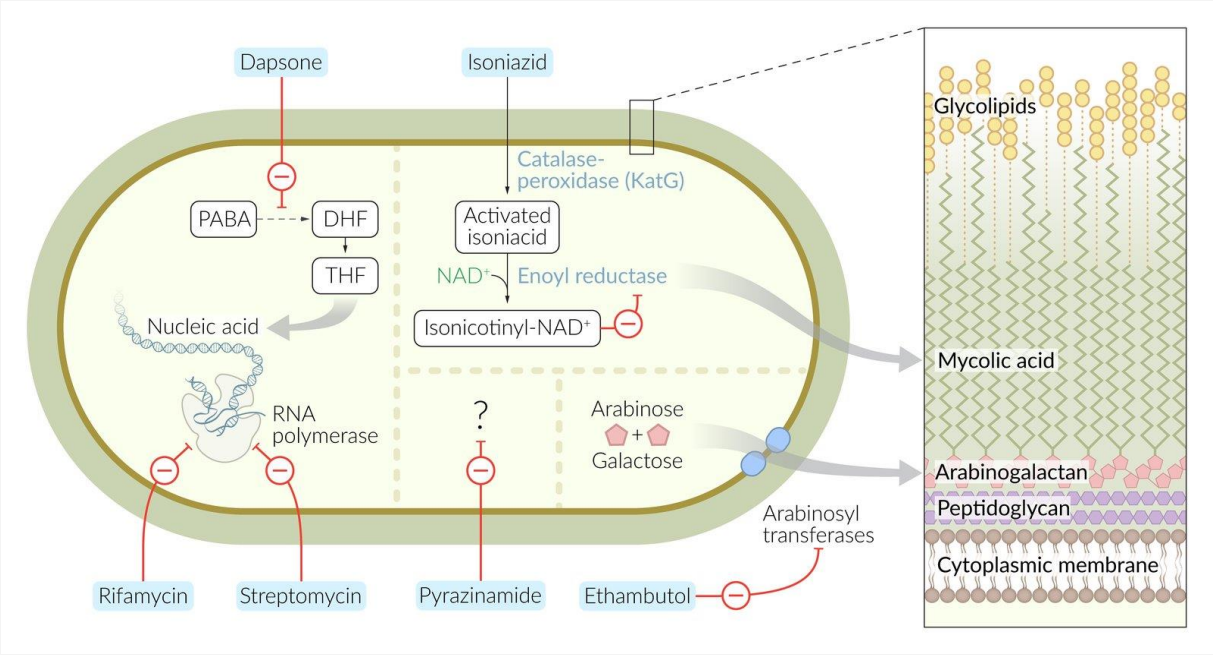


Anti-TB Agents

Examples: Isoniazid , Rifampin , Pyrazinamide , Ethambutol

Mechanism of Action

- Inhibits RNA polymerase (Rifampin)
- Inhibits mycolic acid synthesis (Isoniazid)
- Mechanism unknown (Pyrazinamide)
- Disrupts bacterial cell wall (Ethambutol)



Anti-TB Agents

Examples: Isoniazid , Rifampin , Pyrazinamide , Ethambutol

Indications

- Tuberculosis (Active & Latent TB)
  - Tuberculosis infection (newer term for latent tuberculosis; "TBI")
  - Tuberculosis disease (newer term for active tuberculosis)
  - Prior to starting treatment for TB infection, we ensure that there are no signs or symptoms of TB disease based on history (eg, fever, cough, weight loss, night sweats) and physical examination; however, over half of people with TB disease do not have symptoms, so it is also important to obtain a chest radiograph to rule out asymptomatic disease. This evaluation is important to avoid undertreatment of TB disease, which can lead to emergence of drug resistance.
  - Regimens for treatment of TBI are associated with hepatotoxicity; the risk of hepatotoxicity is greatest with INH and less so for the rifamycin-based regimens.
  - Peripheral neuropathy occurs in up to 2 percent of patients taking INH due to interference with metabolism of pyridoxine and can be prevented with pyridoxine supplementation [26]. For individuals on an TBI regimen containing INH with risk factors for INH neurotoxicity (diabetes, uremia, alcoholism, malnutrition, HIV infection, pregnancy, seizure disorder), we coadminister pyridoxine (25 to 50 mg with each dose of INH)

Regimens for treatment of tuberculosis infection (latent tuberculosis) in nonpregnant adults without HIV[*]

Regimen	Dosing	Clinical considerations
Rifamycin-based regimens[¶] (preferred)		
Rifampin (daily for 4 months; 4R)	▪ Rifampin 10 mg/kg (600 mg maximum) orally daily for 4 months	Better completion rates and less toxicity (relative to isoniazid monotherapy)
Isoniazid[Δ] and rifampin (daily for 3 months; 3HR)	▪ Isoniazid 5 mg/kg (300 mg maximum) orally daily for 3 months ▪ Rifampin 10 mg/kg (600 mg maximum) orally daily for 3 months	Better completion rates and less toxicity (relative to isoniazid monotherapy)
Isoniazid[Δ] and rifapentine (weekly for 3 months; 3HP)	▪ Isoniazid (orally once weekly for 3 months; direct observation is preferred): • 15 mg/kg, rounded up to the nearest 50 or 100 mg; 900 mg maximum ▪ Rifapentine (orally once weekly for 3 months; direct observation is preferred): • 10 to 14 kg: 300 mg • 14.1 to 25.0 kg: 450 mg • 25.1 to 32.0 kg: 600 mg • 32.1 to 49.9 kg: 750 mg • ≥50 kg: 900 mg maximum	Better completion rates (relative to isoniazid monotherapy) Important side effects of 3HP include hypersensitivity or flu-like symptoms (eg, light headedness, dizziness, headache, nausea or vomiting, syncope, rash, or angioedema). For this reason, 3HP usually is administered via directly observed therapy, to facilitate side effect review and treatment withholding if needed. Self-administration of 3HP may be acceptable for patients who can reliably take their medications on schedule and inform their providers promptly of side effects (while withholding the next dose pending provider review).
Alternative regimens		
Isoniazid[Δ]	▪ Isoniazid 5 mg/kg (300 mg maximum) orally daily for 9 months[◇] ▪ Isoniazid 5 mg/kg (300 mg maximum) orally daily for 6 months[◇] ▪ Isoniazid 15 mg/kg (900 mg maximum) orally twice weekly[§] for 9 or 6 months	Fewer drug interactions (relative to rifamycin-based regimens)
Levofloxacin[¥]	▪ Levofloxacin (orally once daily for 6 months): • <50 kg: 500 mg • ≥50 kg: 750 mg	Regimen for patients with exposure to individuals with rifampin-resistant or multidrug-resistant tuberculosis. This regimen may also be used for individuals in whom rifamycins cannot be given, as an alternative to INH monotherapy.

Treatment of drug-susceptible pulmonary tuberculosis in HIV-uninfected adults: Traditional regimen (minimum six months)

Intensive phase[*]		Continuation phase[¶]		Range of total doses (minimal duration)	Comments[Δ◇]
Drugs	**Interval and doses[§] (minimal duration)**	**Drugs**	**Interval and doses[§] (minimal duration)**		
Regimen 1					
INH RIF PZA EMB	**Daily for 8 weeks** 7 days per week for 56 doses (8 weeks), or 5 days per week for 40 doses (8 weeks)[¥]	INH RIF	7 days per week for 126 doses (18 weeks), or 5 days per week for 90 doses (18 weeks)	182 to 130 (26 weeks)	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.

Anti-TB Agents

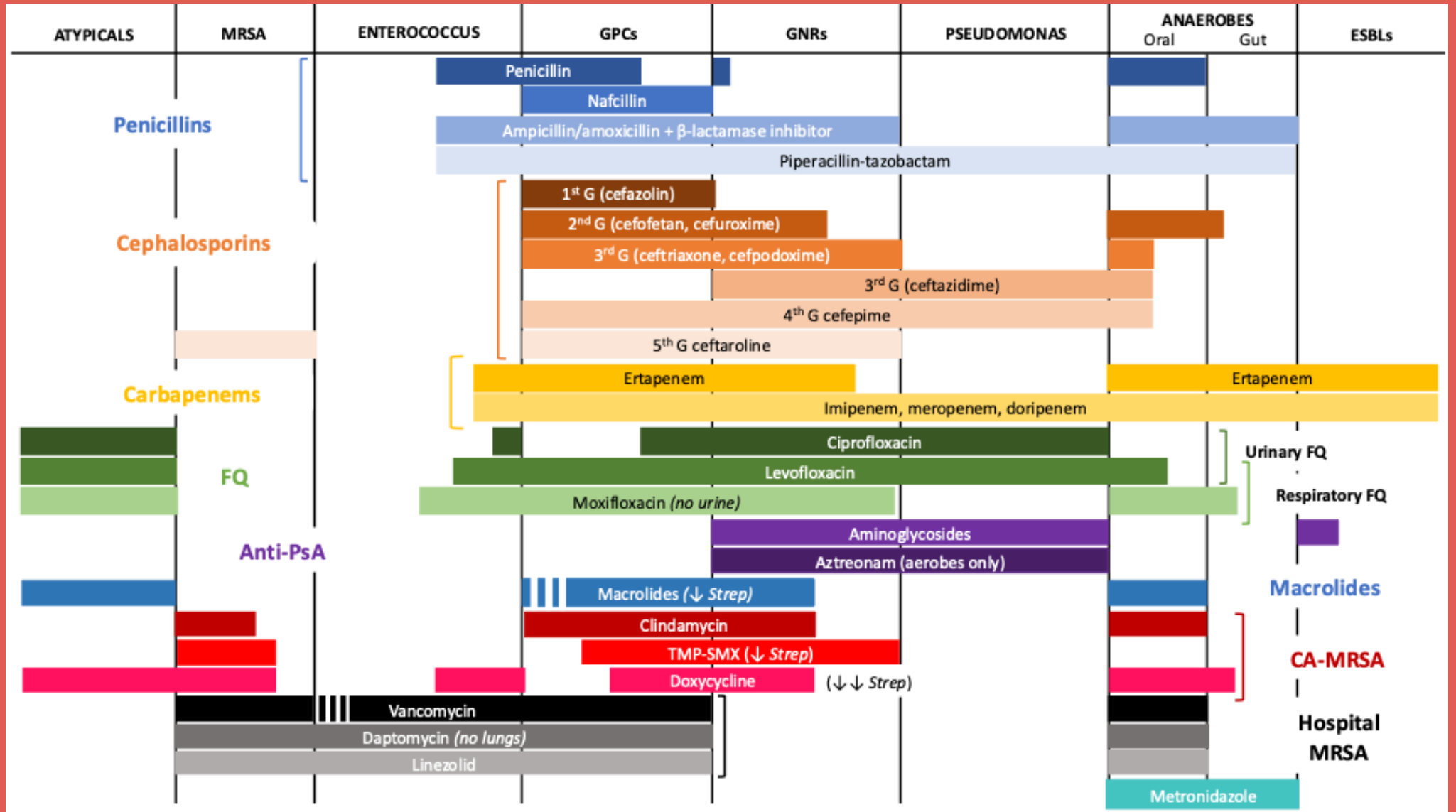
Examples: Isoniazid , Rifampin , Pyrazinamide , Ethambutol

Adverse Effects

- Hepatotoxicity (Isoniazid, Rifampin)
- Optic neuritis (Ethambutol)
- Hyperuricemia (Pyrazinamide)

Contraindications

- Liver disease (Isoniazid, Rifampin)
- Optic neuritis (Ethambutol)


ATYPICALS
MRSA
ENTEROCOCCUS
GPCs
GNRs
PSEUDOMONAS
ANAEROBES
Oral
Gut
ESBLs
Penicillins
Penicillin
Nafcillin
Ampicillin/amoxicillin + β-lactamase inhibitor
Piperacillin-tazobactam
Cephalosporins
1st G (cefazolin)
2nd G (cefofetan, cefuroxime)
3rd G (ceftriaxone, cefpodoxime)
3rd G (ceftazidime)
4th G cefepime
5th G ceftaroline
Carbapenems
Ertapenem
Ertapenem
Imipenem, meropenem, doripenem
FQ
Ciprofloxacin
Urinary FQ
Levofloxacin
Moxifloxacin (no urine)
Respiratory FQ
Anti-PsA
Aminoglycosides
Aztreonam (aerobes only)
Macrolides (↓ Strep)
Macrolides
Clindamycin
TMP-SMX (↓ Strep)
CA-MRSA
Doxycycline
(↓↓ Strep)
Vancomycin
Hospital MRSA
Daptomycin (no lungs)
Linezolid
Metronidazole

Recap

Recap

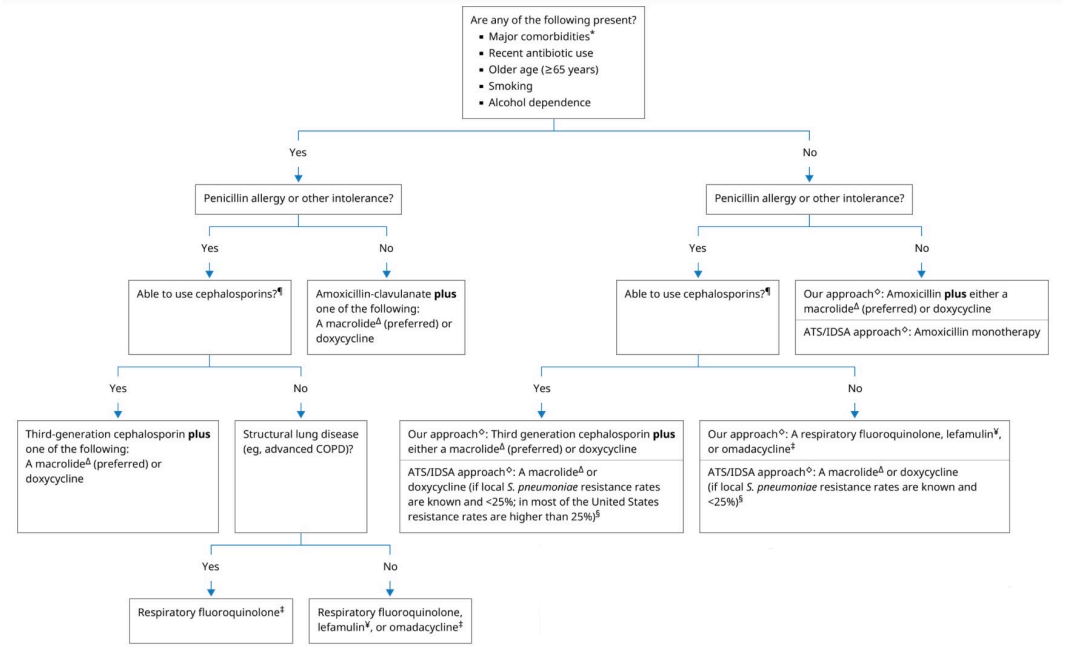
High Yield Points

- Beta-Lactams (PCNs, Cephalosporins) → First-line for most bacterial PNAs
- Macrolides (Azithromycin) or Doxycycline → Atypical pneumonia (Mycoplasma, Legionella, Chlamydia)
- FQ (Levofloxacin, Moxifloxacin) → For severe cases due to resistance risk
- HAP/VAP → Require Pseudomonal (Pip-Tazo, Cefepime) & MRSA coverage (Vancomycin or Linezolid)
- Aspiration pneumonia → Anaerobic coverage (Ampicillin-Sulbactam, Clindamycin, Metronidazole)
- TB treatment (RIPE therapy) → Prolonged therapy and close monitoring for hepatotoxicity
- PCP pneumonia (HIV, CD4 <200) → TMP-SMX; steroids if severe hypoxia
- Fungal pneumonias (Aspergillus, Cryptococcus) → Amphotericin B or Voriconazole.
- Oseltamivir (Tamiflu) →Most effective if w/in 48 hours of flu symptoms

Pneumonia Terminology & Definitions

Term	Definition
Classification by site of acquisition	
Community-acquired pneumonia (CAP)	An acute infection of the pulmonary parenchyma acquired outside of health care settings
Nosocomial pneumonia	An acute infection of the pulmonary parenchyma acquired in hospital settings, which encompasses hospital-acquired pneumonia and ventilator-associated pneumonia
Hospital-acquired pneumonia (HAP)	Pneumonia acquired ≥48 hours after hospital admission; includes both HAP and VAP
Ventilator-associated pneumonia (VAP)	Pneumonia acquired ≥48 hours after endotracheal intubation
Health care-associated pneumonia (HCAP)	Retired term, which referred to pneumonia acquired in health care facilities (eg, nursing homes, hemodialysis centers) or after recent hospitalization*
Classification by etiology	
Atypical pneumonia	Pneumonia caused by "atypical"¶ bacterial pathogens including *Legionella* spp, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Chlamydia psittaci*, and *Coxiella burnetii*
Aspiration pneumonia	Pneumonia resulting from entry of gastric or oropharyngeal fluid, which may contain bacteria and/or exogenous substances (eg, ingested food particles or liquids, mineral oil, salt or fresh water) or be of low pH, into the lower airways
Chemical pneumonitis	Aspiration of substances (eg, acidic gastric fluid) that cause an inflammatory reaction in the lower airways, independent of bacterial infection
Bacterial aspiration pneumonia	An active infection caused by inoculation of large amounts of bacteria into the lungs via orogastric contents

Treatment of Community-Acquired Pneumonia (CAP)



Antibiotic class	Drug	Oral dosing (may need adjustment for renal or hepatic dysfunction)
Penicillins	Amoxicillin	1 g three times daily
Extended-spectrum beta-lactams	Amoxicillin-clavulanate	2000 mg (extended release) twice daily
		875 mg orally twice daily
	Cefpodoxime (3rd generation)	200 mg twice daily
	Cefditoren (3rd generation)	400 mg twice daily
Macrolides	Azithromycin	500 mg on first day then 250 mg daily
	Clarithromycin	500 mg twice daily or 1g (extended release) once daily
Tetracyclines	Doxycycline	100 mg twice daily
	Omadacycline	300 mg twice daily on day 1, then 300 mg once daily
Respiratory fluoroquinolones	Levofloxacin	750 mg once daily
	Moxifloxacin	400 mg once daily
	Gemifloxacin	320 mg once daily
Pleuromutilin	Lefamulin	600 mg twice daily

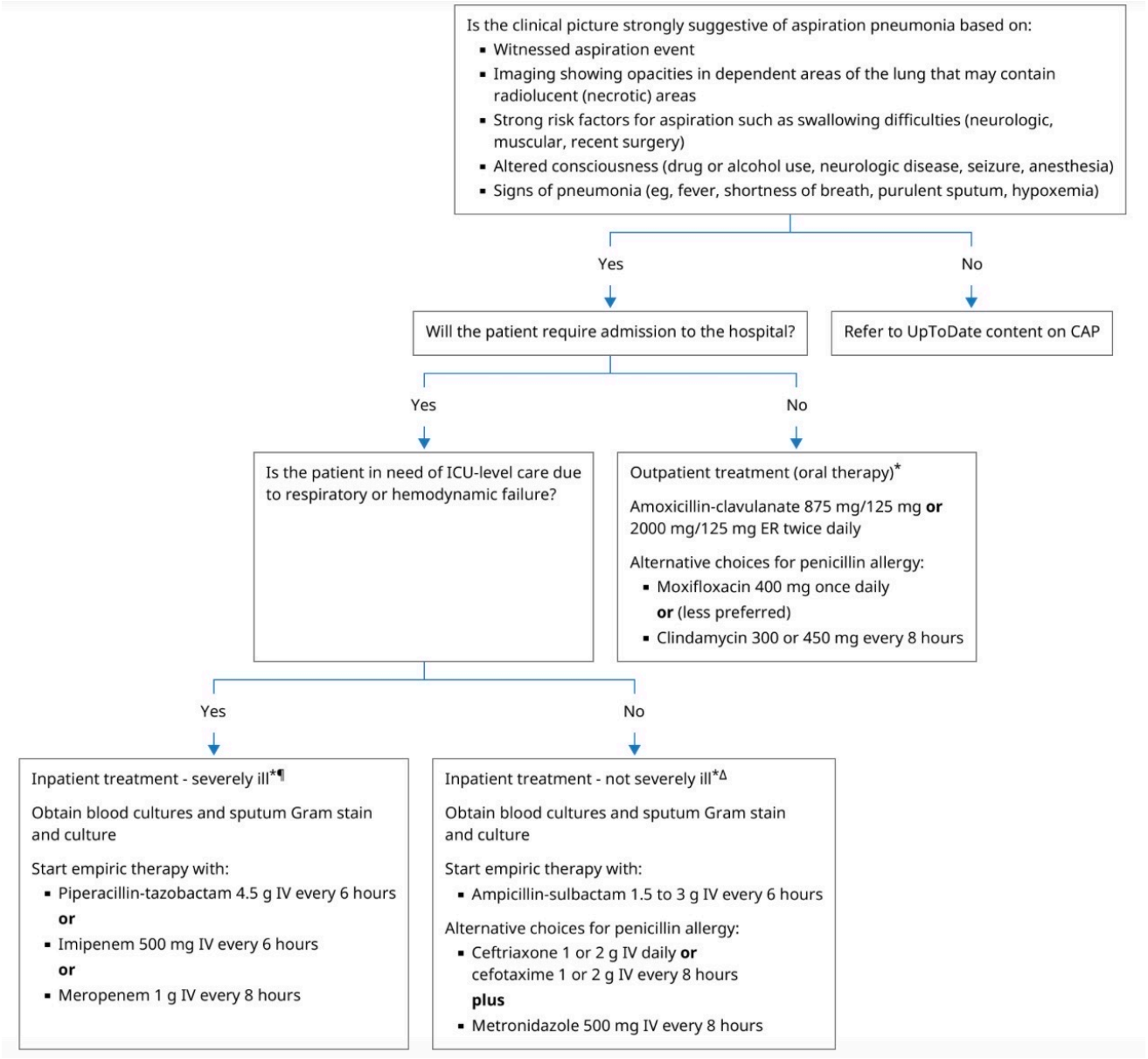
A 5-day course is sufficient for most outpatients. In general, a follow-up visit or communication is indicated within a few days of starting treatment to ensure that the patient is afebrile and improving.

For all patients, our empiric regimens are designed to target:◇
- *Streptococcus pneumoniae* (most common bacterial CAP pathogen)
- Atypical pathogens (eg, *Legionella* spp, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*)

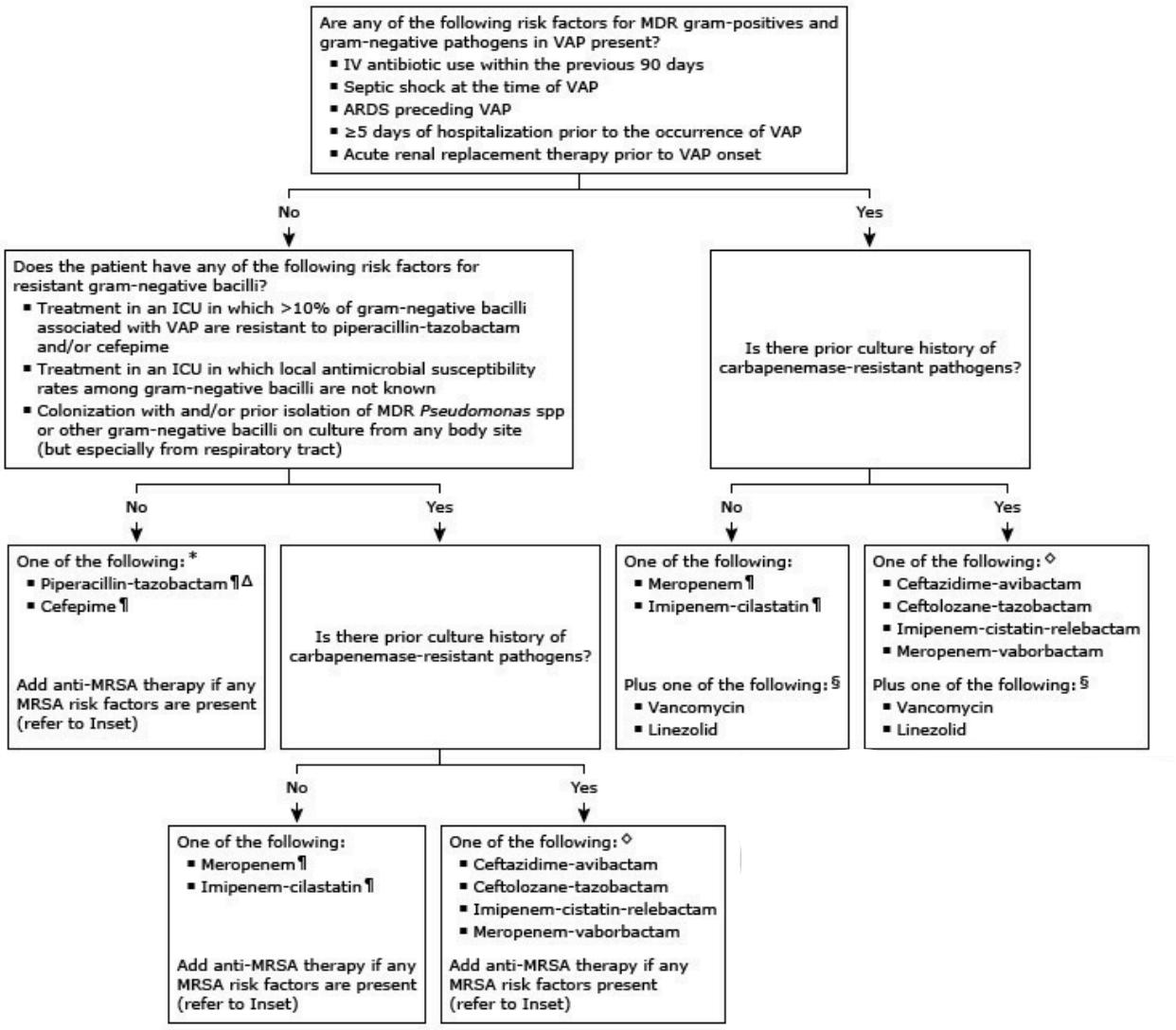
Coverage is expanded in those with comorbidities, older age, or recent antibiotic use to include or better treat:
- Beta-lactamase-producing *Haemophilus influenzae*
- *Moraxella catarrhalis*
- Methicillin-susceptible *Staphylococcus aureus*

For patients with structural lung disease (eg, advanced COPD), coverage is further expanded to include Enterobacteriaceae, such as *Escherichia coli* and *Klebsiella* spp.

Treatment of Aspiration Pneumonia



Treatment of Ventilator-Associated Pneumonia (VAP)

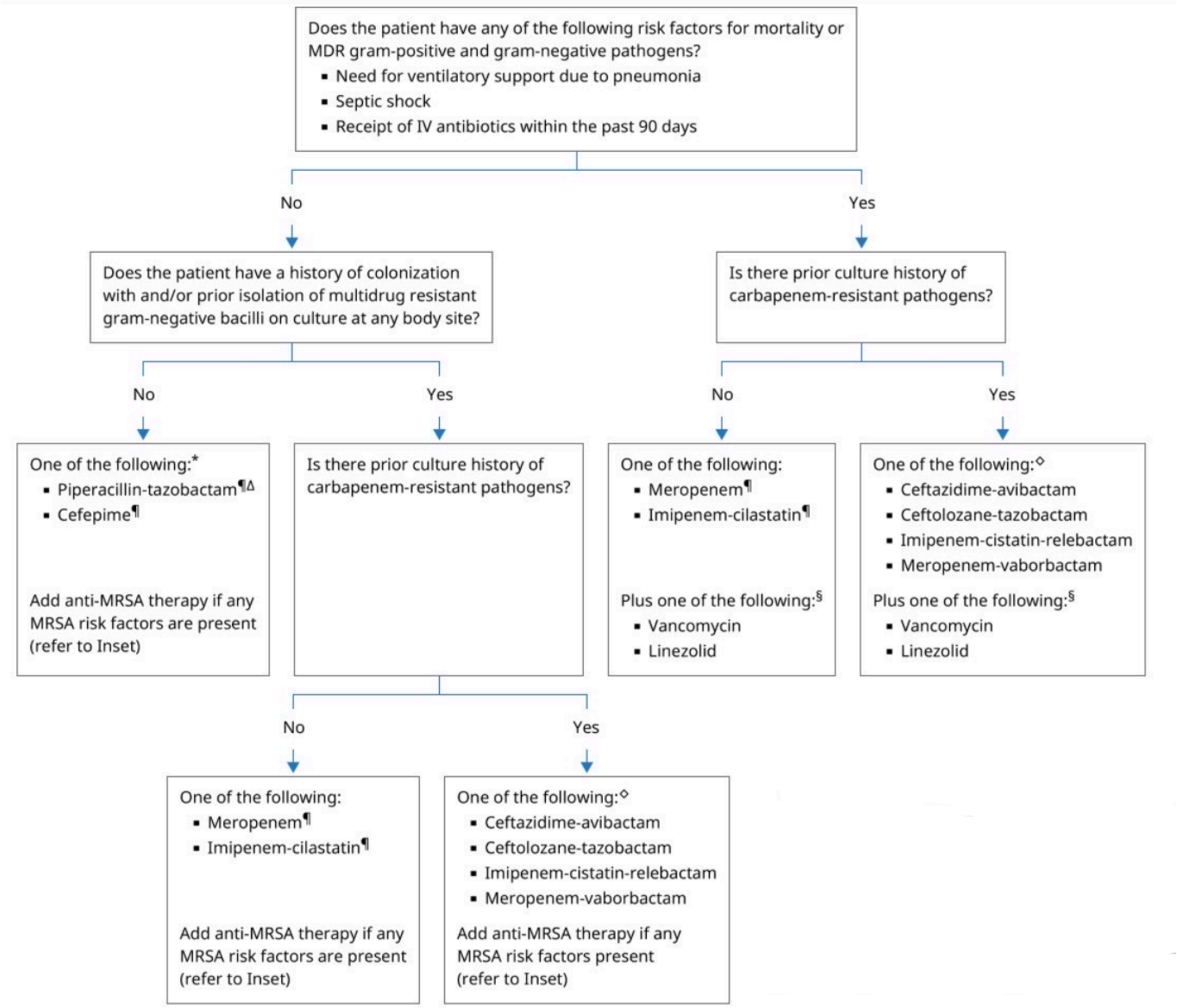


ARDS: acute respiratory distress syndrome; HAP: hospital-acquired pneumonia; ICU: intensive care unit; IDSA/ATS: Infectious Diseases Society of America/American Thoracic Society; IV: intravenous; MDR: multidrug-resistant; MRSA: methicillin-resistant Staphylococcus aureus; VAP: ventilator-associated pneumonia.

* We generally prefer piperacillin-tazobactam or cefepime because they are more likely to have activity against gram-negative bacilli than levofloxacin. However, levofloxacin 750 mg IV daily may be preferred if there is a high suspicion for Legionella spp infection and local resistance rates of S. aureus, P. aeruginosa, and other gram-negative bacilli to fluoroquinolones are low. The IDSA/ATS guidelines also include imipenem and meropenem as options, but we generally reserve these agents for patients with a high likelihood of infection with extended-spectrum beta-lactamase (ESBL)-producing gram-negative bacilli.

Inset	
Dosing of preferred antibiotics	
Piperacillin-tazobactam ¶	4.5 g IV every 6 hours
Cefepime ¶	2 g IV every 8 hours
Meropenem ¶	1 g IV every 8 hours
Imipenem-cilastatin ¶	500 mg IV every 6 hours
Ceftazidime-avibactam	2.5 g IV every 8 hours
Ceftolozane-tazobactam	3 g IV every 8 hours
Imipenem-cilastatin-relebactam	1.25 g IV every 6 hours
Meropenem-vaborbactam	4 g IV every 8 hours
Add anti-MRSA therapy if patient has one of the following risk factors for MRSA: ▪ Treatment in a unit in which >10 to 20% of *S. aureus* isolates associated with VAP are methicillin resistant ▪ Treatment in a unit in which the prevalence of MRSA is not known ▪ Colonization with and/or prior isolation of MRSA on culture from any body site (but especially the respiratory tract)	
Anti-MRSA therapy consists of one of the following: §	
Vancomycin	Generally 15 to 20 mg/kg every 8 to 12 hours for most patients with normal kidney function. Interval adjustments should be based on AUC-guided (preferred) or trough-guided serum concentration monitoring. The vancomycin loading dose is based on actual body weight; the dose is rounded to the nearest 250 mg increment and not exceeding 2000 mg. Within this range, we use a higher dose for critically ill patients.
Linezolid	600 mg IV every 12 hours

Treatment of Hospital-Acquired Pneumonia (HAP)



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Linezolid	600 mg IV every 12 hours

Treatment of *Pneumocytis jerovecii*

- TMP-SMX is the preferred regimen for the treatment of PJP.
    - Therapy should be administered for 21 days.
    - Trimethoprim is a dihydrofolate reductase inhibitor, and sulfamethoxazole is a dihydropteroate synthetase inhibitor; when coupled together they are synergistic in eradicating P. jirovecii.
- The standard dose of TMP-SMX is 15 to 20 mg/kg/day orally or intravenously in three or four divided doses.
    - Dosing of TMP-SMX is based upon the TMP component and expressed as mg/kg per day of TMP.
    - The severity of disease dictates whether oral or intravenous therapy should be used.
- Corticosteroids given in conjunction with anti-Pneumocystis therapy in moderate-severe disease and can decrease the incidence of mortality and respiratory failure associated with PJP.
    - Without steroids, patients with PJP may worsen clinically after two to three days of therapy, presumably due to increased inflammation in response to dying organisms.
    - Corticosteroids should be initiated concurrently with anti-Pneumocystis therapy for 21-day oral regimen:
        - Prednisone 40 mg twice daily for 5 day, followed by Prednisone 40 mg daily for 5 days, followed by Prednisone 20 mg daily for 11 days
        - Intravenous methylprednisolone can be substituted for oral prednisone at 75 percent of the prednisone dose if IV therapy is necessary.
- In women who may become pregnant, folic acid 4 mg per day is administered as a supplement to prevent folate deficiency in case they were to become pregnant while receiving TMP-SMX

Treatment of Aspergillus Pneumonia

- For initial therapy of invasive aspergillosis, we recommend voriconazole if a resistant pathogen is not suspected.
- Amphotericin B is alternative to voriconazole but it carries the risk of nephrotoxicity and is only available intravenously.
    - Amphotericin B is generally reserved for patients at risk for drug interactions with azoles, severe hepatotoxicity, or isolates suspected to be triazole-resistant.
- Lipid formulations of amphotericin B is favored over amphotericin B deoxycholate, since amphotericin B deoxycholate is associated with severe nephrotoxicity.
    - There are two currently marketed lipid formulations of amphotericin B:
        - Liposomal amphotericin B (AmBisome)
        - Amphotericin B lipid complex (Abelcet)
    - The main advantage of the lipid formulations is the ability to administer larger doses of amphotericin B with fewer toxicities.
    - Amphotericin B lipid complex and liposomal amphotericin B also have fewer infusion-related side effects than amphotericin B deoxycholate.
    - The lipid formulations, although less toxic, have not been definitively shown to result in better outcomes compared with conventional amphotericin B.
- When using a lipid formulation of amphotericin B for the treatment of invasive aspergillosis, we prefer liposomal amphotericin B (AmBisome) at an initial dose of 3 to 5 mg/kg IV per day; amphotericin B lipid complex (Abelcet) at a dose of 5 mg/kg IV per day is an appropriate alternative.

Recap

Avoid Pitfalls

⚠ FQ → Tendon rupture, QT prolongation, C. difficile risk
⚠ Macrolides → QT prolongation
⚠ Aminoglycosides → Nephrotoxicity, Ototoxicity; avoid in renal impairment
⚠ Beta-lactams → Hypersensitivity; cross-reactivity in PCN allergy
⚠ Vancomycin → Red Man Syndrome
⚠ Rifampin → CYP450 inducer; ↓ warfarin, OCP, HIV drug efficacy
⚠ Isoniazid → Needs B6 to prevent peripheral neuropathy
⚠ Ethambutol → Optic neuritis; monitor vision
⚠ Broad-spectrum overuse → MDR, C. difficile risk
⚠ Escalation/de-escalation failure → Tx failure, resistance

Recap

🎯 Final Takeaways

- ☑ Drug classes for pulmonary infections and their mechanisms.
- ☑ How to choose the right antibiotic for different respiratory infections.
- ☑ Common side effects and drug interactions to be aware of.
- ☑ When to escalate or de-escalate therapy based on clinical response.

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