
بسم الله الرحمن الرحيم

Common Antibacterials in Veterinary Medicine

Antibacterials play a crucial role in veterinary medicine, treating bacterial infections in animals, protecting their health, and safeguarding public health.

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Basic principals of chemotherapy

History and definition

Paul Ehrlich (1865-1915)

“Selective toxicity”

Target sites” for antibacterials

A) Cell wall

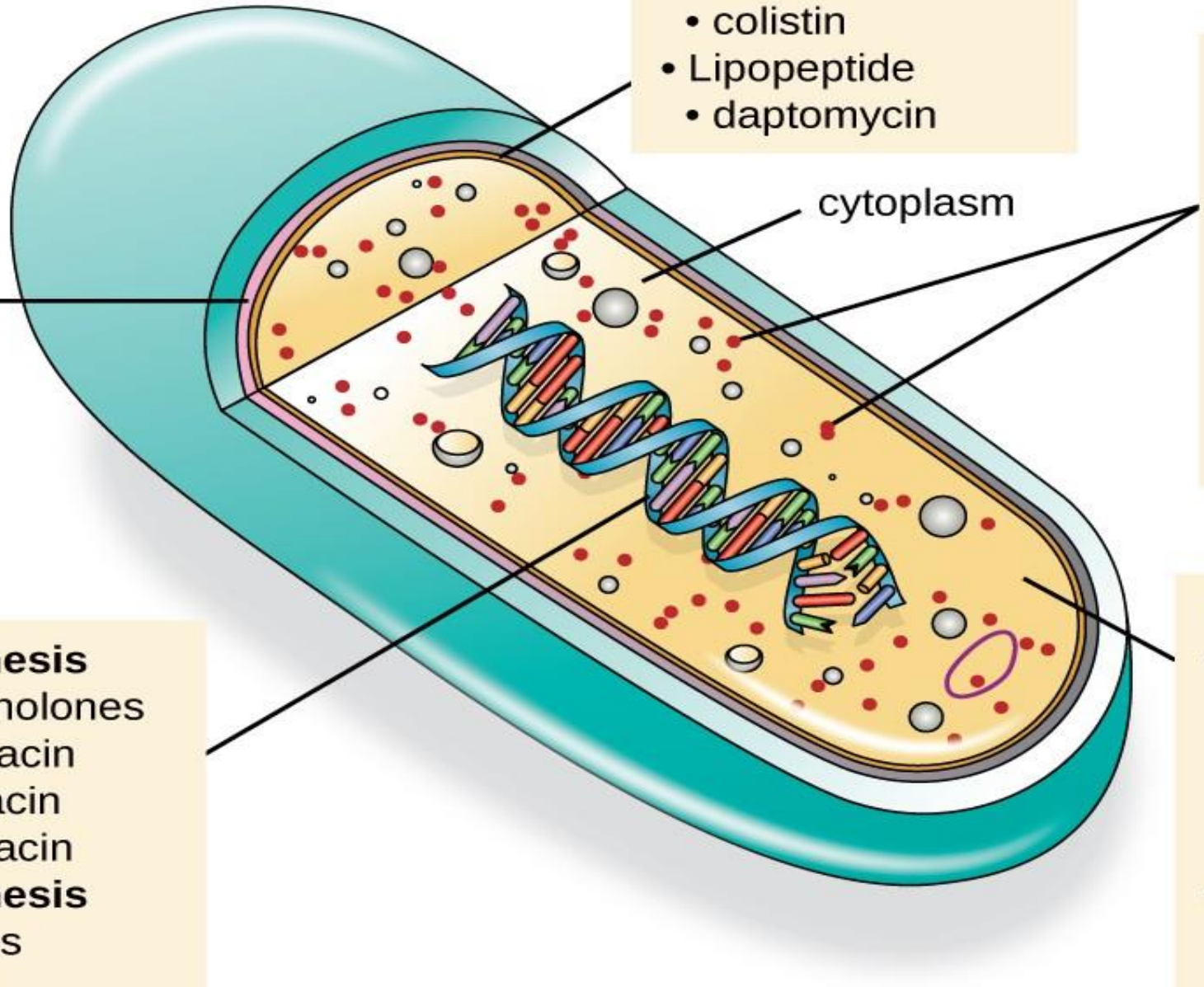
B) Cytoplasmic membrane

C) Protein synthesis

D) Metabolism of nucleic acids

Plasma membrane
- Polymyxins
  - polymyxin B
  - colistin
- Lipopeptide
  - daptomycin

Cell wall
- β-lactams
  - penicillins
  - cephalosporins
  - monobactams
  - carbapenems
- Glycopeptides
  - vancomycin
- Bacitracin



Ribosomes
- 30S subunit
  - aminoglycosides
  - tetracyclines
- 50S subunit
  - macrolides
  - lincosamides
  - chloramphenicol
  - oxazolidinones

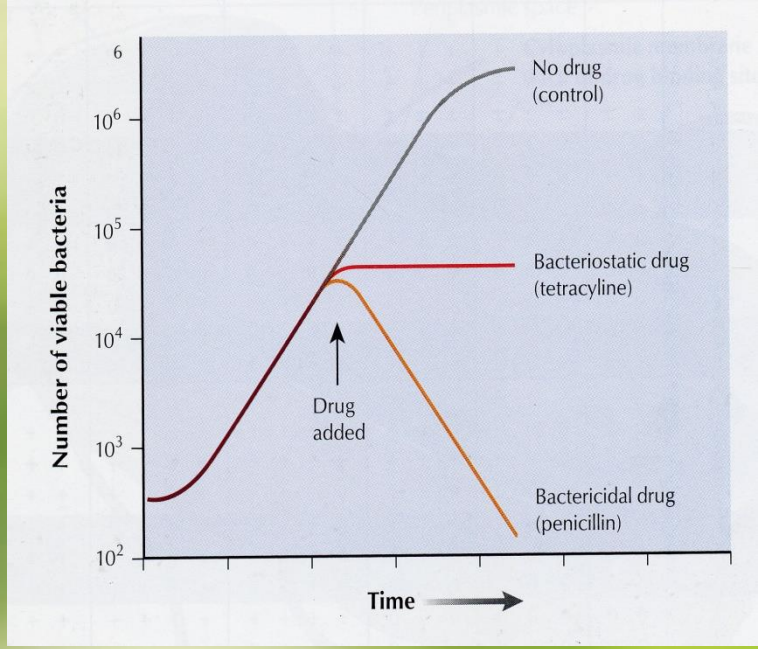
DNA synthesis
- Fluoroquinolones
  - ciprofloxacin
  - levofloxacin
  - moxifloxacin

RNA synthesis
- Rifamycins
  - rifampin

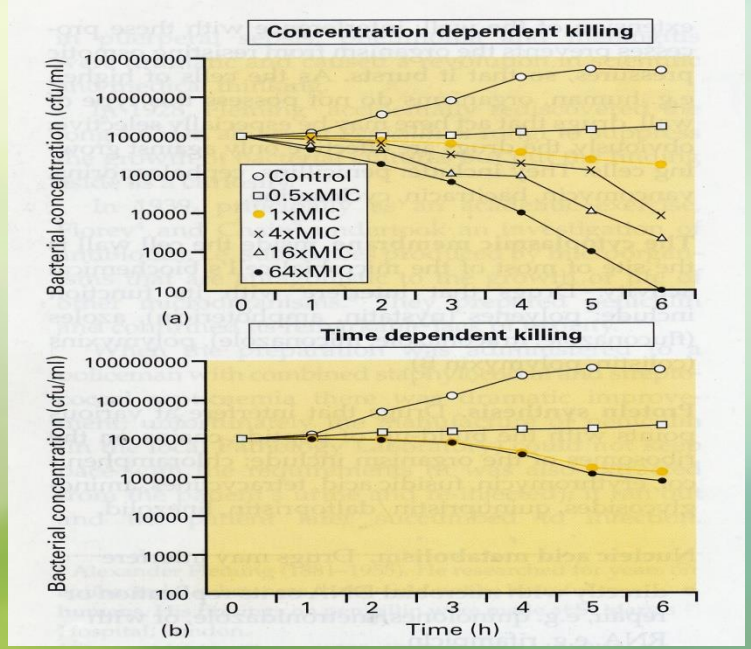
Metabolic pathways
- Folic acid synthesis
  - sulfonamides
  - sulfones
  - trimethoprim
- Mycolic acid synthesis
  - izoniazid

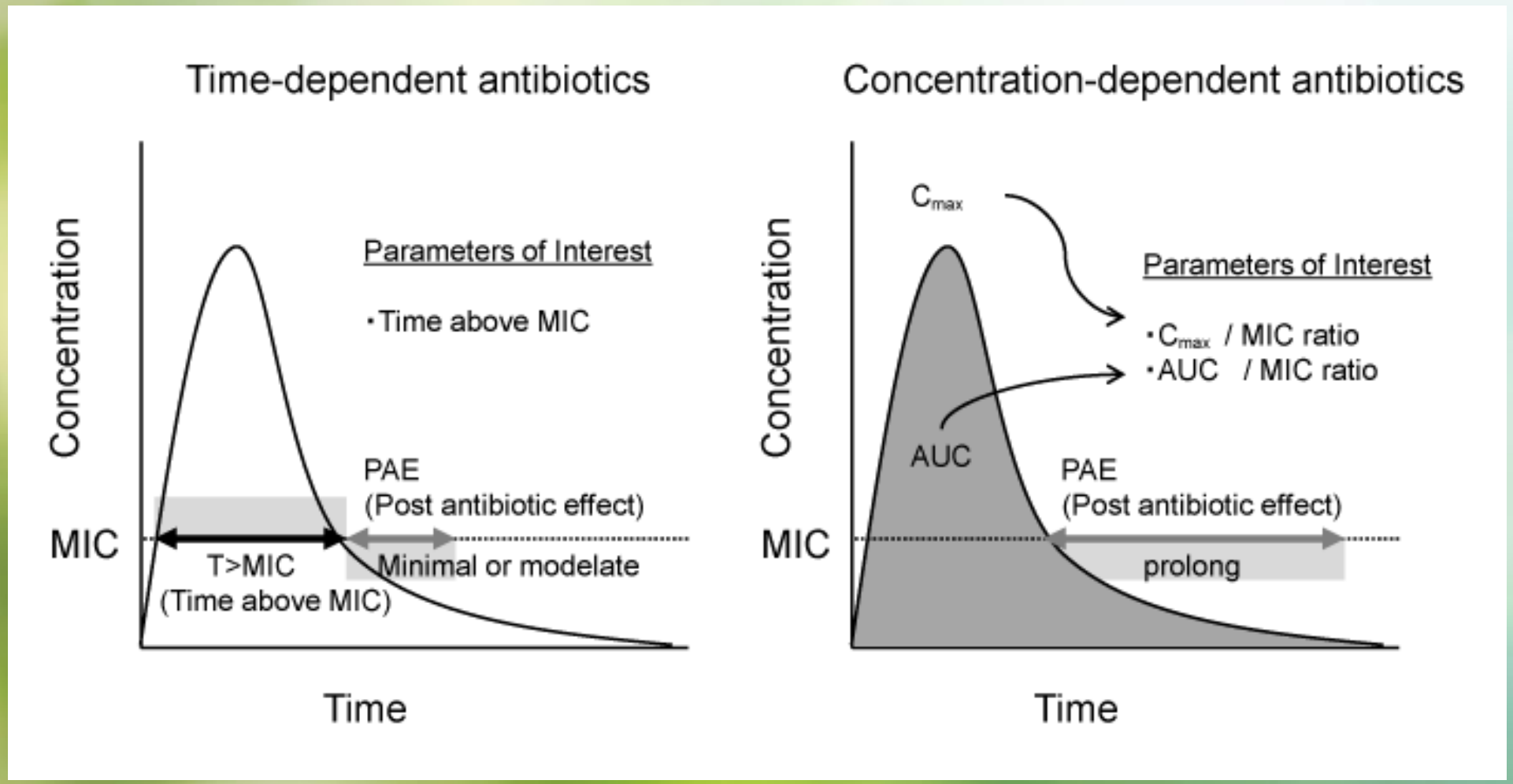
•*Classification of antibacterial agents:*

- *Bacteriostatic* or *Bactericidal* agents



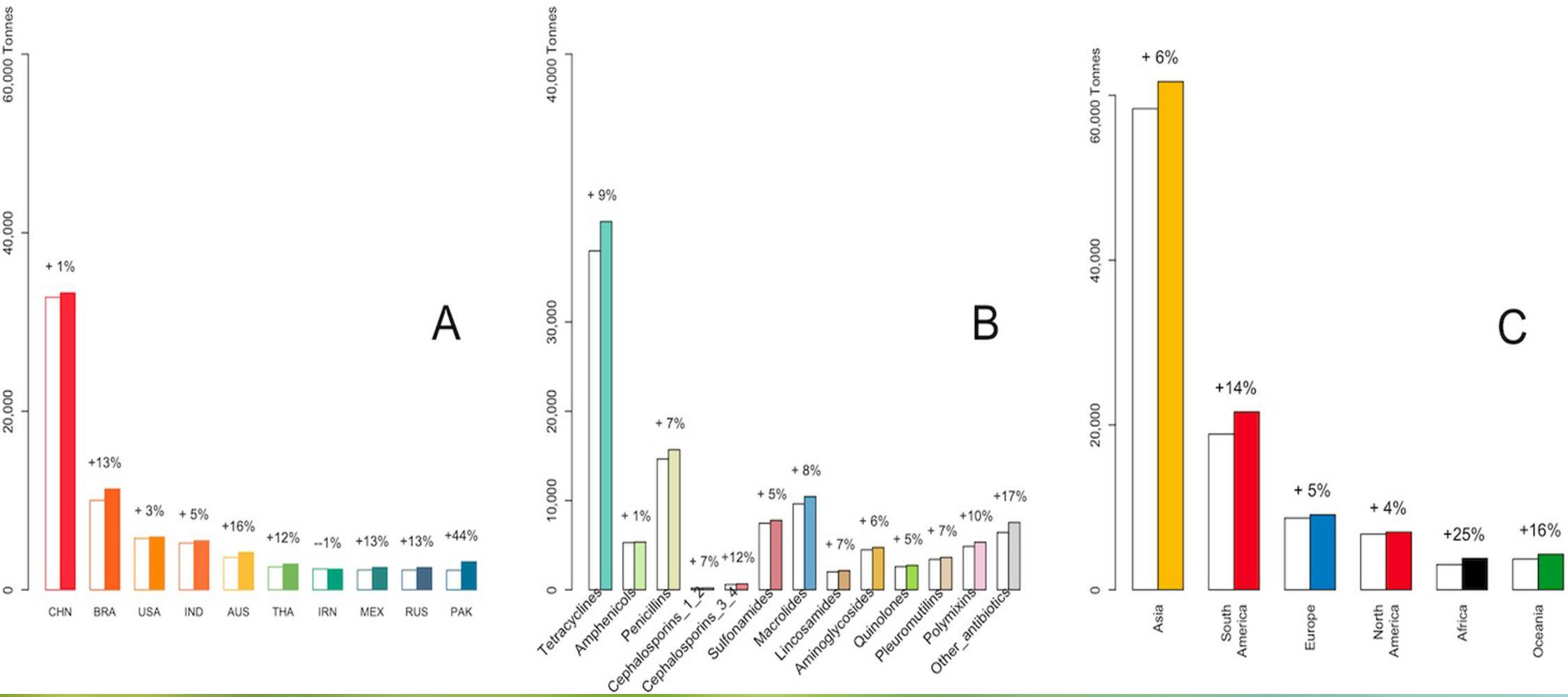
- *Concentration-dependent* vs. *time-dependent* effects



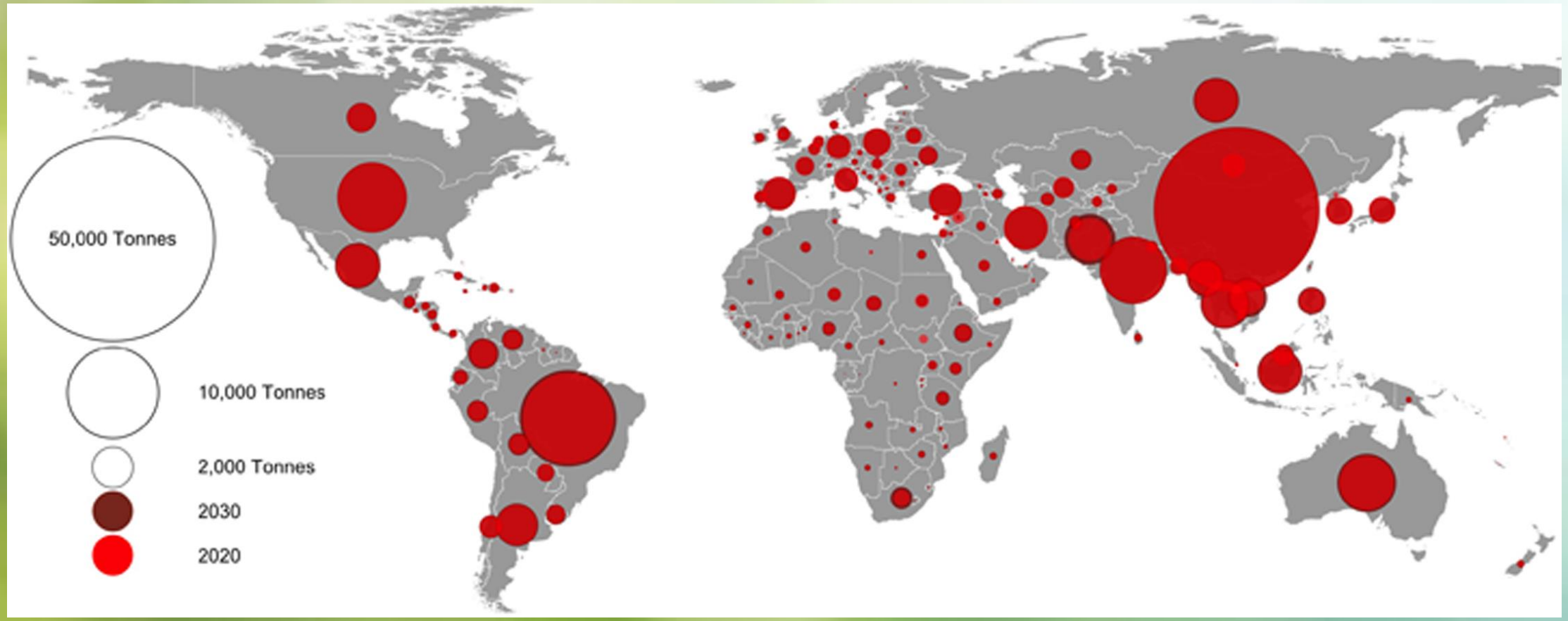

Time-dependent antibiotics
Concentration
MIC
Parameters of Interest
・Time above MIC
PAE
(Post antibiotic effect)
T>MIC
(Time above MIC)
Minimal or modelate
Time
Concentration-dependent antibiotics
Concentration
MIC
Cmax
Parameters of Interest
・Cmax / MIC ratio
・AUC / MIC ratio
AUC
PAE
(Post antibiotic effect)
prolong
Time

Excessive use of antibacterials especially in food animals and its consequences

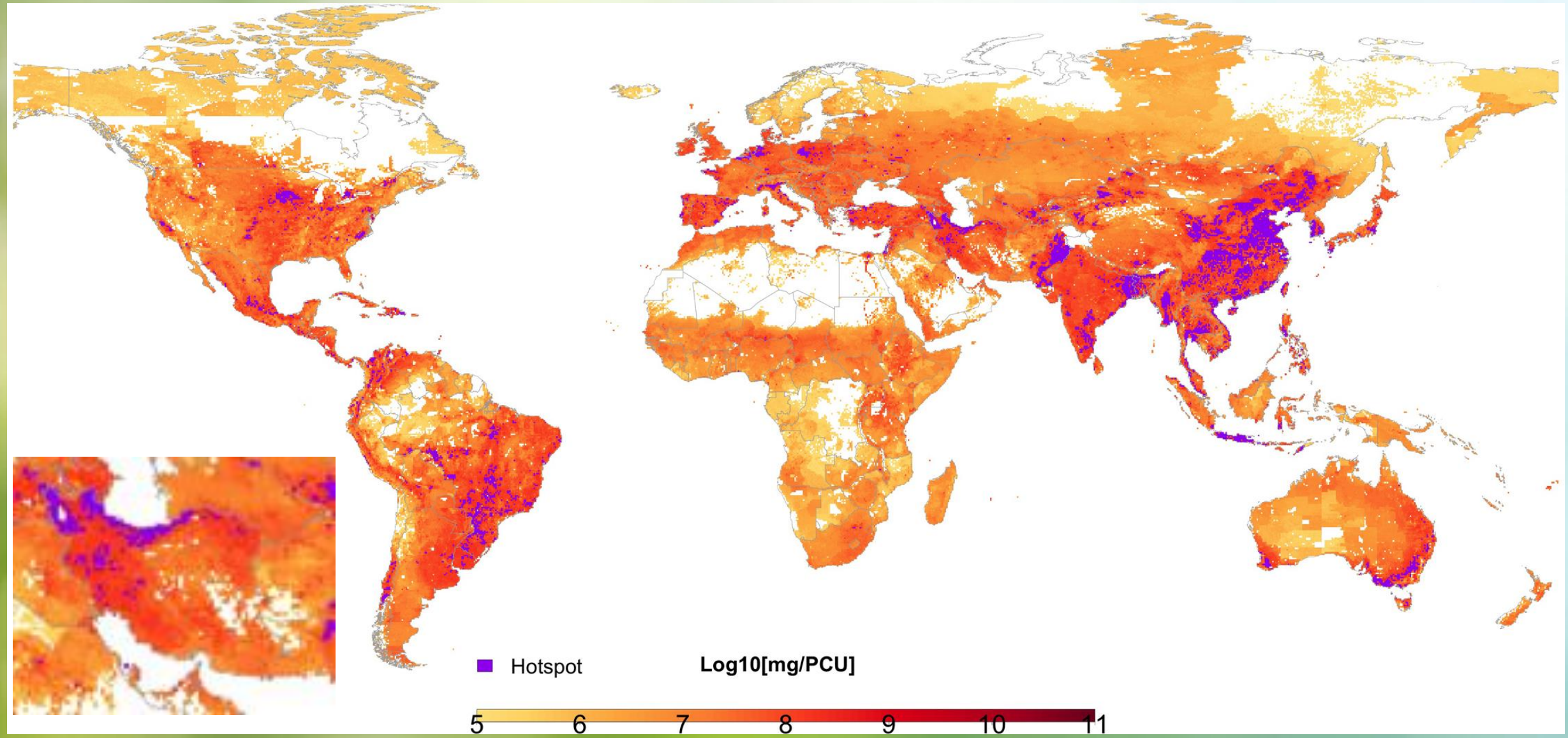
- Globally, antimicrobial usage in food producing animals including for cattle, sheep, chicken, and pigs was estimated at 99,502 tons (95% CI 68,535–198,052) in 2020 and is projected, based on current trends, to increase by 8.0% to 107,472 tons (95% CI: 75,927–202,661) by 2030.
- Hotspots of antimicrobial use were overwhelmingly in Asia (67%), while <1% were in Africa.



veterinary antimicrobial consumption in 2020 (white bars) and their projected consumption for 2030 (coloured bars) by (A) country (top 10), (B) antimicrobial class, and (C) continent. CHN, China; BRA, Brazil; IND, India; USA, United States; AUS, Australia; IRN, Iran; THA, Thailand; PAK, Pakistan; JPN, Japan; MEX, Mexico. https://doi.org/10.1371/journal.pgph.0001305



Circles are proportional to quantity of antimicrobials used. Red circles correspond to the quantity used in 2020, and outer dark red ring corresponds to the projected increase in consumption in 2030.



Global distribution of veterinary antimicrobial consumption at 10 x 10 kilometers resolution expressed in milligrams per biomass (population correction units).

BASIC GROUNDS

- Currently, the average annual consumption of antibiotics per kilogram of animal product worldwide is estimated to be 45 mg/kg for cattle vs. 148 mg/kg for chickens.

- Antibiotic resistance – when antibiotics stop functioning – is threatening millions of human lives and the health, welfare and productivity of our livestock.
- The more we use antibiotics, the greater the chance that antibiotic resistance will develop. Therefore, it is important that we use antibiotics only when they are really needed.

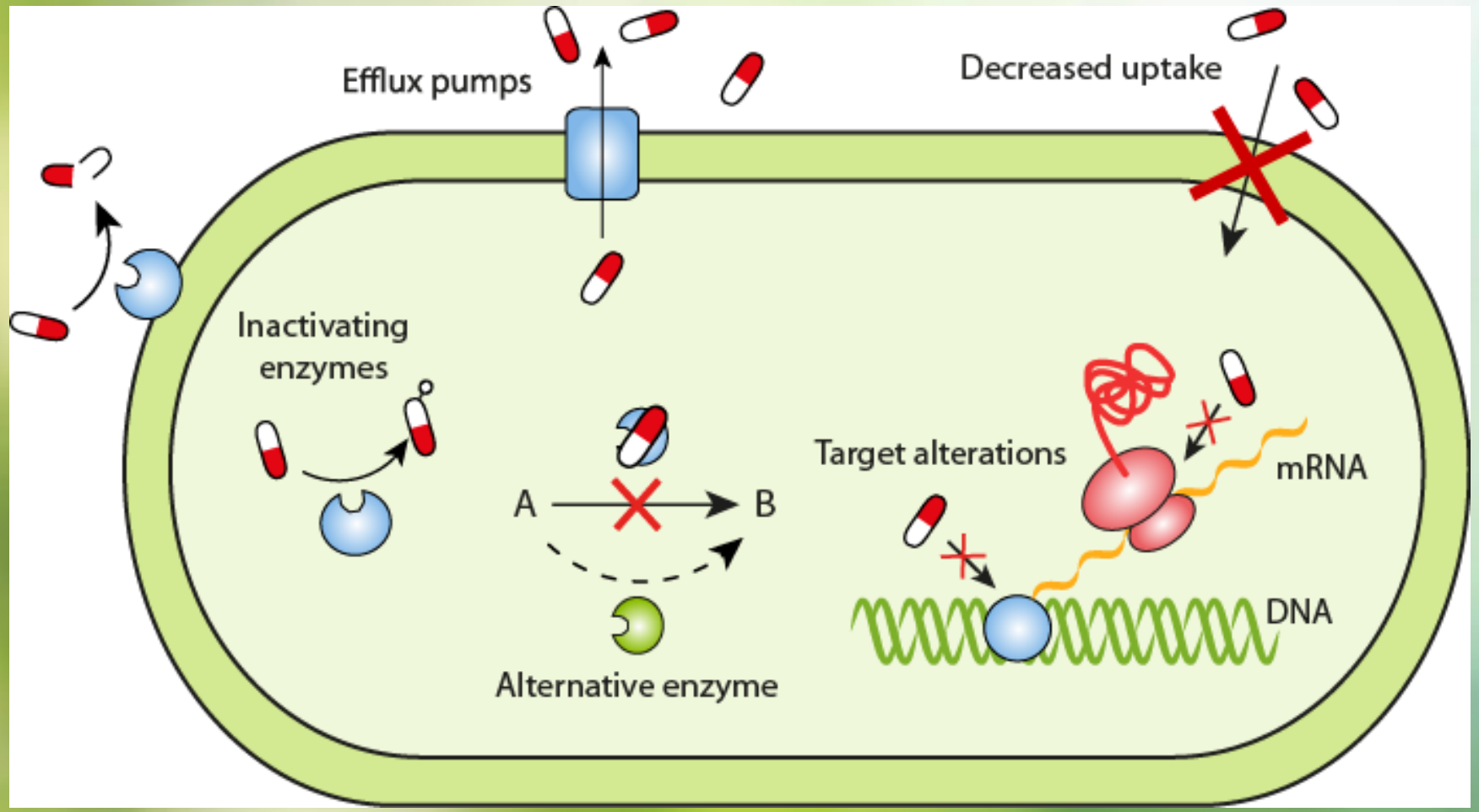
- Microbial resistance:

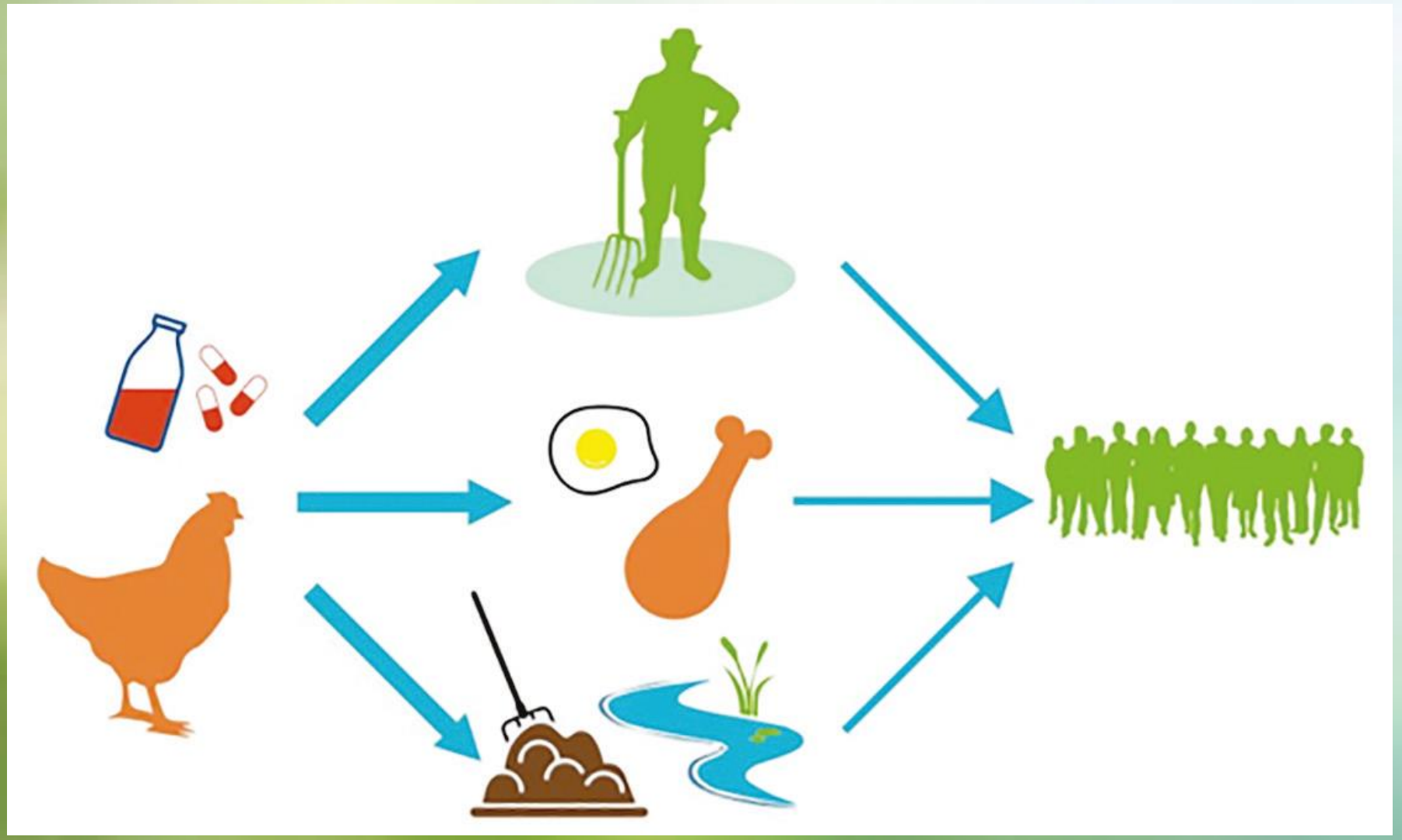
-Mechanisms of resistance :

a) Natural resistance
b) Spontaneous mutations
c) Gene transfer

-

Biochemical mechanisms of resistance





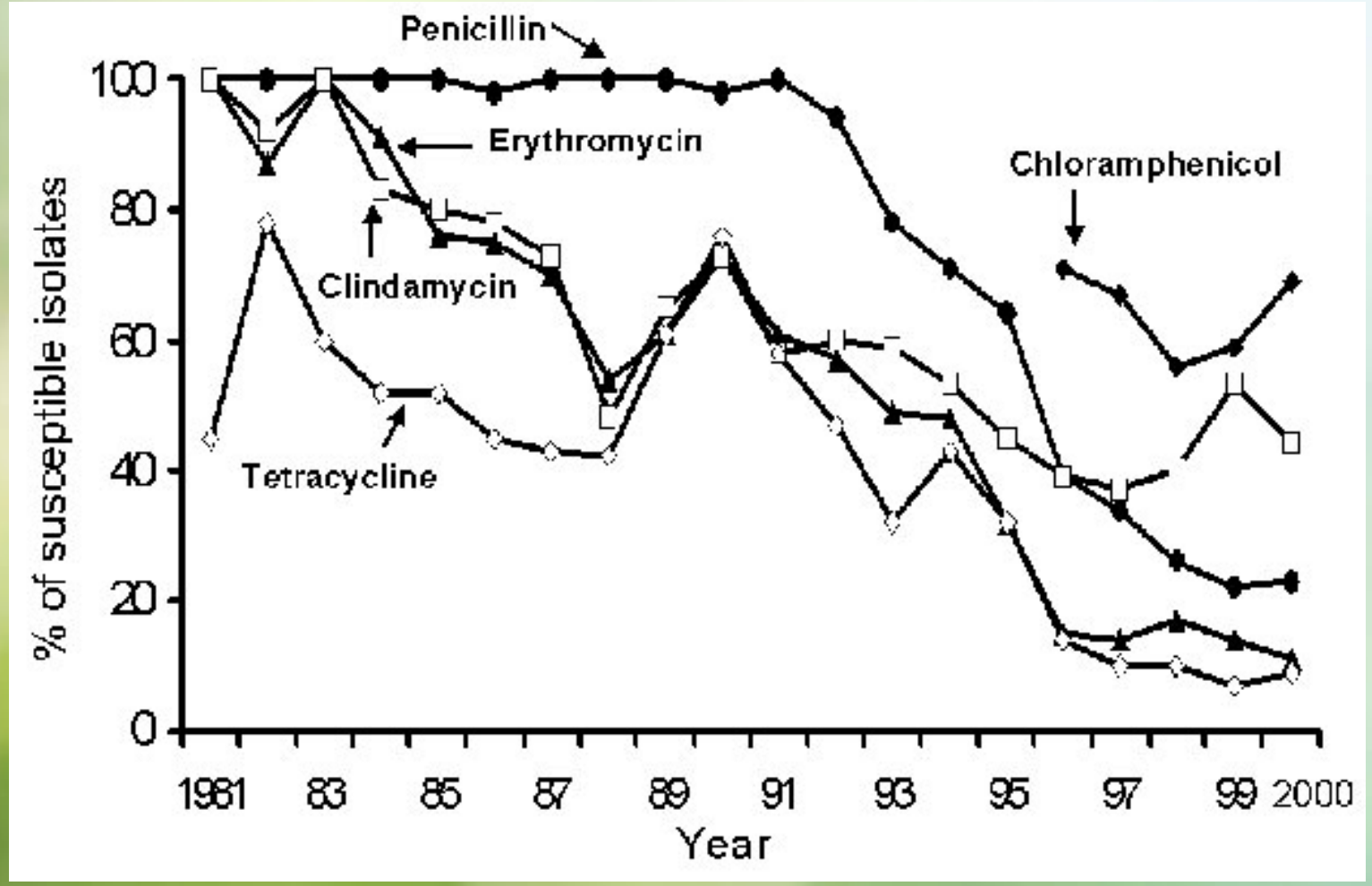
Resistant bacteria can move from poultry to humans: (i) via direct contact with the farmer; (ii) via food products; or (iii) via the environment. The routes via direct contact and food products are regarded as the most important.

- Antimicrobial resistance is an urgent global public health threat, killing at least 1.27 million people worldwide and associated with nearly 5 million deaths in 2019, according to a report released in The Lancet.
- (Global Covid deaths until December 2023 was roughly 7 million)!!!
- The six leading pathogens for deaths associated with resistance were Escherichia coli, followed by Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa.

Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022 Feb 12;399(10325):629-655.

Magnusson, U., Sternberg, S., Eklund, G., Rozstalnyy, A. 2019. Prudent and efficient use of

antimicrobials in pigs and poultry. FAO Animal Production and Health Manual 23. Rome. FAO.



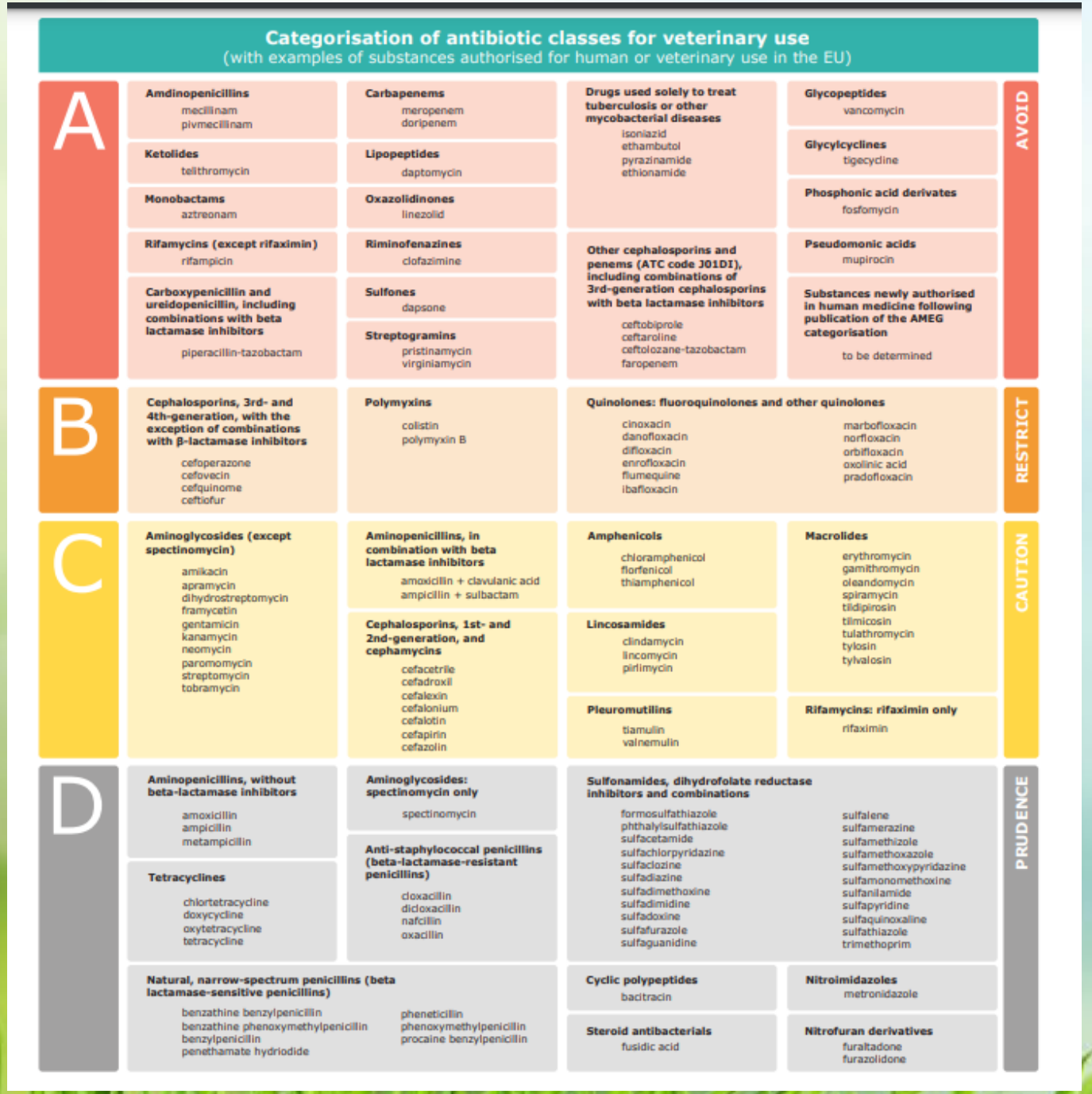
Prevalence of susceptibility to five antimicrobial agents for Streptococcus pneumoniae isolates at the National Taiwan University Hospital, 1981–2001. Susceptibility testing was performed with the disk diffusion method. For penicillin susceptibility testing, the 10-U penicillin disk was used from 1981 to 1989, and the 1-µg oxacillin disk since 1990.

Hsueh P, Luh K. Antimicrobial Resistance in Streptococcus pneumoniae, Taiwan. Emerging Infectious Diseases. 2002;8(12):1487-1491. doi:10.3201/eid0812.020178.

ANTIMICROBIAL STEWARDSHIP AND PRUDENT USE OF ANTIBIOTICS

- The World Health Organization (WHO) categorizes fluoroquinolones, third- and fourth- generation cephalosporins, macrolides, glycopeptides, and polymyxins as “highest priority critically important” antibiotics for human medicine.

European Medicines Agency (EMA)



Categorisation of antibiotic classes for veterinary use

(with examples of substances authorised for human or veterinary use in the EU)

A — AVOID

Amdinopenicillins
- mecillinam
- pivmecillinam

Ketolides
- telithromycin

Monobactams
- aztreonam

Rifamycins (except rifaximin)
- rifampicin

Carboxypenicillin and ureidopenicillin, including combinations with beta lactamase inhibitors
- piperacillin-tazobactam

Carbapenems
- meropenem
- doripenem

Lipopeptides
- daptomycin

Oxazolidinones
- linezolid

Riminofenazines
- clofazimine

Sulfones
- dapsone

Streptogramins
- pristinamycin
- virginiamycin

Drugs used solely to treat tuberculosis or other mycobacterial diseases
- isoniazid
- ethambutol
- pyrazinamide
- ethionamide

Other cephalosporins and penems (ATC code J01DI), including combinations of 3rd-generation cephalosporins with beta lactamase inhibitors
- ceftobiprole
- ceftaroline
- ceftolozane-tazobactam
- faropenem

Glycopeptides
- vancomycin

Glycylcyclines
- tigecycline

Phosphonic acid derivates
- fosfomycin

Pseudomonic acids
- mupirocin

Substances newly authorised in human medicine following publication of the AMEG categorisation
- to be determined

B — RESTRICT

Cephalosporins, 3rd- and 4th-generation, with the exception of combinations with β-lactamase inhibitors
- cefoperazone
- cefovecin
- cefquinome
- ceftiofur

Polymyxins
- colistin
- polymyxin B

Quinolones: fluoroquinolones and other quinolones
- cinoxacin
- danofloxacin
- difloxacin
- enrofloxacin
- flumequine
- ibafloxacin
- marbofloxacin
- norfloxacin
- orbifloxacin
- oxolinic acid
- pradofloxacin

C — CAUTION

Aminoglycosides (except spectinomycin)
- amikacin
- apramycin
- dihydrostreptomycin
- framycetin
- gentamicin
- kanamycin
- neomycin
- paromomycin
- streptomycin
- tobramycin

Aminopenicillins, in combination with beta lactamase inhibitors
- amoxicillin + clavulanic acid
- ampicillin + sulbactam

Cephalosporins, 1st- and 2nd-generation, and cephamycins
- cefacetrile
- cefadroxil
- cefalexin
- cefalonium
- cefalotin
- cefapirin
- cefazolin

Amphenicols
- chloramphenicol
- florfenicol
- thiamphenicol

Lincosamides
- clindamycin
- lincomycin
- pirlimycin

Pleuromutilins
- tiamulin
- valnemulin

Macrolides
- erythromycin
- gamithromycin
- oleandomycin
- spiramycin
- tildipirosin
- tilmicosin
- tulathromycin
- tylosin
- tylvalosin

Rifamycins: rifaximin only
- rifaximin

D — PRUDENCE

Aminopenicillins, without beta-lactamase inhibitors
- amoxicillin
- ampicillin
- metampicillin

Tetracyclines
- chlortetracycline
- doxycycline
- oxytetracycline
- tetracycline

Aminoglycosides: spectinomycin only
- spectinomycin

Anti-staphylococcal penicillins (beta-lactamase-resistant penicillins)
- cloxacillin
- dicloxacillin
- nafcillin
- oxacillin

Natural, narrow-spectrum penicillins (beta lactamase-sensitive penicillins)
- benzathine benzylpenicillin
- benzathine phenoxymethylpenicillin
- benzylpenicillin
- penethamate hydriodide
- pheneticillin
- phenoxymethylpenicillin
- procaine benzylpenicillin

Sulfonamides, dihydrofolate reductase inhibitors and combinations
- formosulfathiazole
- phthalylsulfathiazole
- sulfacetamide
- sulfachlorpyridazine
- sulfaclozine
- sulfadiazine
- sulfadimethoxine
- sulfadimidine
- sulfadoxine
- sulfafurazole
- sulfaguanidine
- sulfalene
- sulfamerazine
- sulfamethizole
- sulfamethoxazole
- sulfamethoxypyridazine
- sulfamonomethoxine
- sulfanilamide
- sulfapyridine
- sulfaquinoxaline
- sulfathiazole
- trimethoprim

Cyclic polypeptides
- bacitracin

Steroid antibacterials
- fusidic acid

Nitroimidazoles
- metronidazole

Nitrofuran derivatives
- furaltadone
- furazolidone

- According to OIE (WOAH)
- Aminoglycosides, third anf 4th generation cephalosporins, macrolides, fluoroquinolones, sulfonamides, tetracyclines, penicillins, Amphenicol derivatives are veterinary critically important antibacterials.

- A review on selected antibacterial agents

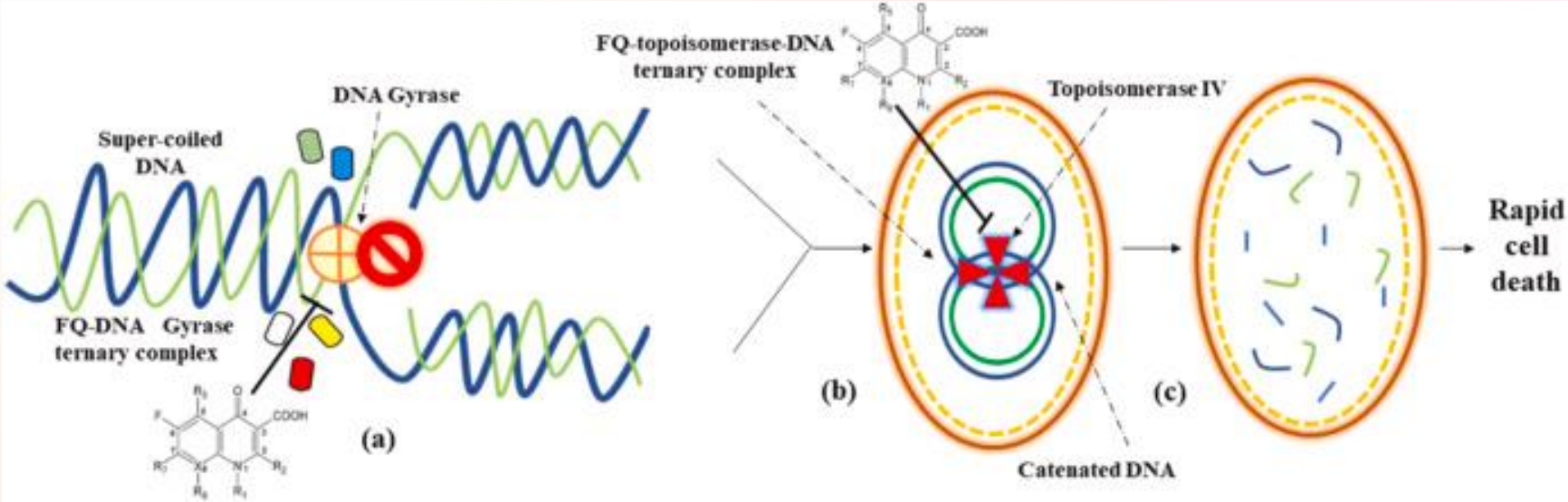
Enrofloxacin

Class

Fluoroquinolone

Mechanism

Bactericidal by inhibiting bacterial DNA replication and transcription.
The most common target site for quinolones is the A subunit of DNA gyrase. Another target is the topoisomerase IV enzyme which is less important in G negative bacteria. Works in concentration dependent manner.
Cmax : MICratio that is at least 8–10 times (i.e., a peak concentration that is 8–10 times the MIC) is desirable. A high Cmax : MIC ratio is optimal to decrease emergence of resistance. (AUC : MIC) may be used to predict efficacy. An AUC : MIC ratio of 125–250 has been associated with the optimum antibacterial effect.



Spectrum

Fluoroquinolones in general exhibit good activity against most gram-negative bacteria, especially those of the Enterobacteriaceae. Gram-positive bacteria are variably susceptible. The newer fluoroquinolones, such as moxifloxacin, gatifloxacin, and the veterinary drug pradofloxacin, have increased activity against gram-positive cocci and anaerobic bacteria.

Other bacteria susceptible to fluoroquinolones include intracellular organisms (Rickettsia spp., Chlamydia, and Mycobacterium spp.) and Mycoplasma spp.

Not effective against anaerobes.

Factors that may affect activity

Cations at the site of infection and low pH.

Cations such as Al+3, Mg+3, Fe+2, and Ca+2 can bind a carboxyl group on the drug and significantly decrease activity.

Low pH at the site of action increases the MIC (acidic urine).

Maximum dose for cats is 5 mg/kg/day. Higher doses are associated with retinal degeneration and blindness.

- Available for use in oral and injectable preparations.

انروفلوکساسین تزریقی رویان دارو قابل استفاده در گاو، گوسفند و بز (برخی شرکت ها برای گوساله هم توصیه به مصرف کرده اند!)

There is a risk that fluoroquinolones may cause damage to the developing cartilage of young animals.

قرص های ۵۰ میلی گرمی انروفلوکساسین برای سگ ها (شرکت تولید داروهای دامی ایران)

در سگ های با سن کمتر از ۱ سال یا به طور استثناء در نژادهای بزرگ سگ که دارای دوره رشد طولانی تر هستند، در سن زیر ۱۸ ماه استفاده نشود چون غضروفهای مفصلی ممکن است طی دوره رشد سریع تحت تاثیر قرار بگیرد.

نکته: جذب خوراکی سیپروفلوکساسین در سگ ها مناسب نیست.

در اسب تجویز انروفلوکساسین توصیه نمی شود.

- قابل استفاده در آب آشامیدنی طیور گوشتی (در مرغ تخمگذار که تخم مرغ به مصرف انسانی می رسد استفاده نشود).

✓The Food and Drug Administration announced it would no longer allow distribution or use of the antimicrobial enrofloxacin after judging that it causes resistance in *Campylobacter jejuni* when used to treat respiratory infections in poultry.

- تجویز انروفلوکساسین در خرگوش، جوندگان و خزندگان مجاز است. (Minimal disruption of GI microflora)

Florfenicol

Class

A derivative of chloramphenicol with the advantage of being used in food animals.

Mechanism

It acts by binding to the 50S ribosome, thereby inhibiting bacterial protein synthesis. Bactericidal against some bacteria but not Ecoli.
AUC/MIC would be the best parameter to predict clinical efficacy.

Spectrum

The list of susceptible bacteria for florfenicol is the same as chloramphenicol. However, some bacteria resistant to chloramphenicol because of inactivation by acetylation may be susceptible to florfenicol.

Gram positive, Gram negative (e. g. Pasteurella and enterobacteriacea), anaerobes, mycoplasma and many Rickettsiae ae susceptible.

- Good absorption, wide distribution, Florfenicol amine is the metabolite that persists longest in tissues of cattle and is used as the marker residue.
- Drug interactions

Other antibiotics that bind to the 50S ribosomal subunit of susceptible bacteria (erythromycin, clindamycin, lincomycin, tylosin, etc.) may potentially antagonize the activity of chloramphenicol or vice versa, but the clinical significance of this potential interaction has not been determined.

- Monitoring Parameters

1) Clinical efficacy 2) Injection site reactions

- محلول تزریقی ۳۰٪: گاو وگوسفند و بز. سگ و گربه
- در گاوهایی شیرده که شیر آنها مصرف انسانـی دارد، منع مصرف دارد

- تزریق داخل وریدی این دارو ممنوع است

- زمان پرهیز از مصرف گوشت: ۲۸ روز پس از تزریـــق عضلانـــی و ۳۸ روز پس از تزریق زیرجلدی
- محلول خوراکی ۱۰٪: آب اشامیدنی طیور. آب محتوی دارو باید هر روز به صورت تازه تهیه و در طول همان روز به طورکامل مصرف شود.
- فلورفنیکل ۵۰٪ (اکوا فلور) ماهیان سردابی medicated feed

Tilmicosin

- Macrolide antibiotic
- Mechanism of action

Inhibition of protein synthesis by binding to the 50S ribosomal subunit

Although most authors have listed macrolides as bacteriostatic at therapeutic concentrations, this effect may be both bacterial species, concentration, and drug dependent.

- Spectrum

The spectrum favors the gram-positive group, a few gram-negative bacteria are susceptible, especially Pasteurella spp. Activity against anaerobic bacteria is only moderate.

Most other gram-negative bacteria, such as those of the Enterobacteriaceae or Pseudomonas spp., are resistant. Mycoplasma are susceptible.

- Like other macrolides, tilmicosin reaches high concentrations in lung tissues and this may account for efficacy treating bovine pneumonia.

Efficacy is probably best attributed to the concentrations at the site of infection

- If administered IM, a local tissue reaction may occur resulting in trim loss. Edema may be noted at the site of subcutaneous injection.

- Injections of tilmicosin to horses, goats, swine, or nonhuman primates can be fatal.
- The heart is the target of toxicity in animals, perhaps mediated via depletion of cardiac intracellular calcium, resulting in a negative inotropic effect
- The risk of cardiac toxicity is particularly important for humans. several people have died as a result of tilmicosin administration.
- Monitoring Parameters

1) Efficacy; 2) Withdrawal times

• تیل مایکوزین ۳۰٪ محلول تزریقی گاو و گوسفند

• تیل مایکوزین ۲۵٪ محلول خوراکی طیور گوشتی، پرندگان زینتی، بوقلمون، گوساله

منع مصرف

طیور:۱۲ روز

بوقلمون: ۱۹ روز

گوساله: ٤٢ روز

ز تجویز در طیور تخم گذار که تخم آنها به مصرف انسان میرسد، خودداری گردد.

Cefazolin

- β-lactam (first generation cephalosporin antibiotic)
- Mechanism of action

β-lactam antibiotics exert their effects by preventing bacterial cell wall synthesis and disrupting bacterial cell wall integrity.

Inhibition of transpeptidation reaction by acetylating the enzyme is one of the sites of action for β-lactam antibiotics. Interference with transpeptidation results in a weak cell wall and rupture of the bacteria.

Bactericidal in a time-dependent manner. The important parameter is considered time above MIC (T > MIC).

Specrtum

- Almost all gram-positive bacteria, except Enterococcus, activity includes β-lactamase-positive staphylococcus. They also have greater activity against members of the Enterobacteriaceae than penicillin G.
- Contraindicated in patient with a history of hypersensitivity (cross reactivity with other betalactams)
- Dosage adjustment may be needed in patients with renal failure.

- Cefazolin is the injectable cephalosporin administered often to companion animals. It could also be used in horses and reptiles.
- Distribution is not impaired in osteomyelotic bone. This advantage of good penetration has allowed it to be used for prevention and treatment of bone infections and as a common antibiotic to use prophylactically prior to orthopedic surgery.
- Human products are used in veterinary species.
- Usually safe. Only monitoring for clinical efficacy is needed.
- Incompatibility with drugs such as amikacin and oxytetracycline in injection solution should be considered.

Clindamycin

- Is a lincosamide antibiotic, usually used in dogs and cats.
- More active against bacteria and better absorption after oral administration than lincomycin.
- Mechanism of action

Protein synthesis inhibition at 50S ribosomal subunit.

Should not be used with macrolides (reduced efficacy).

- Spectrum

Most aerobic Gram positive bacteria, mycoplasma and toxoplasma, anaerobes (but not C. difficile).

- Penetrates into abscesses and white blood cells.
- Has good activity in wounds, abscesses and osteomyelitis due to S. aureus and also pathogenic anaerobes.
- Contraindicated in rabbits, hamsters, chinchillas guinea pigs, horses and ruminants because of the seriouse gastrointestinal effects.
- Usually should not be used in neonates.
- Adverse effects include gastroenteritis. Solid formulations may cause esophageal injury in cats if administered without water or food.
- C. difficile-associated pseudomembranouse colitis with clindamycin is not a significant risk in dogs and cats.

- Monitoring is for clinical efficacy, severe diarrhea and liver and kidney function tests if used for more than one month.
- Clindamycin palmitate is more palatable than HCl salt.
- Clindamycin phosphate is the injectable formulation.

Oxytetracycline

- Tetracycline antibiotic. Mechanism of action

Tetracyclines possess antimicrobial activity by binding to the 30S ribosomal subunit of susceptible organisms. After binding to the ribosome, the tetracyclines interfere with the binding of aminoacyl-tRNA to the messenger RNA molecule/ribosome complex, thereby interfering with bacterial protein synthesis in growing or multiplying organisms.

These drugs are generally considered bacteriostatic.

- Spectrum
- Wide spectrum but many bacteria are now resistant. It is useful against mycoplasma, rickettsia, spirochetes and chlamydia.
- In birds, doxycycline is the drug of choice for treatment of Chlamydophila psittaci (formerly called Chlamydia psittaci).
- Drug of choice for equine monocytic or granulocytic ehrlichiosis.
- Adverse effects: GI distress, staining of developing teeth and bones and retardation of bone growth (extreme caution in pregnancy), superinfections, cats do not tolerate tetracyclines well. Oral use in horses under stress is associated with severe diarrhea. IM injection in ruminants may cause local reactions, necrosis and yellow staining. Should be used cautiously in patients with renal or hepatic insufficiency.
- Raid IV injection of undiluted propylene glycol –based products has been associated with intra vascular hemolysis nd cardiodepressant effects in ruminants and only should be used by IM injection.
- Long acting (LA) formulations of the drug are also available

- Divalent or trivalent cations (oral anti acids, saline, cathartics, iron, zinc, Mg etc.) should be administered At least 2 hours apart.
- Monitoring
- 1) Clinical efficacy 2) Adverse effects 3) Periodic liver and kidney function tests in long-term use or in susceptible patients.
- The drug becomes unstable in solutions with pH>6 particularly in those containing calcium.

- اکسی تتراسایکلین تزریقی ۲۰٪ (طولانی اثر) گاو گوسفند و بز- عضلانی
- اکسی تتراسایکلین تزریقی ۱۰٪ گاو گوسفند و بزاسب- IM, IV, SC
- اکسی تتراسایکلین خوراکی ۲۰٪ پودر محلول در آب- طیور نشخوارکنندگان ماهی زنبور عسل
- اکسی تتراسایکلین خوراکی ۵۰٪ طیور مخلوط در دان

Amoxicillin

Class

Aminopenicillin (beta-lactam)

Mechanism

Amoxicillin is a time-dependent, bactericidal agent that acts by inhibiting cell wall synthesis.

Spectrum

Aminopenicillins (ie, broad-spectrum or ampicillin penicillins) have increased activity against many strains of gram-negative aerobes not covered by natural penicillins or penicillinase-resistant penicillins, including some strains of Escherichia coli, Klebsiella spp, and Haemophilus spp. Like the natural penicillins, aminopenicillins are susceptible to inactivation by beta-lactamase–producing bacteria (eg, many Staphylococcus spp, E coli). Although not as active as natural penicillins, aminopenicillins have activity against many anaerobic bacteria, including clostridial organisms.

Like other beta-lactam antibiotics, penicillins are generally considered more effective against actively growing bacteria.

Amoxicillin/clavulanate is often used in small animals because of its enhanced efficacy against many beta-lactamase –producing bacteria.

Higher serum concentrations may be attained with amoxicillin as compared with ampicillin because amoxicillin is better absorbed orally (in nonruminants).

Oral beta-lactam antibiotics and macrolides should not be administered to rabbits, guinea pigs, chinchillas, hamsters, or other small mammals, as severe enteritis and clostridial enterotoxemia may occur.

Most common adverse effects are GI-related, but hypersensitivity and other adverse effects can occur (rare).

- Urine culture may be considered after 5 to 7 days when treating bacterial cystitis for longer periods of time (relapsing cases).
- It is important to note that positive cultures taken at this time should prompt questioning the owner about compliance and further investigation as to why the infection has not been eliminated (eg, underlying pathology [eg, cystic calculi, neoplasia]); a positive culture at this time should not simply prompt a change in antibiotic choice.
- A negative culture during this time frame does not necessarily guarantee resolution of the infection.

- آموکسی سیلین تری هیدرات پودر قابل حل در آب مرغ، بوقلمون و اردک
- آموکسی سیلین طولانی اثر تزریقی دام و سگ و گربه

Gentamicin

Class

Aminoglycoside Antibiotic

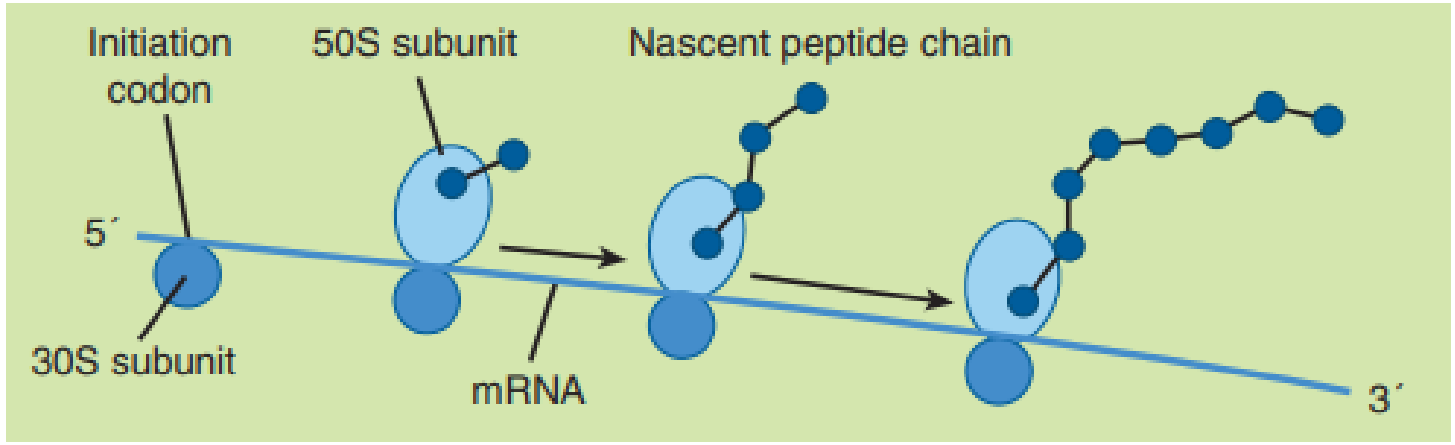
Mechanism

Gentamicin acts on susceptible bacteria presumably by irreversibly binding to the 30S ribosomal subunit, thereby inhibiting protein synthesis.

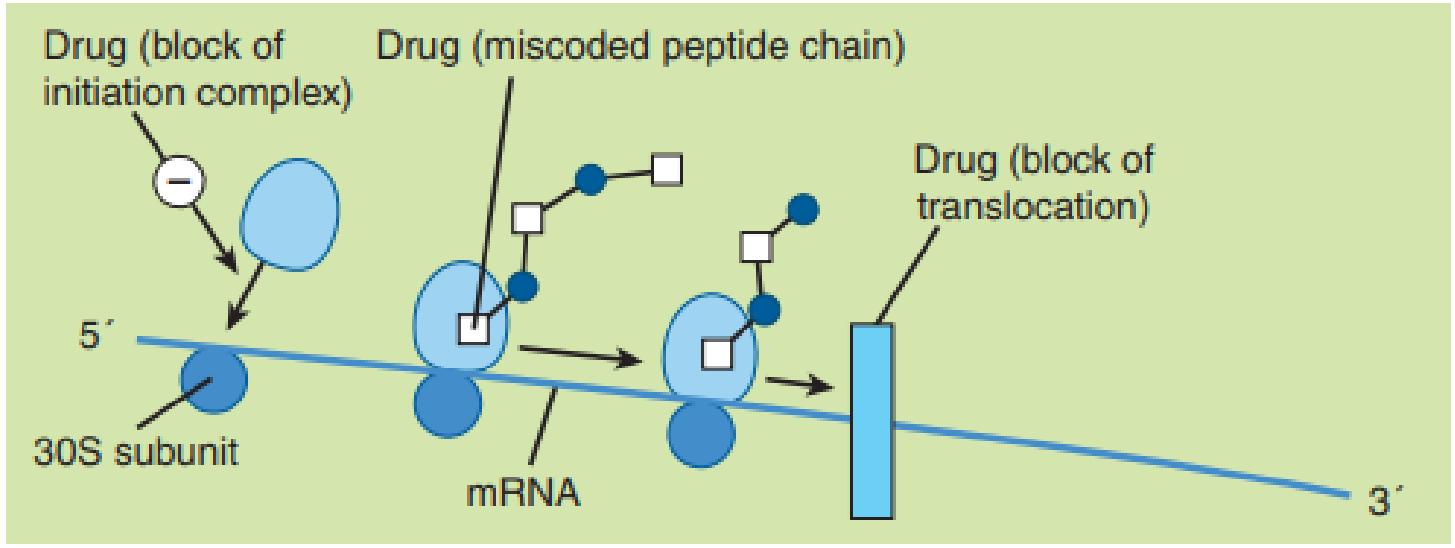
It is considered a bactericidal concentration-dependent antibiotic. A ratio of 10 or greater for peak plasma concentration to MIC is believed to be optimal for antibacterial efficacy.

Antimicrobial activity of the aminoglycosides is enhanced in an alkaline environment. The presence of pus, necrotic tissue, or cellular debris reduce aminoglycoside efficacy.

Normal bacterial cell



Aminoglycoside-treated bacterial cell



Spectrum

Parenteral aminoglycoside antibiotic that is active against a variety of bacteria, predominantly gram-negative aerobic bacilli but also many staphylococci.

Reserved for serious infections because of potential adverse effects (nephrotoxicity, ototoxicity, and neuromuscular blockade)

▶Cats may be more sensitive to toxic effects, especially vestibular effects.

Gentamicin, like other aminoglycosides, is not appreciably absorbed after oral or intrauterine administration.

SC injection results in slightly delayed peak concentrations and more variability than after IM injection.

Aminoglycosides tend to accumulate in certain tissues, such as the inner ear and kidneys, which may explain their toxicity.

Elimination of aminoglycosides after parenteral administration occurs almost entirely by glomerular filtration. Patients with decreased renal function can have significantly prolonged half-lives.

They should be used with extreme caution in patients with preexisting renal disease, with concomitant monitoring and dosage interval adjustments made.

Other risk factors for the development of toxicity include age (both neonatal and geriatric patients), fever, hypokalemia, treatment duration, sepsis, hypotension, and dehydration.

- Monitor renal function prior to and during therapy. If signs of acute kidney injury (eg, renal casts in urine sediment, glucosuria, low urine-specific gravity, azotemia) are noted, therapy should be halted if possible, and alternative antibiotic therapy should be instituted.
- Dosing adjustments (ie, prolonging dosing interval) can be used in situations where the risks for ongoing treatment outweigh renal concerns.
- Dosing is best based on measurement of peak and trough drug levels.

- Because aminoglycosides can cause irreversible ototoxicity, they should be used with caution in working or service dogs (eg, seeing-eye, herding, dogs for the hearing impaired) and should be avoided for treatment of otitis if an intact tympanic membrane is not known to be present.
- Gentamicin is considered *more ototoxic* than *amikacin*.

- Aminoglycosides should be used with caution in patients with neuromuscular disorders (eg, myasthenia gravis) because of their neuromuscular blocking activity. They should not be used in animals with botulism.
- Sighthound dogs may require reduced dosages of aminoglycosides, as they have significantly smaller volumes of distribution.

- IM injections in horses have caused muscle irritation and IV injections are preferred. IV administration may be associated with allergic and anaphylactic reactions in horses.
- The injection should be pre-warmed and administered slowly. If clinical signs occur, corticosteroid treatment may be necessary. The risk for antibiotic-associated diarrhea/colitis in horses caused by gentamicin is thought to be low, but gentamicin may enhance beta-2 toxin production by Clostridium perfringens and may increase the severity of colitis.

- Nephrotoxicity is usually reversible once the drug is discontinued, but development of oliguric acute kidney injury portends a poor prognosis. Although gentamicin may be more nephrotoxic than some other aminoglycosides, the risk for nephrotoxicity with all systemic aminoglycosides requires equal caution and monitoring.

- Strategies to reduce the potential for nephrotoxicity in animals with uncompromised renal function include once-daily administration, renal function monitoring, hydration and electrolyte balance, avoidance of other nephrotoxic drugs, and employment of therapeutic drug monitoring to adjust dosages and/or dosing intervals to maintain low trough concentrations (preferably less than 1 – 2 µg/mL).

- Aminoglycoside ototoxicity (eighth (vestibulocochlear) cranial nerve toxicity) can manifest by either auditory and/or vestibular clinical signs and may be irreversible.
- Cats are apparently very sensitive to the vestibular effects of the aminoglycosides and can exhibit signs of vertigo, head tilt, ataxia, impaired righting reflex, and post-rotatory righting reflex.
- Concurrent use with loop diuretics may increase the nephrotoxic or ototoxic potential of the aminoglycosides.

- Therapeutic drug monitoring (TDM) when possible in patients with uncompromised renal function; highly recommended for patients with risk factors for nephrotoxicity.
- Peak and trough levels are determined through samples collected 30 minutes after administration (peak) and immediately before administration of the next dose (trough).
- Generally, peak levels (≈30 to 60 minutes post IV dose) should be greater than 32 µg/mL and trough levels less than 1 – 2 µg/mL.

- جنتامایسین تزریقی وریدی یا عضلانی گاو گوسفند اسب بز سگ و گربه
- سوسپانسیون تزریقی اموکسی سیلین جنتامایسین دامی (جنتاموکس)

Sulfadiazine/Trimethoprim

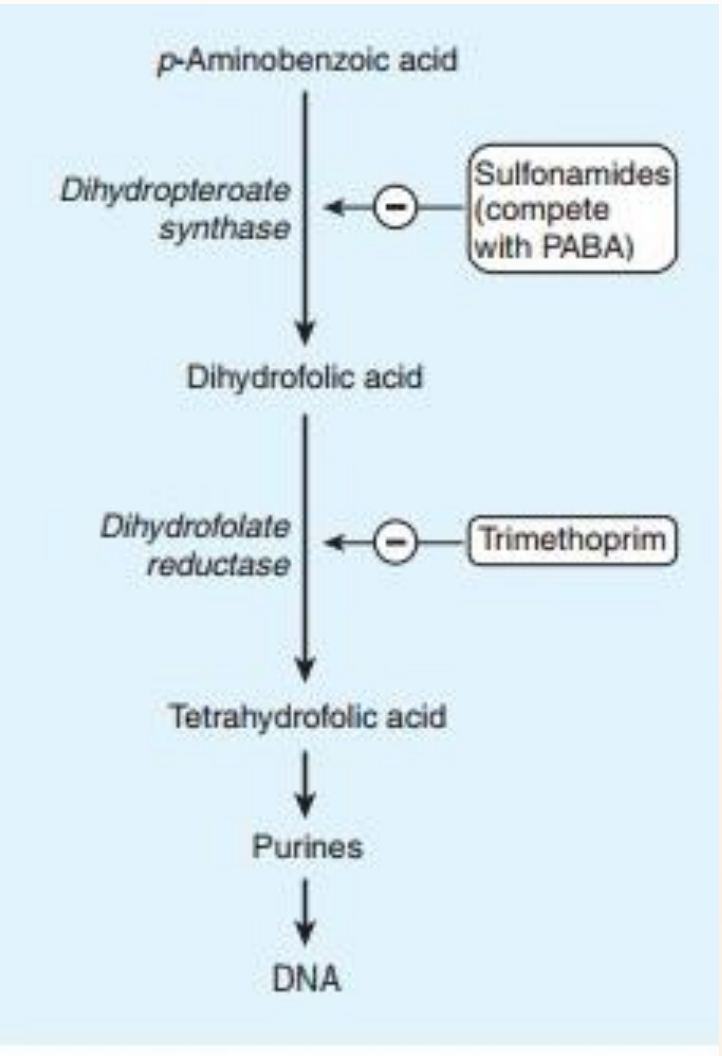
Class

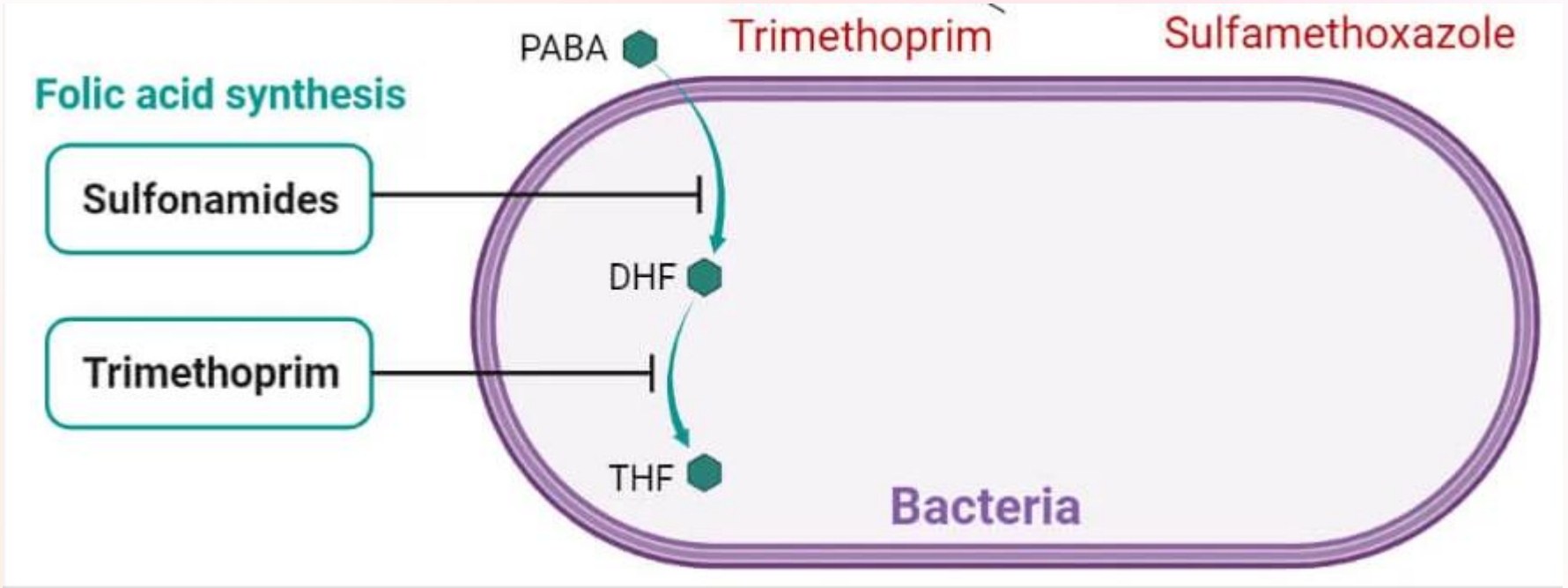
Potentiated Sulfonamide

Mechanism

Sulfonamides are bacteriostatic agents while trimethoprim is bactericidal; both agents are time-dependent antibiotics. When used in combination, the resulting potentiated sulfonamides are bactericidal. Potentiated sulfonamides sequentially inhibit enzymes in the folic acid pathway, inhibiting bacterial thymidine synthesis. Sulfonamides compete with para-aminobenzoic acid (PABA) to reduce bacterial dihydrofolic acid (DFA) formation, and trimethoprim blocks the conversion of DFA to tetrahydrofolic acid by preferentially inhibiting bacterial dihydrofolate reductase.

Infected tissue and cellular debris can inhibit the activity of sulfa-/trimethoprim by secreting PABA and thymidine. The effects of sulfa-/trimethoprim on the equine GI microbiome appear to be reversible.





Spectrum

Potentiated sulfonamides have a fairly broad spectrum of activity. Generally susceptible gram-positive bacteria include most streptococci and staphylococci and Nocardia spp.
Many gram-negative organisms of the Enterobacteriaceae family are inherently susceptible to potentiated sulfonamides but acquired resistance can occur.
Sulfa-/trimethoprim is ineffective against Pseudomonas aeruginosa. Some protozoa (ie, Pneumocystis jiroveci, Coccidia spp, Neospora spp, Toxoplasma spp) are also inhibited.
Potentiated sulfonamides appear to have little activity against most atypical bacteria and anaerobes; methicillin-resistant staphylococci are usually resistant. Enterococcus spp infections may appear to be susceptible to sulfonamide-containing antibiotics in vitro; however, they are intrinsically resistant, so sulfa-/trimethoprim should not be used for these bacteria.

Sulfadiazine/trimethoprim should not be used in dogs or horses with marked liver parenchymal damage, impaired hepatic function, blood dyscrasias, or a history of sulfonamide or trimethoprim sensitivity.

Sulfa-/trimethoprim should be used with caution in patients with

pre-existing hepatic or renal disease or folate deficiency.

Sulfadiazine has potential for crystallization in the urine, so use should be avoided in dogs with uroliths, at increased risk for developing uroliths, with highly concentrated urine (from dehydration), or with acidic urine.

- Horses receiving sulfadiazine/trimethoprim that are under conditions of stress may develop potentially fatal acute diarrhea.
- Discontinue antimicrobial therapy if acute diarrhea or persistent changes in fecal consistency are observed and initiate appropriate treatment.
- Sulfadiazine/trimethoprim should not be administered to horses with drug-induced cardiac arrhythmias (eg, anesthetic and sedative agents) and it should not be given IV concurrently or with previous administration of CNS depressants (eg, anesthetic agents, phenothiazines).

- Adverse effects noted in dogs include keratoconjunctivitis sicca (KCS; which may be irreversible), acute neutrophilic hepatitis with icterus, vomiting, anorexia, diarrhea, fever, hemolytic anemia, urticaria, polyarthritis, facial swelling, polydipsia, polyuria, and cholestasis. Potentiated sulfonamides may cause clinical hypothyroidism in dogs, particularly with extended therapy. Acute hypersensitivity reactions manifesting as type I (ie, anaphylaxis) or type III (ie, formation of antigen:antibody complexes) reactions can be seen.
- Hypersensitivity reactions appear to be more common in large- breed dogs. Doberman pinschers, Samoyeds, and miniature schnauzers appear to be more susceptible to sulfonamide-induced polysystemic immune complex disease.

Monitoring

■ Clinical efficacy

■ Adverse effects

■ Renal function (creatinine, BUN) and potassium

■ If prolonged therapy (ie, greater than 7 days) is anticipated, the following is recommended:

■ Baseline and periodic CBC and hepatic profile

■ In dogs, baseline Schirmer tear testing, with periodic re-evaluation (eg, in 5 days, then every 2-3 weeks) and owner monitoring for ocular discharge

■ Thyroid function tests should also be considered (baseline and ongoing) in dogs

- سولفادیازین ۲۰٪ + تری متوپریم ٤٪ محلول استریل تزریقی گاو اسب سگ و گربه
- سولفادیازین ٤۰٪+ تری متوپریم ۸٪ سوسپانسیون تزریقی دامی
- سولفادیازین ۲۵٪+ تری متوپریم.٪۵ دان
- سولفادیازین ٤۰٪+ تری متوپریم ۸٪پودر محلول در آب طیور

Doxycycline

Class

Tetracycline antibiotic

Mechanism

Like other tetracyclines.

Longer half-life, wide volume of distribution, higher CNS penetration), and safety profile, as compared with tetracycline or oxytetracycline, make it the preferred choice in small animal species when a tetracycline is indicated, particularly in azotemic patients.

Doxycycline’s elimination from the body is relatively unique. The drug is primarily excreted into the feces via nonbiliary routes in an inactive form.

Doxycycline does not accumulate in patients with renal dysfunction.

Doxycycline use has been associated with the development of esophageal stricture, particularly in cats. If using oral tablets in cats, pilling should be followed by at least 5 mL of water or food. Dry pilling should be avoided.

Oral doxycycline monohydrate may have a lower risk for causing esophagitis than the hyclate salt, as it is much less acidic and slower to dissolve in neutral solutions; however, it is recommended that all oral formulations administered to cats should be followed by a water or food swallow, regardless of the salt used.

- In horses, IV injection of even relatively low doses of doxycycline has been associated with cardiac arrhythmias, collapse, and death.
- In goats, IM injection has led to severe edema and pain at the injection site.

- Doxycycline therapy is part of the American Heartworm Society’s recommended canine heartworm treatment protocol. Dirofilaria immitis harbors Wolbachia spp organisms as endosymbiotic bacteria. The presence of Wolbachia spp—even in very low numbers— appears necessary for filarial embryogenesis. In addition, Wolbachia spp organisms contribute to pulmonary and renal inflammation of filarial disease. Doxycycline greatly reduces Wolbachia spp organisms in filarial nematodes, which can result in amicrofilaremia for up to 12 months.

- محلول تزریقی داکسی سایکلین ۱۰٪ گاو گوسفند و بز عضلانی
- محلول خوراکی قابل مصرف در آب آشامیدنی داکسی سایکلین ۱۰٪ مرغ گوشتی


از توجه شما سپاسگزارم.