CHAPTER 13

Medications in Infectious Disease

13.1 Antibacterial Agents

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I. Cell Wall Inhibitors

Ia. Beta-Lactams

MOA: They interfere with the last step (cross-linkage) of cell wall synthesis by binding to Penicillin binding proteins

> COMMENT BOX
> **Beta-Lactams** are **bactericidal** agents.

1) Penicillins

Side Effects: Hypersensitivity reaction (if severe, IgE-mediated then it is contraindicated); cross sensitivity; GI irritation (orally); renal failure; seizures (rare)

> COMMENT BOX
> **Penicillins** are considered as **Pregnancy Category (B)** drugs.

a. Narrow Spectrum Penicillins (Natural Penicillins) (Penicillin G, Penicillin V)

Route of Administration: Penicillin G (Benzylpenicillin)—IV, IM (acid-labile; not to be given orally);
Penicillin V (Phenoxymethylpenicillin)—oral (on empty stomach)
Coverage: Gram-positive organisms; Gram-negative cocci; non-β-lactamase-producing anaerobes; little activity against Gram-negative rods; susceptible to hydrolysis by β-lactamases

b. Penicillinase-Resistant Penicillins (Antistaphylococcal) (Nafcillin, Oxacillin)

Route of Administration: Nafcillin—IV, IM; Oxacillin—IV
Route of Excretion: Urine or bile
Coverage: Active against streptococcus and staphylococcal (resistant to hydrolysis by β-lactamases); not active against enterococci, anaerobes, and Gram-negative cocci and rods

c. Broad Spectrum Penicillins (Aminopenicillins) (Amoxicillin, Ampicillin)

Route of Administration: Amoxicillin—oral; Ampicillin—oral (on empty stomach), IV, IM
Route of Excretion: Urine
Dosage Range: Amoxicillin—immediate release: 500 mg to 1 g q8-12hrs; extended release: 775 mg once daily; Ampicillin—oral: 250-500mg q6hrs; IV or IM: 1-2g q4-6hrs, max 12g/day
Coverage: They retain the antibacterial spectrum of Penicillin; improved activity against some Gram-negative rods (but not Pseudomonas); relatively susceptible to hydrolysis by β-lactamases

> COMMENT BOX
> **Broad spectrum Penicillins** should be used with caution in infectious **mononucleosis** patients due to an increased risk of **erythematous rash**.

COMMENT BOX
Broad spectrum Penicillins should be used with caution in infectious **mononucleosis** patients due to an increased risk of **erythematous rash**.

d. Extended Spectrum Penicillins (Piperacillin, Ticarcillin, Carbenicillin)

Piperacillin/Tazobactam

Route of Administration: IV
Route of Excretion: Urine (primarily), feces
Coverage: Includes the activity of Aminopenicillin; active against P.aeruginosa and Klebsiella species
Additional Side Effects: Leukopenia/neutropenia (with prolonged use)

Ticarcillin/Clavulanate

Route of Administration: IV
Route of Excretion: Urine
Coverage: Includes the activity of Aminopenicillin; active against P.aeruginosa
Additional Side Effects: Hypokalemia (should be monitored)

COMMENT BOX
Aminopenicillins and **Extended Spectrum Penicillins** are susceptible to hydrolysis by β-lactamases; that is why they are often combined with β -lactamase inhibitors like **Tazobactam**, **Sulbactam**, or **Clavulanate**.

COMMENT BOX
Clavulanate does **not** affect the half-life of **Ticarcillin**.

COMMENT BOX
Extended Spectrum Penicillins should be **discontinued** if **bleeding disorders** occur.

Beta-Lactamase Inhibitors

- **Clavulanate**—with Amoxicillin called Augmentin; with Ticarcillin called Timentin
- **Tazobactam**—with Piperacillin called Tazocin
- **Sulbactam**—with Ampicillin called Unasyn
- **Avibactam**—with Ceftazidime called Avycaz

MOA: They bind to and inactivate beta-lactamases and inhibit them (not all types); they have no significant anti-bacterial activity and are thus combined with other beta-lactams

2) Cephalosporins

Side Effects: Hypersensitivity reaction (if severe, IgE-mediated then it is contraindicated); cross sensitivity; GI irritation (orally); renal failure; seizures (rare)

COMMENT BOX
Cephalosporins are similar to Penicillins but are more **stable** to many bacterial beta-lactamases; therefore, they have a **broader spectrum** of activity. They are considered as **Pregnancy Category (B)** drugs.

a. First Generation Cephalosporins (Cefadroxil, Cefazolin, Cefalexin, Cephalothin (prototype))

Route of Administration: Cefadroxil/Cefalexin—oral; Cefazolin—IV, IM

Route of Excretion: Urine

Coverage: Very active against Gram-positive cocci (streptococci and staphylococci); some activity against Gram-negative bacteria (like E coli, K.pneumoniae, Proteus mirabilis); not active against MRSA and enterococci

Additional Side Effects: Cefazolin and Cefalexin are associated with increased INR

b. Second Generation Cephalosporins (Cefaclor, Cefuroxime, Cefoxitin, Cefotetan)

Route of Administration: Cefaclor—oral; Cefuroxime—oral, IV, IM; Cefoxitin/Cefotetan—IV, IM

Route of Excretion: Urine (primarily)

Coverage: Same as first-generation drugs but they have extended Gram-negative coverage (Klebsiella species including those resistant to first-generation cephalosporins); active against anaerobes (Cefoxitin and Cefotetan); not active against MRSA and enterococci

> **COMMENT BOX**
> These drugs should be used with **Caution** in patients with **renal impairment**, **colitis**, and **seizure disorders**.

COMMENT BOX
None of the **first** or **second** generation Cephalosporins is active against **P.aeruginosa** species.

c. Third Generation Cephalosporins (Ceftriaxone, Cefotaxime, Ceftazidime, Cefoperazone, Cefixime, Cefdinir, Cefpodoxime)

Route of Administration: Ceftriaxone/Cefotaxime/Ceftazidime/Cefoperazone—IV, IM;
Cefixime/Cefdinir/Cefpodoxime—oral

Route of Excretion: Urine (primarily), bile (Cefoperazone and Ceftriaxone)

Coverage: They have expanded Gram-negative coverage compared to second-generation agents (like Haemophilus and Neisseria species); not active against MRSA and enterococci

COMMENT BOX
Among third generation Cephalosporins, only **Ceftazidime** and **Cefoperazone** are **active** against **P.aeruginosa**.

d. Fourth Generation Cephalosporins (Cefepime, Cefpirome)

Route of Administration: Cefepime—IV, IM; Cefpirome—IV

Route of Excretion: Urine (Cefepime)

Coverage: Good activity against P.aeruginosa, Enterobacter (resistant to hydrolysis by β-lactamases produced by Enterobacter unlike second and third generations which are facing newly-emerging resistance against this species), and S pneumoniae; highly-active against Haemophilus and Neisseria; not active against MRSA and enterococci
Additional Side Effects: Positive direct Coombs test (hemolytic anemia); neurotoxicity; increased INR

e. Fifth Generation Cephalosporins (Ceftaroline Fosamil)

MOA: Cell wall inhibitor through inhibition of PBP2a
Route of Administration: IV (slow infusion)
Route of Excretion: Urine
Coverage: Active against MRSA; some in-vitro activity against enterococci; some Gram-negative activity (but not active against pseudomonas or ESBL)
Additional Side Effects: Positive direct Coombs test

3) Carbapenems
(Imipenem, Meropenem, Ertapenem, Doripenem)

Side Effects: Hypersensitivity (because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty); **seizures**

> COMMENT BOX
> **Meropenem**, **Ertapenem**, and **Doripenem** are considered as **Pregnancy Category (B)** drugs, while **Imipenem** is considered as **Pregnancy Category (C)** drug.

Imipenem/Cilastatin

Route of Administration: IV infusion only
Route of Excretion: Urine (primarily)
Half-life: 60 mins
Coverage: Active against most Gram-negative rods (including P.aeruginosa); Gram-positive organisms; anaerobes
Additional Side Effects: Decreased hematocrit and hemoglobin; thrombocytopenia; increased AST and ALT; CNS effects

> COMMENT BOX
> **Imipenem** is metabolized in the kidney to produce **toxic metabolites**; **Cilastatin** prevents that metabolism.

Meropenem

Route of Administration: IV
Route of Excretion: Urine (primarily)
Half-life: 60 mins

Coverage: Similar to Imipenem with slightly greater activity against Gram-negative aerobes and slightly less activity against Gram-positives
Additional Side Effects: Can rarely cause CNS effects and dermatological effects (Stevens-Johnson syndrome and toxic epidermal necrosis)

Ertapenem

Route of Administration: IV infusion, IM
Route of Excretion: Urine (primarily)
Half-life: 4 hours (advantage of being given once daily)
Coverage: Similar to other carbapenems but does not have activity against P.aeruginosa, Acinetobacter, Enterococcus spp., and Penicillin-resistant strains of S.pneumonia
Additional Side Effects: GI effects (diarrhea)

4) Monobactams (Aztreonam)

Route of Administration: IV, IM
Route of Excretion: Urine (primarily)
Coverage: Limited to aerobic Gram-negative organisms (including P.aeruginosa); no activity against Gram-positive bacteria or anaerobes (unlike other β-lactam antibiotics)
Side Effects: Neutropenia; increased serum transaminases

> COMMENT BOX
> **Monobactams** are considered as **Pregnancy Category (B)** drugs.

Ib. Glycopeptides (Vancomycin, Teicoplanin)

> COMMENT BOX
> **IV Vancomycin** is considered as **Pregnancy Category (C)** drug, while **oral Vancomycin** and **Teicoplanin** are considered as **Pregnancy Category (B)** drugs.

Vancomycin

MOA: Binds to the D-ala-D-ala portion of cell wall precursor, preventing glycopeptide polymerization
Route of Administration: IV, PO, rectal (off-label)
Route of Excretion: IV—renal; PO—fecal (primarily)
Coverage: Gram-positive species including MRSA and other Gram-positive anaerobes including C.difficile
Side Effects: PO—abdominal pain; dysgeusia (solution); nausea; IV—Cardiovascular (hypotension with rapid IV administration less than 1.5 hours); red man syndrome; nephrotoxicity; ototoxicity; neutropenia; thrombocytopenia

> COMMENT BOX
> **Vancomycin** displays **time-dependent** antimicrobial killing activity (slowly bactericidal). However, it has **no** activity against **Gram-negative** bacteria because of its **huge structure** that prevents it from penetrating the outer membrane of these organisms.

II. Protein Synthesis Inhibitors

IIa. Macrolides

MOA: Inhibition of protein synthesis via binding to the 50S ribosomal subunit

Side Effects: They have been associated with rare Qt prolongation and ventricular arrhythmias

> COMMENT BOX
> **Macrolides** are mainly **bacteriostatic** agents.

Erythromycin

Route of Administration: Oral, IV (infusion only)

Route of Excretion: Fecal (primarily)

Coverage: Gram-positive bacteria (especially pneumococci, streptococci, staphylococci, and corynebacteria); Mycoplasma pneumoniae; Chlamydia trachomatis; H pylori; Gram-negative organisms such as Neisseria species

Additional Side Effects: Signs of liver disease

> COMMENT BOX
> **Erythromycin** may be **bactericidal** at **higher concentrations**.

Azithromycin

Route of Administration: IV (infusion), oral

Route of Excretion: Fecal (primarily)

Coverage: Slightly less active than Erythromycin against staphylococci and streptococci and slightly more active against H influenzae

Additional Side Effects: Diarrhea; nausea; abdominal pain; use with caution in patients with renal disease, liver disease and cholestatic jaundice (especially associated with prior Azithromycin use), and myasthenia gravis

COMMENT BOX
Azithromycin should **not** be given long-term to prevent **bronchiolitis obliterans** syndrome in patients with cancers of the blood or lymph nodes who undergo stem cell transplant because of increased rate of **relapses** of hematological malignancies and death.

Telithromycin

Route of Administration: Oral
Route of Excretion: Urine
Coverage: Has better activity against macrolide-resistant species of S.pneumoniae, staphylococci, enterococci, Chlamydia trachomatis, and Neisseria gonorrhoeae
Additional Side Effects: GI effects (Diarrhea)
Contraindications: Myasthenia gravis (risk of respiratory failure)

COMMENT BOX
Azithromycin and **Erythromycin** are considered as **Pregnancy Category (B)** drugs. **Telithromycin**, however, is considered as **Pregnancy Category (C)** drug.

IIb. Aminoglycosides

(Tobramycin, Gentamicin, Amikacin, Streptomycin)

MOA: Inhibition of protein synthesis via binding the 30S ribosomal subunit

Route of Administration: IV infusion, IM

Route of Excretion: Urine

Coverage: Mainly Gram-negative bacteria (including P.aeruginosa); Amikacin is resistant to many enzymes that inactivate Gentamicin and Tobramycin and has slightly better activity than them; Streptomycin is not currently useful due to developing resistance in most species with the exception of a few like M.tuberculosis (second-line agent) and Brucella

Side Effects: Neurotoxicity (ototoxicity, irreversible); nephrotoxicity (usually reversible); neuromuscular blockade; local skin reactions with IM injection (should be administered in a large muscle)

COMMENT BOX

Aminoglycosides have a **concentration-dependent bactericidal** effect and a significant **post-antibiotic effect**. They are considered as **Pregnancy Category (D)** drugs.

COMMENT BOX

Aminoglycosides are almost always used in **combination** with a **β-lactam** antibiotic to extend empiric coverage and to take advantage of the potential **synergism** between these two classes.

IIc. Tetracyclines

(Tetracycline, Minocycline, Doxycycline, Tigecycline)

MOA: Protein synthesis inhibition via binding to the 30S ribosomal subunit

Route of Administration: Tetracycline—oral (on empty stomach); Doxycycline/Minocycline—oral, IV; Tigecycline—IV only

Coverage: Broad spectrum including Gram-positive (including MRSA) and Gram negative bacteria, certain anaerobes, rickettsia, chlamydia, and mycoplasmas (Tigecycline has an improved activity compared to other Tetracyclines)

Side Effects: GI discomfort; light hypersensitivity; permanent teeth discoloration (in children); increased BUN; hepatotoxicity (more with Tetracycline and Minocycline than Doxycycline); tissue hyperpigmentation (with Doxycycline); autoimmune syndromes (with Minocycline)

Contraindications: Severe hepatic dysfunction; pregnancy 2nd and 3rd trimesters (although recent data supported the use of these drugs in some cases of pregnant women with life-threatening infections); breast feeding; children less than 8 years; avoid administration along with dairy products and divalent cations (Ca+2, Mg+2, Fe+2, Al+3)

COMMENT BOX

Tetracyclines are **bacteriostatic** agents. They are also considered as **Pregnancy Category (D)** drugs.

IId. Lincosamides

(Clindamycin, Lincomycin)

MOA: Protein synthesis inhibition via binding to the 50S ribosomal subunit

Route of Administration: Clindamycin—oral, IV (never administer undiluted as bolus), IM; Lincomycin—IV, IM, subconjunctival injection

Coverage: Active against Gram-positive bacteria (esp. streptococci, staphylococci (including MRSA), and pneumococci); not active against Enterococci and Gram-negative aerobic organisms

Side Effects: Colitis (C.difficile-associated diarrhea); hypersensitivity; impaired liver function

> COMMENT BOX
> **Clindamycin** is considered as **Pregnancy Category (B)** drug, while **Lincomycin** is considered as **Pregnancy Category (C)** drug. They both are **bacteriostatic** agents.

IIe. Oxazolidinones (Linezolid)

MOA: Binds to the ribosomal RNA of the 50S subunit

Route of Administration: Oral, IV (do not mix or infuse with other medications)

Route of Excretion: Urine, feces

Coverage: Active against Gram-positive organisms (including staphylococci, streptococci, enterococci, and Gram-positive anaerobic cocci); also active against M.tuberculosis

Side Effects: Diarrhea; bone marrow suppression (decreased WBCs, RBCs, and platelets); skin reactions; neuropathy; serotonin syndrome (increased risk when used with other serotonergic agents)
Contraindications: Concurrent use or within 2 weeks of MAO-inhibitors; hypertensive patients; patients with carcinoid syndrome

> COMMENT BOX
> **Linezolid** is **bacteriostatic** against **enterococci** and **staphylococci** and **bactericidal** against most strains of **streptococci**. It is considered as **Pregnancy Category (C)** drug.

III. Antimetabolites (Sulfonamides combinations)

Sulfamethoxazole (SMX)–Trimethoprim (TMP) or Co-Trimoxazole

MOA: They inhibit the formation of tetrahydrofolate (THF)
Route of Administration: Oral, IV
Route of Excretion: Urine
Coverage: Active against Gram-negative (esp. Salmonella and Shigella); most Gram-positive especially Nocardia and Listeria (also including MRSA but **not** streptococcus group A); Pneumocystis jiroveci Pneumonia
Side Effects: GI upset; crystalluria; hepatotoxicity; hyperbilirubinemia; hyperkalemia; use during the last 2 weeks of pregnancy is associated with increased risk of neonates with prolonged physiological jaundice

Contraindications: Hypersensitivity to any sulfa drug; concomitant use with other sulfonamides; blood dyscrasias

> **COMMENT BOX**
> Each one of **SMX** or **TMP** is **bacteriostatic** when used alone; however, when **combined**, they are often **bactericidal**. SMX-TMP is considered as **Pregnancy Category (C)** drug.

IV. Nucleic Acid Synthesis Inhibitors

IVa. Fluoroquinolones

- First Group—Norfloxacin
- Second Group—Ciprofloxacin, Levofloxacin, Ofloxacin, Enoxacin
- Third Group—Gemifloxacin, Moxifloxacin, Gatifloxacin

MOA: They inhibit bacterial DNA gyrase and topoisomerase IV
Route of Administration: Oral, IV infusion
Route of Excretion: Mixed (renal and nonrenal)
Coverage: Generally, they have excellent Gram-negative coverage and variable Gram-positive coverage;

- **First group**—least active against both Gram-negative and Gram-positive organisms
- **Second group**—excellent Gram-negative activity (including P.aeruginosa, with Ciprofloxacin being the most active) and moderate to good Gram-positive activity (including S.pneumonia, with Levofloxacin being the most active)

- **Third group**—improved activity against Gram-positive organisms (esp. S pneumoniae) and atypical pneumonia agents like Chlamydia, Mycoplasma, and Legionella (alongside Levofloxacin, they are called **Respiratory Fluoroquinolones**)

Side Effects: Hypersensitivity; QT prolongation; dysglycemia; hepatotoxicity; phototoxicity; CNS effects; peripheral neuropathy; GI effects; psychiatric effects; mental illness; tendonitis and tendon rupture (DC in patient who display these effects)
Contraindications: Previous tendonitis associated with quinolones use; concomitant administration with antacids, dairy products, and metal cations

> COMMENT BOX
> **Fluoroquinolones** have many **drug-drug interactions**. Also, their side effects can be **irreversible.** All of this largely participated in **discouraging** their use in practice in case a less toxic alternative is available.

IVb. Rifampin/Rifampicin

MOA: Blocks RNA transcription via binding to RNA polymerase
Route of Administration: Oral (on empty stomach), IV infusion
Route of Excretion: Feces (primarily), urine
Coverage: Active against Gram-positive organisms; some Gram-negative organisms (including Neisseria and Haemophilus species); also active against M.tuberculosis and Brucella
Side Effects: Rash; thrombocytopenia; nephritis; flu-like symptoms; orange-colored urine, sweat, and tears (harmless)

> COMMENT BOX
> **Rifampin** is a **bactericidal** agent. It is considered as **Pregnancy Category (C)** drug. They also have a lot of **drug-drug interactions**.

V. Miscellaneous

Fosfomycin

MOA: It is a phosphonic acid derivative that Inactivates the enzyme pyruvyl transferase, which is critical in the synthesis of cell walls by bacteria

Route of Administration: Oral, IV

Coverage: Has activity against both Gram-positive and Gram-negative organisms

Side Effects: Headache; diarrhea; vaginitis

> COMMENT BOX
> **Fosfomycin** is considered as **Pregnancy Category (B)** drug.

Nitrofurantoin

MOA: Nitrofurantoin is reduced by bacterial flavoproteins to reactive intermediates that inactivate or alter bacterial ribosomal proteins

Route of Administration: Oral (with meals)

Coverage: Active against E. coli, Enterococci, Staphylococcus aureus, and certain strains of Klebsiella and Enterobacter species

Side Effects: Anorexia; nausea; vomiting

> COMMENT BOX
> **Nitrofurantoin** is considered as **Pregnancy Category (B)** drug.

Isoniazid

MOA: Inhibition of mycolic acid synthesis (an essential component of cell wall)
Route of Administration: Oral (on empty stomach), IM
Coverage: M.tuberculosis
Side Effects: Increased serum transaminases; risk of hepatitis and pancreatitis; peripheral neuropathy (usually given with Vitamin B6)

> **COMMENT BOX**
> **Isoniazid** is considered as **Pregnancy Category (C)** drug.

Ethambutol

MOA: Inhibits arabinosyl transferase resulting in impaired mycobacterial cell wall synthesis
Route of Administration: Oral
Coverage: Mycobacterial species (combined with other agents)
Side Effects: Visual disturbances (including color blindness, visual field defects, and optic neuritis)

> **COMMENT BOX**
> **Ethambutol** is considered as **Pregnancy Category (B)** drug.

VI. Clinical Pearls

- In this section, we will mention briefly the antimicrobials that are used **empirically** in certain site-specific infections
- It is important to weigh-out **risk against benefit** before starting empirical antimicrobial therapy, and to do cultures to establish the particular microbial diagnosis when possible
- Once the causative organism and its susceptibility for antimicrobials are identified, the antimicrobial regimen should be **narrowed down** to the narrowest possible coverage
- Note that the choice of antimicrobial agents should be guided by the **common microorganisms** causing the disease and their **susceptibility** to different antimicrobials in that specific community or hospital according to **data** collected as well as the **clinical status** of the patient, **site of infection**, and **drug properties** (e.g. site penetration)
- Certain antimicrobials have **synergistic** effects when **combined** together
- The treatments that we will mention are typically the first-line regimens for **immunocompetent** adults (unless otherwise mentioned)

1) Bacterial Meningitis/Meningoencephalitis

Choice of Empirical Antimicrobial:

- **Community acquired** (in immunocompetent patients <50 years)—Third Generation Cephalosporin + Vancomycin
- **Healthcare acquired** (greater coverage of gram negative is required)—Vancomycin + Meropenem or Ceftazidime or Cefepime

Common Causative Microbes: Pneumococcus, Meningococcus, H.influenza, herpes, CMV

Duration of Treatment: Typically 7-21 days depending on causative organism and clinical status of patient

COMMENT BOX

Add **Ampicillin** for patients **>50 year** old to cover **L. Monocytogenes**. If **encephalitis** is present, **herpetic infection** should be suspected and patient should be started on **Acyclovir** (it can be difficult to differentiate between meningitis and encephalitis).

COMMENT BOX

Moxifloxacin can be used in patients with **Penicillin** or **Cephalosporin allergy**.

2) Sinusitis/Acute Otitis Media

Choice of Empirical Antimicrobial: Amoxicillin-clavulanate; others include Doxycycline and Fluoroquinolones

Common Causative Microbes: Streptococcus pneumonia, H.influenza, Moraxella catarrhalis

Duration of Treatment: Typically 5-10 days

3) Pneumonia

Community Acquired Pneumonia (CAP)		Hospital Acquired Pneumonia
Outpatient	**Inpatient**	**3-drug regimen:** Beta-Lactam antipseudomonal (e.g. Ceftazidime or Imipenem or Piperacillin-Tazobactam) + Anti–MRSA (Vancomycin or Linezolid) + Aminoglycoside (e.g. Amikacin)
No risk factors (1)**:** Macrolide or Doxycycline **Risk factors** (2)**:** (Beta-lactam + Macrolide) **or** a respiratory Fluoroquinolone	**First-line:** (Beta-lactam or Carbapenem) + (Macrolide or respiratory Fluoroquinolone) **Suspected Pseudomonas** (3)**:** (Levofloxacin/Ciprofloxacin + Carbapenem) **or** (Piperacillin-Tazobactam) **or** Cefepime **or** (Levofloxacin + Aminoglycoside + Aztreonam) (4) **Suspected MRSA** (5)**:** add Vancomycin or Linezolid to the above regimen	

(1): Immunocompetent patient, no comorbidities, bacterial resistance less than 26%, and no use of antibiotics in the last 3 months
(2): e.g. COPD
(3): e.g. COPD, Gram-negative bacilli in sputum
(4): The last regimen is used in case of Penicillin allergy
(5): e.g. recent influenza infection

Common Causative Microbes (CAP): Streptococcus pneumonia, Chlamydia, Mycoplasma, Legionella, viral; more virulent organisms include Staphylococcus, Pseudomonas, Enterobacteria, and certain strains of influenza virus

Duration of treatment: 7-10 days (can be longer); CAP—typically 5 days (3 days for Azithromycin 500 mg)

> COMMENT BOX
> **Avoid** using **Fluoroquinolones** in the outpatient treatment of **CAP** if possible to **slow** the development of microbial **resistance** against these drugs.

> COMMENT BOX
> **Macrolides** and **Fluoroquinolones** have high **oral bioavailability** so they can be used in patients **orally** rather than parentally.

4) Infective Endocarditis

Choice of Empirical Antimicrobial: Varies; as per culture (blood cultures are typically positive in more than 90% of cases and empirical antibiotic is not necessary if the patient is clinically stable)

Common Causative Microbes: MRSA, MSSA, Enterococci, Streptococci, HACEK, Brucella

Duration of Treatment: Typically 6 weeks, but can be shorter in uncomplicated right-sided IE or with less virulent organisms

> COMMENT BOX
> Once cultures are **positive**, treatment options include **Penicillin G** +/- **Gentamycin** or **Ceftriaxone** for **S.Viridans**, **Nafcillin** for **MSSA** or **coagulase-negative Staphylococcus**, **Vancomycin** for **MRSA**, and **Gentamycin** + **Ampicillin** or **Vancomycin** for **Enterococcus**.

5) Septic arthritis

Choice of Empirical Antimicrobial: Typically Vancomycin + third generation Cephalosporin (Vancomycin can be substituted with Clindamycin in clinically stable patients aged >3 months) if sensitive organism)

Common Causative Microbes: MRSA, Enterobacteria, Gonococcus, H.influenza

Duration of Treatment: 3-4 weeks in adults

COMMENT BOX

Cefepime must be used instead of third generation Cephalosporin in case **P.aeruginosa** is suspected (e.g. in patient with history of penetrating injury).

COMMENT BOX

Joint aspiration and **blood cultures** should be sent before starting antibiotic therapy if possible. **IV antibiotic** therapy is then started until the patient is clinically stable. After the patient reaches a good clinical status, therapy can be then switched to **oral** as **outpatient** (**as per culture**).

6) Osteomyelitis

Choice of Empirical Antimicrobial: Typically Vancomycin + third generation cephalosporin or Cefepime (as per culture)

Common Causative Microbes: Staphylococcus, Gram-negatives

Duration of Treatment: Typically 8 weeks (IV) in adults

COMMENT BOX
An attempt for **surgical debridement** is typically done before antibiotic therapy to allow better **penetration** of the antimicrobial agent by removing necrotic tissue, and for sampling to establish microbiological diagnosis.

COMMENT BOX
The treatment varies if a **prosthesis** is present, which if not removed surgically could involve added **Rifampicin** for its great biofilm penetrance (for **S.aureus**).

7) Cellulitis

Choice of Empirical Antimicrobial: Cefazolin (IV) or Cephalexin (oral). If there is pus or an abscess, MRSA should be covered (Vancomycin or Clindamycin or Linezolid)
Common Causative Microbes: Group B Streptococcus, Staphylococcus
Duration of Treatment: Typically 5-14 days

COMMENT BOX
Choice of **oral vs. IV** therapy should be guided by the **clinical status** of the patient and the presence of **risk factors** (severely ill or immunocompromised patients should receive IV antibiotics).

COMMENT BOX
If there is an **abscess**, it should be **drained** first and the antibiotics may or may not be initiated depending on the clinical picture.

Antibiotic groups according to their activity against specific microorganisms

Anti-pseudomonas activity	Anti-MRSA activity	Anti-TB activity
Carbapenems (NOT Ertapenem)	Glycopeptides (Vancomycin, Teicoplanin)	Rifampicin
Aminoglycosides	Ceftaroline Fosamil	Isoniazid
Ticarcillin/Clavulanate, Piperacillin/Tazobactam	SMX-TMP	Ethambutol
Monobactams	Clindamycin	Pyrazinamide
Third generation Cephalosporin (Ceftazidime and Cefoperazone)	Tetracycline (Tigecycline, minocycline)	Streptomycin
Cefepime	Linezolid	Fluoroquinolones
Ciprofloxacin	Rifampicin	Aminoglycosides
Colistin	Daptomycin	Para-amino salicylic acid