Aantimicrobial agents

ANTIMICROBIAL AGENTS

- **Anti microbial agents:**
- includes **synthetic** as well as **naturally** obtained drugs that supress growth or kill microorganisms.

classification

- Anti-bacterial.
- Anti-viral.
- Anti-fungal.
- Anti-parasitic agents.

Mechanism of Action

- **Agents that inhibit synthesis of bacterial cell walls**

  Penicillins & cephalosporins

  Vancomycin

  Azole antifungal agents (clotrimazole, fluconazole, itraconazole)

- **Agents that act directly on the cell membranes of the microorganisms**

  Polyene antifungal agents

  (Nystatin, Amphotericin B)

Alter cell memb. Permeability and lead to leakage of intracellular comp.

Gram-Positive Cocci		
Streptococcus pneumoniae[7] (pneumococcus)	Penicillin[6]	Macrolide,[2] a cephalosporin,[8] vancomycin, clindamycin, a tetracycline,[3] respiratory fluoroquinolones[1]
Streptococcus, hemolytic, groups A, B, C, G	Penicillin[6]	Macrolide,[2] a cephalosporin,[8] vancomycin, clindamycin
Viridans streptococci	Penicillin[6] ± gentamicin	Cephalosporin,[8] vancomycin
Staphylococcus, methicillin-resistant	Vancomycin	TMP-SMZ,[4] doxycycline, minocycline, linezolid[11], tedizolid[11], daptomycin[11], televancin[11], dalbavancin[11], oritavancin[11], ceftaroline
Staphylococcus, non-penicillinase-producing	Penicillin[6]	A cephalosporin,[8] clindamycin
Staphylococcus, penicillinase-producing	Penicillinase-resistant penicillin[9]	Vancomycin, a cephalosporin,[8] clindamycin, amoxicillin-clavulanic acid, ampicillin-sulbactam, piperacillin-tazobactam, TMP-SMZ[4]
Enterococcus faecalis	Ampicillin ± gentamicin[10]	Vancomycin ± gentamicin
Enterococcus faecium	Vancomycin ± gentamicin[10]	Linezolid,[11] quinupristin-dalfopristin,[11] daptomycin,[11] tigecycline,[11] tedizolid,[11] oritavancin[11]

Suspected or Proved Etiologic Agent	Drug(s) of First Choice	Alternative Drug(s)
Gram-Negative Cocci		
Moraxella catarrhalis	Cefuroxime, a fluoroquinolone[1]	Ceftriaxone, cefuroxime axetil, a macrolide,[2] a tetracycline,[3] amoxicillin-clavulanic acid, TMP-SMZ[4]
Neisseria gonorrhoeae (gonococcus)	Ceftriaxone plus azithromycin or doxycycline	Cefixime plus azithromycin or doxycycline[5]
Neisseria meningitidis (meningococcus)	Penicillin[6]	Ceftriaxone, ampicillin

- **Agents that affect the function of 30S or 50S ribosomal subunits to cause a reversible inhibition of protein synthesis**
- Bacteriostatic drugs

  Chloramphenicol, Tetracyclines, Erythromycin, Clindamycin.

- **Agents that bind to 30S ribosomal subunit & alter protein synthesis, which eventually leads to cell death**

  Aminoglycosides

- **Agents that affect bacterial nucleic acid metabolism**.

  Rifamycins which inhibit RNA polymerase

  Quinolones which inhibit topoisomerases

- Metronidazole diffuses into the organism, inhibits protein synthesis by interacting with DNA and causing a loss of helical DNA structure and strand breakage. Therefore, it causes cell death in susceptible organisms

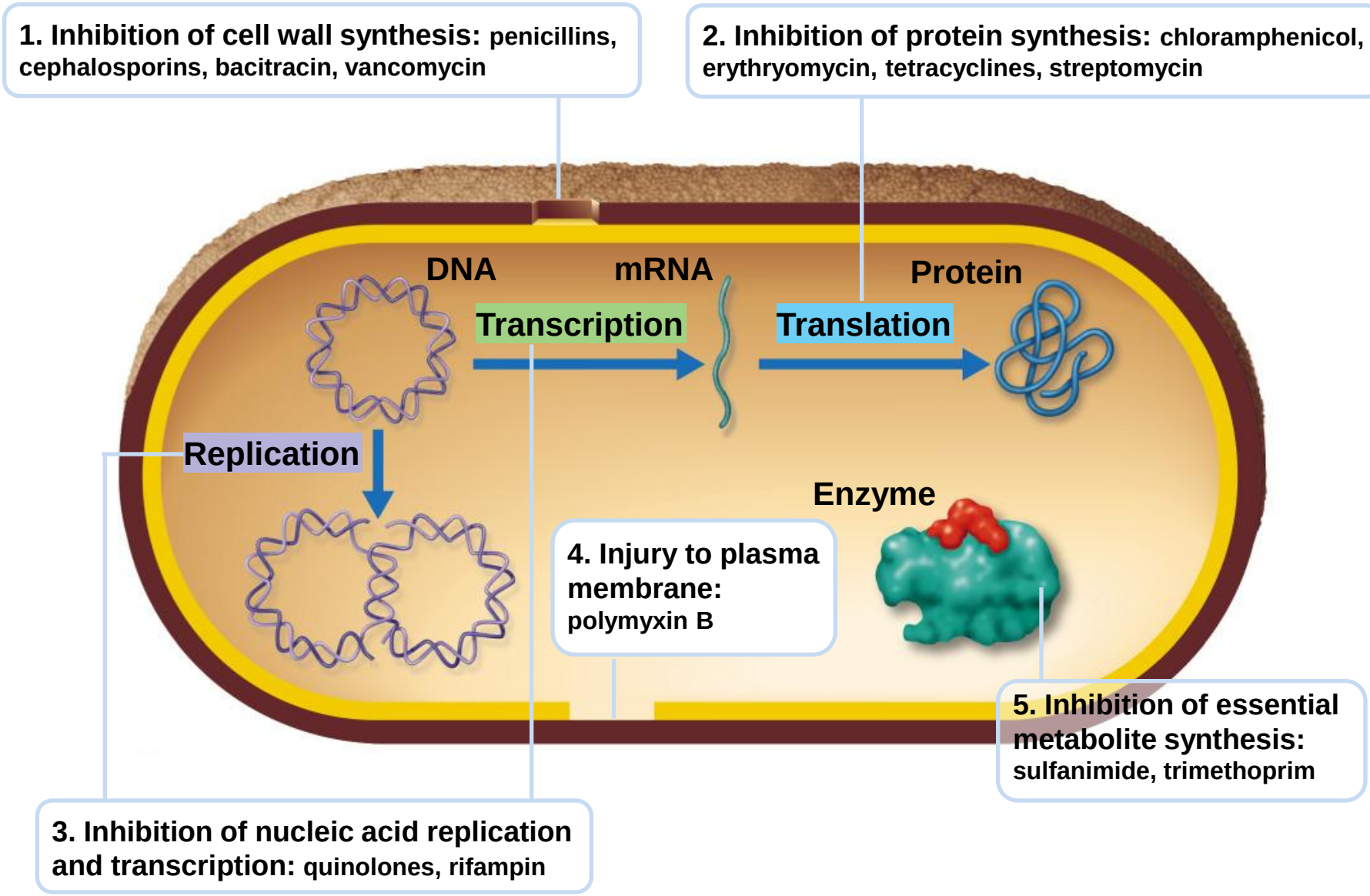
Bacteroides, gastrointestinal strains	Metronidazole	Ampicillin-sulbactam, piperacillin-tazobactam, carbapenem

- **Anti-metabolites**
  including trimethoprim & sulphonamides

Antiviral agents

- Nucleic acid analogues.
- Non-nucleoside reverse transcriptase inhibitors.
- Inhibitors of viral enzymes

Figure 20.2 Major Action Modes of Antimicrobial Drugs.



Type of action

Bacteriostatic Agents

Bactericidal Agents

Bacteriostatic Agents

Sulphonamides

Tetracyclines

Chloramphenicol

Erythromycin

Ethambutol

Bactericidal Agents

Penicillins/Cephalosporins.

Aminoglycosides

Rifampin

- **Isoniazid**
- **Pyrazinamide**

Othe bactericidal ab

Cephalosporins

Vancomycin

Nalidixic acid

Ciprofloxacin

Metronidazole

& Cotrimoxazole

Successful Antimicrobial Therapy

- **Concentration:** site of infection

  Concentration should inhibit microorganisms

  simultaneously it should be below the level toxic to human beings.
- **Host Defences**

  Immunity intact - Bacteriostatic Agents

  Impaired immunity - Bactericidal Agents

Factors to consider when prescribing an antibiotic

- Any history of allergy, toxicity?
- Is it appropriate for the spectrum I want to cover?
- What route of admin: oral or i.v?
- Any factors affecting absorption ?
- Is it going to reach the site of infection?
- Any drug interactions?
- Any serious toxicity eg, hepatic, renal?
- Does it need monitoring eg aminoglycosides, vancomycin, streptomycin?

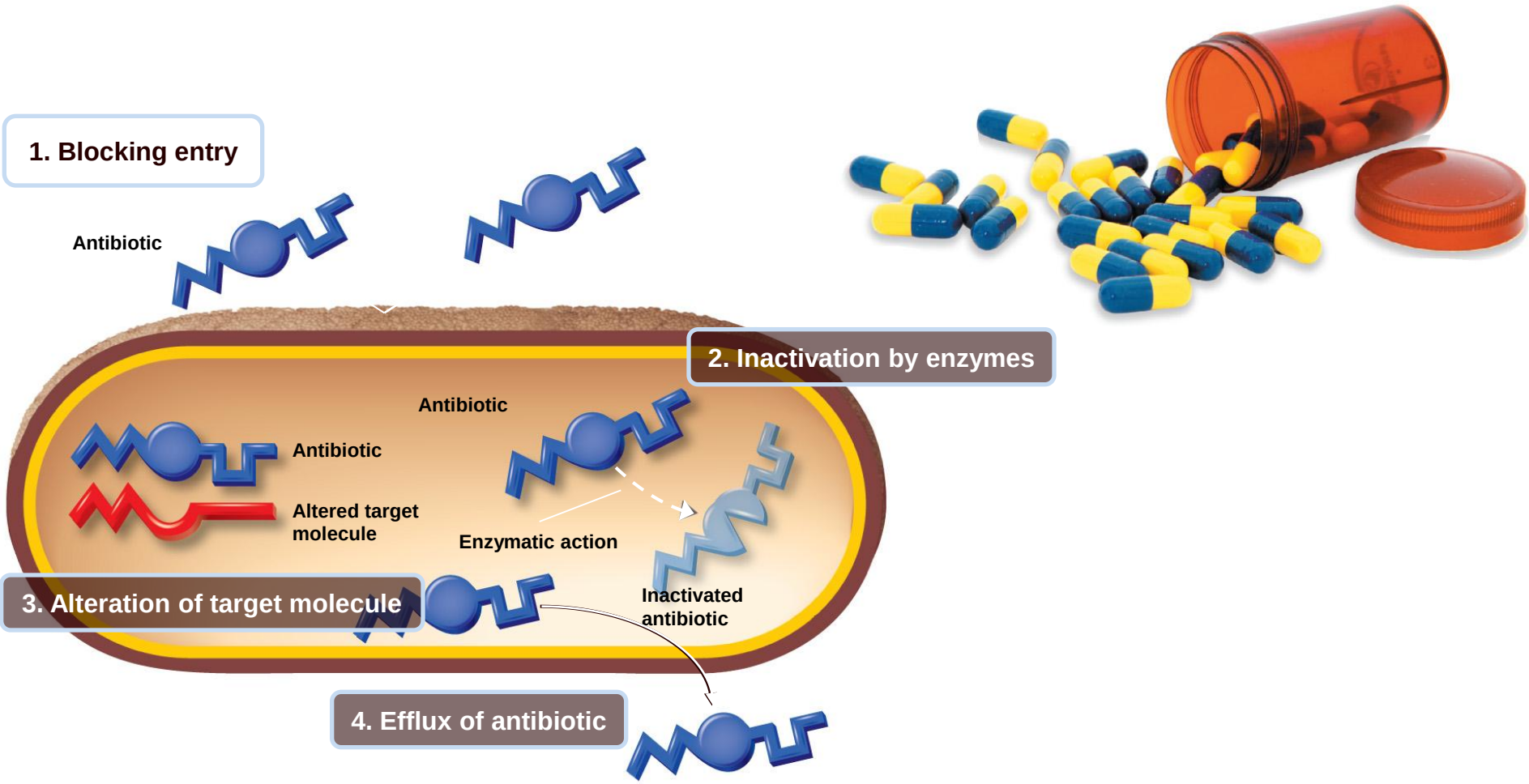
Effects of Combinations of Drugs

- **Synergism** occurs when the effect of two drugs together is greater than the effect of either alone
- **Antagonism** occurs when the effect of two drugs together is less than the effect of either alone

Pneumonia, acute, community-acquired, non-ICU hospital admission	Pneumococci, *M pneumoniae*, *Legionella*, *C pneumoniae*	Ceftriaxone, 1 g intravenously every 24 hours or ampicillin, 2 g intravenously every 6 hours) **plus** azithromycin, 500 mg intravenously every 24 hours; **or** a respiratory fluoroquinolone[3] alone

Resistance

Figure 20.20 Bacterial Resistance to Antibiotics.



Prevention of drug resistance

Prevention drug resistance

- Use of AMAs should not be:

  indiscriminate.

  inadequate .

  unduly prolonged.
- Use rapidly acting & narrow spectrum (Selective) AMA whenever possible.

Prevention DRUG RESISTANCE

- **Combination AMA**
  - whenever prolonged therapy is undertaken. Tuberculosis, SABE
- Infection by organism notorious for developing resistance Staph, E. Coli, M. Tuberculosis must be **treated intensively.**

Pseudomonas aeruginosa	Piperacillin-tazobactam or ceftazidime or cefepime, or imipenem or meropenem or doripenem or aztreonam ± aminoglycoside[12]	Ciprofloxacin (or levofloxacin) ± piperacillin-tazobactam; ciprofloxacin (or levofloxacin) ± ceftazidime; ciprofloxacin (or levofloxacin) ± cefepime; ceftazidime-avibactam[13]; ceftolozane-tazobactam[13]

Cystitis	*Escherichia coli*, *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, *Proteus* species, other gram-negative rods or enterococci	Nitrofurantoin monohydrate macrocrystals 100 mg twice daily for 5–7 days (unless pregnant); fosfomycin 3 g orally as a single dose	Cephalexin, 0.5 g orally four times daily for 7 days, for uncomplicated cystitis. Due to increasing resistance, TMP-SMZ and fluoroquinolones should not be used as first-line therapy for empiric treatment
Pyelonephritis	*E coli*, *K pneumoniae*, *Proteus* species, *S saprophyticus*	Fluoroquinolones[4] for 7 days if prevalence of resistance among uropathogens is < 10%	TMP-SMZ,[1] one double-strength tablet twice daily for 7–14 days for susceptible pathogens. Oral beta-lactams are considered less effective

Pharyngitis	Group A streptococcus	Phenoxymethyl penicillin, 0.5 g orally four times daily, **or** amoxicillin, 0.5–1 g orally three times daily, for 10 days	For patients with history of mild penicillin allergy, cephalexin, 0.5 g orally four times daily for 10 days; for patients with more severe penicillin allergy, clindamycin, 300 mg orally four times daily for 10 days; **or** azithromycin, 500 mg on day 1 and 250 mg on days 2–5; **or** azithromycin for susceptible isolates
Otitis media	*Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*	Amoxicillin, 0.5–1 g orally three times daily for 10 days	Augmentin,[2] 0.875 g orally twice daily; **or** cefuroxime, 0.5 g orally twice daily; **or** cefpodoxime, 0.2–0.4 g daily; **or** doxycycline, 100 mg twice daily
Acute sinusitis	*S pneumoniae, H influenzae, M catarrhalis*	Augmentin,[2] 0.875 g orally twice daily	For patients allergic to penicillin, doxycycline, 100 mg twice daily for 10 days, or secondarily, some fluoroquinolones[5] can be considered. Due to increasing resistance among pneumococci, monotherapy with a macrolide, a cephalosporin, or TMP-SMZ is not recommended

- Thank you