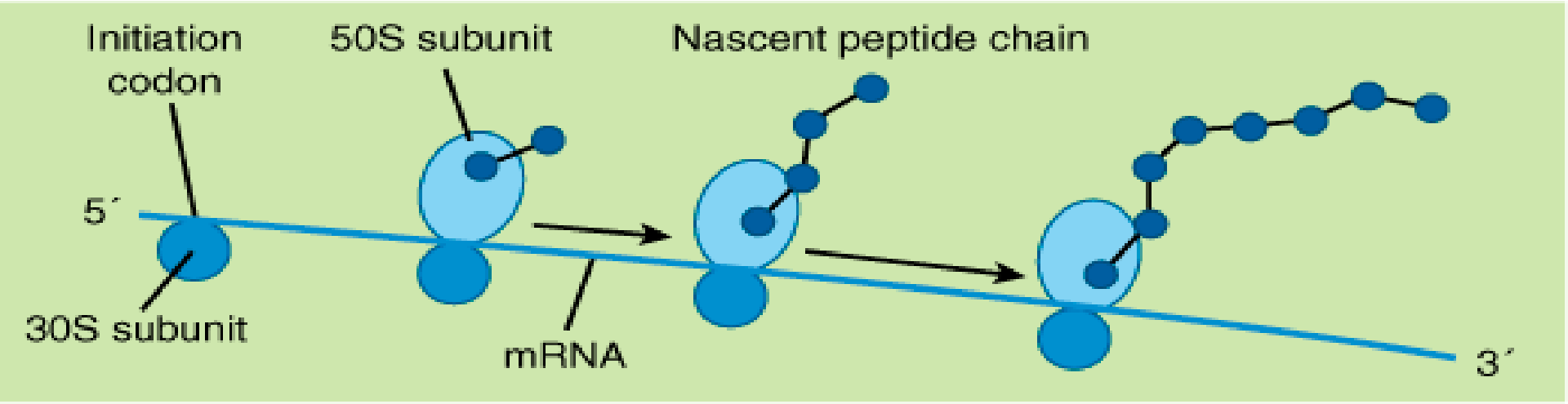
Aminoglycosides

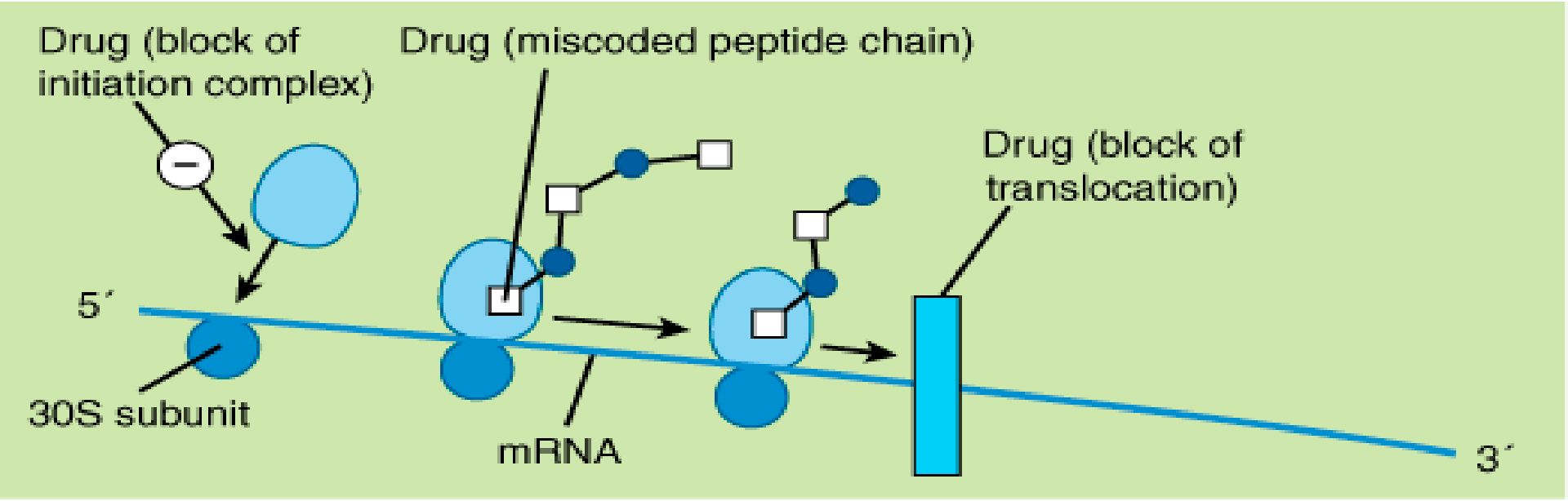
- **The only bactericidal protein synthesis inhibitors.**
- **They bind to the ribosomal 30S subunit.**
- **Inhibit initiation of peptide synthesis and cause mis-reading of the genetic code.**
- **Streptomycin is the oldest member of the group, 1947**
- **Amikacin**
- **Gentamicin**
- **Tobramycin**
- **Netilmycin**
- **Neomycin.**

- **Spectrum includes many aerobic Gram-negative and some Gram-positive bacteria.**

Normal bacterial cell



Aminoglycoside-treated bacterial cell



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition*: http://www.accessmedicine.com

Clinical Uses of Aminoglycosides

- Widely used in the empirical treatment of infections suspected of being due to aerobic gram-negative bacilli.
- Gram –ve bacillary infection, septicemia, pelvic & abdominal sepsis
- Bacterial endocarditis
- Enterococcal, streptococcal or staphylococcal pneumonia.
- Tuberculosis
- Plague, Brucellosis
- To sterilize the bowel of patients who receive immunosuppressive therapy, before surgery & in hepatic coma

Aminoglycosides

- **Aminoglycosides are poorly absorbed from all sites of administration including the GI tract.**
- **They are usually administered intramuscularly or intravenously, or topically. They can be given orally to act locally in sterilizing the GIT.**
- **Serious dose-related side-effects occur with the aminoglycosides,**
- **The main hazards are Nephrotoxicity and Ototoxicity, may also cause n.m. blockade**

Clinical Uses of Aminoglycosides

- **Gentamycin is usually the first choice due to its low cost, reliable activity and long experience of use. Used in infected burns, otitis externa, acute pyelonephritis.**
- **Tobramycin is the most active against *Pseudomonas* infections**
- **Amikacin has the broadest antibacterial spectrum. Preferred in serious nosocomial G –ve bacillary infection in hospitals where Tobramycin & Gentamicin have developed resistance.**
- **Neomycin is reserved for topical applications because of its serious systemic toxicity.**

Clindamycin

- **Active against Gram-positive cocci, including penicillin-resistant staphylococci, and many anaerobic bacteria.**

- **Binds to the 50S ribosomal subunit and inhibits the correct attachment of the amino acid end of aminoacyl-tRNA.**
- **Mainly used in infections caused by *Bacteroides* organisms and in staphylococcal infections of bones and joints.**
- **Nearly completely absorbed (90%), and penetrates deeply into the soft tissues of the body, as well as bone, where dental infections reside.**

Clinical Uses of Clindamycin

- **Penetrating wounds of the abdomen and the gut.**
- **Female genital tract infections, like septic abortion.**
- **Aspiration pneumonia.**
- **Highly effective in dental infections.**

Side-effects of Clindamycin

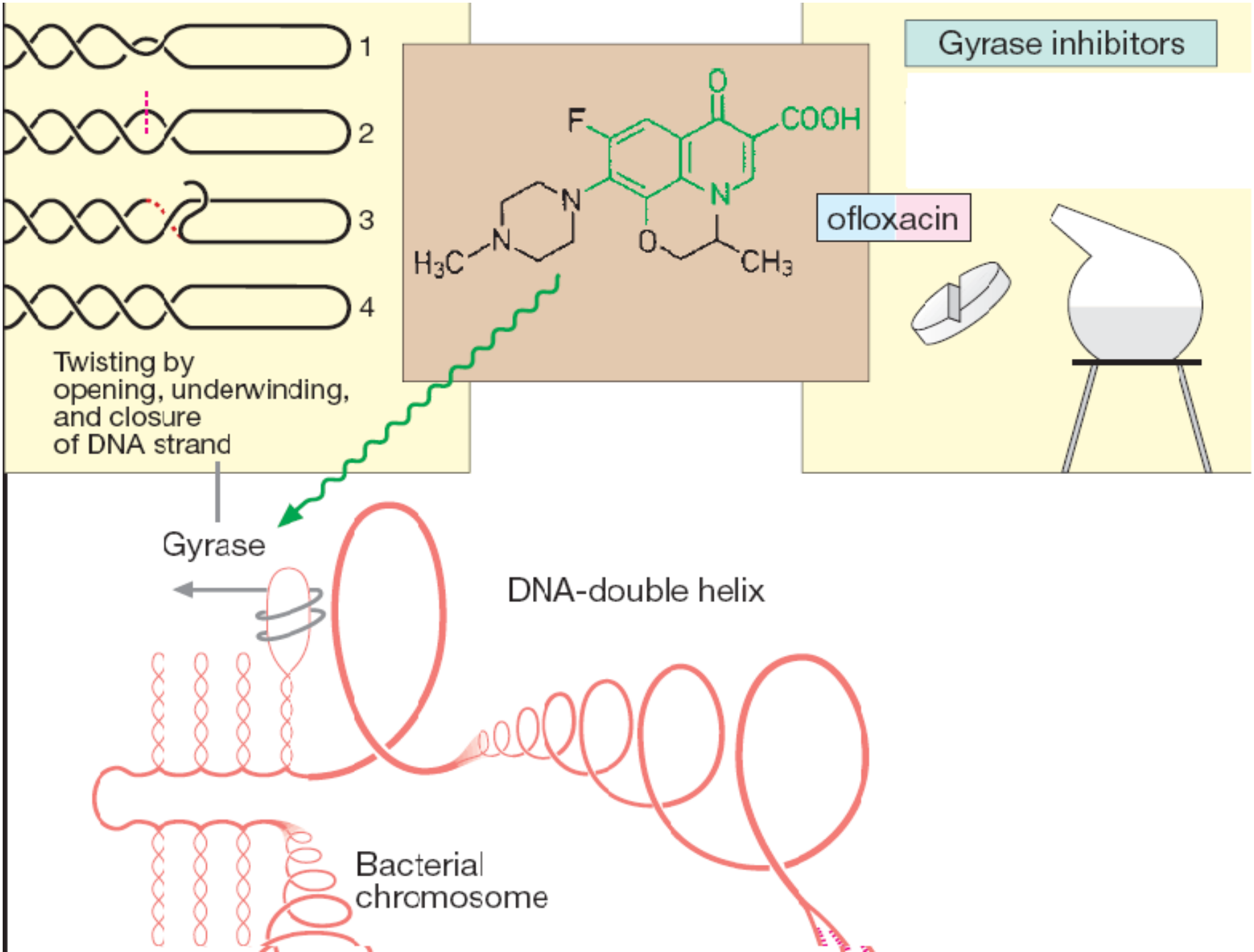
- **Pseudomembranous colitis: This is a very serious condition. *Clostridium difficile* outbreak can spreadin hospital patients within a week.**
  With weakened intestinal flora due to antibiotics, *C. difficile* could be fatal. Immediately upon finishing a course of clindamycin, or any antibiotic, one should take probiotics(beneficial bacteria) to repopulate the intestines. Eat your yogurt!

Quinolones

- **First oral antibiotics effective against gram-negative bacteria.**
- **Ciprofloxacin is the most commonly used fluoroquinolone.**
- **Ciprofloxacin is the most active member against gram-negatives, *Pseudomonas aeruginosa* in particular**
- **Ofloxacin**
- **Levofloxacin**
- **Gemifloxacin**
- **Moxifloxacin**
- **These have improved activity against gram-positive organisms, particularly *S. pneumoniae* and some staphylococci.**

Quinolones

- **Specific inhibitors of DNA gyrase by trapping the enzyme in its cleavable complex.**
- **Bacterial DNA gyrase is a type II topoisomerase that produces transient double strand breaks in DNA.**
- **Inhibition of DNA gyrase prevents the relaxation of positively supercoiled DNA required for normal transcription and replication.**
- **Quinolones are broad spectrum antibiotics, active against both Gram-negative and Gram-positive bacteria.**
- **More active against Gram-negative species.**


1
2
3
4
Twisting by
opening, underwinding,
and closure
of DNA strand
Gyrase
F
COOH
O
N
N
O
H_3C
CH_3
Gyrase inhibitors
ofloxacin
DNA-double helix
Bacterial
chromosome

Clinical Uses of Quinolones

Complicated urinary tract infections

Respiratory infections in patients with cystic fibrosis

Levofloxacin,, gemifloxacin, and moxifloxacin, so-called respiratory fluoroquinolones, have enhanced activity against gram-positive bacteria and atypical pneumonia agents (e.g. chlamydia, mycoplasma, and legionella), nowadays are increasingly used for treatment of upper and lower respiratory tract infections.

Infections of soft tissues, bones, and joints and intra-abdominal infections

Bacterial prostatitis and cervicitis

Bacterial diarrhoea caused by shigella, salmonella, and *E. coli*.

Side Effects of Quinolones

- **Mainly cause GI symptoms (nausea, vomiting, and diarrhea) and skin rashes.**

- **Arthropathy, may damage growing cartilage, particularly in young individuals.**

  So, contraindicated in children (under 18) except in special cases.

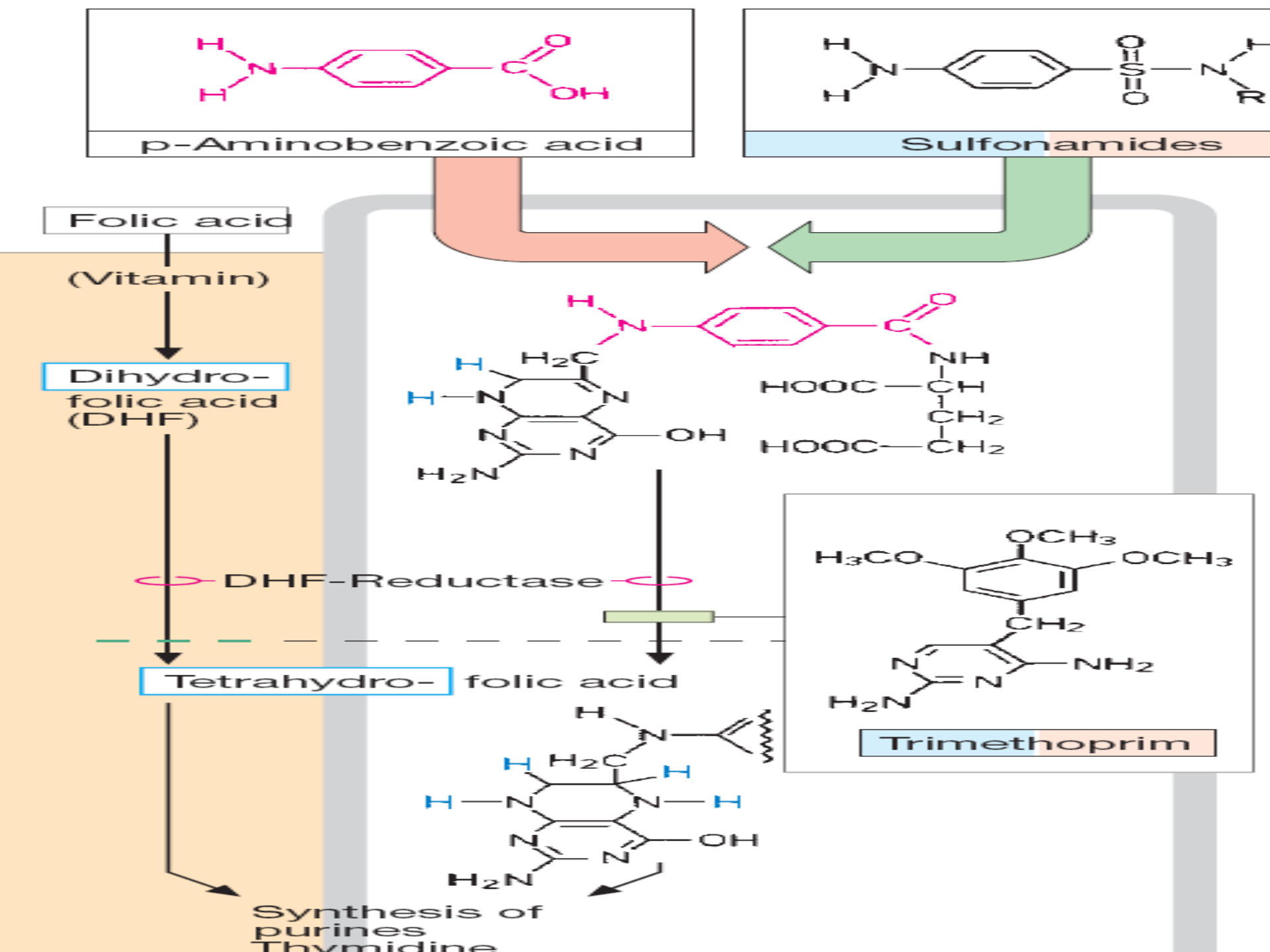
Sulphonamides

- **Sulphonamides have a similar structure to p-aminobenzioc acid (PAPA), which is a precursor of Folic acid.**

- **Compete with PAPA for the bacterial enzyme, dihydropteroate synthetase. Thus, they inhibit the synthesis of bacterial folic acid, and the end result is interference with nucleic acid synthesis**

- **The sulphonamides are bacteriostatic.**

- **Resistance is common, mainly via up-regulation of the synthesis of PABA and by mutations in dihydropteroate synthetase.**


p-Aminobenzoic acid
Sulfonamides
Folic acid
(Vitamin)
Dihydro-
folic acid
(DHF)
DHF-Reductase
Tetrahydro-
folic acid
Trimethoprim
Synthesis of
purines
Thymidine

Sulphonamides

Orally Absorbable Agents:

Sulfisoxazole and sulfamethoxazole are almost exclusively used in urinary tract infections.

Orally Nonabsorbable Agents:

Sulfasalazine, and salicylazosulfapyridine are widely used in ulcerative colitis, enteritis, and other inflammatory bowel disease

-Topical Agents:

Silver sulfadiazine is used for burn wound infections.

Sulphonamides

- **Sulphonamides have mild to moderate side-effects including, nausea, vomiting, headache, and depression.**

- **More serious side-effects include hepatitis, hypersensitivity reactions, bone marrow depression, and aplastic anemia.**

- **Sulfonamides may provoke hemolytic reactions in patients with glucose-6-phosphate dehydrogenase deficiency.**

VRE and more

- **Teicoplanin** is used in the prophylaxis and treatment of serious infections caused by Gram-positive bacteria, including **methicillin-resistant *Staphylococcus aureus* and *Enterococcus faecalis*.**

- **Linezolid** is approved for **vancomycin-resistant *E faecium* infections**; nosocomial pneumonia; community-acquired pneumonia; and skin infections, complicated or uncomplicated.

  It should be reserved for treatment of infections caused by multidrug-resistant gram-positive bacteria.

- **Daptomycin** is active against vancomycin-resistant strains of enterococci and *S aureus*.

Commonly prescribed ABX in the community setting

- Oral infections: penicillin, clindamycin, erythromycin, amoxicillin, cephalexin
- UTI: ciprofloxacin, SMX/TMP
- RTI's, sinusitis: clarithromycin, azithromycin, 2nd or 3rd gen Cephs, amoxi/clav, levo-/moxifloxacin
- Skin/nail/bites: cephalexin, cloxacillin, amoxi/clav
- Travellers' diarrhea: azithromycin, ciprofloxacin, norfloxacin
- H. pylori: amoxi+clarithromycin, metronidazole+clarithromycin, tetracycline+metronidazole

Commonly prescribed ABX in the community setting

- **Bacterial vaginosis: metronidazole, clindamycin**
- **Chlamydia: single dose azithromycin, 7-day course doxycycline, ofloxacin**
- **Gonorrhea: cefixime, ceftriaxone**
- **Acne: tetracyclines, erythromycin**
- **Acute otitis media: Macrolides, amoxicillin, amoxi/clav, 2nd gen Cephs**
- **Patients with penicillin allergy: clindamycin or erythromycin.**
- **Intraabdominal infections: ciprofloxacin, metronidazole, 3rd gen Cephs**
- **C. difficile diarrhea: metronidazole, vancomycin**