Antibiotics

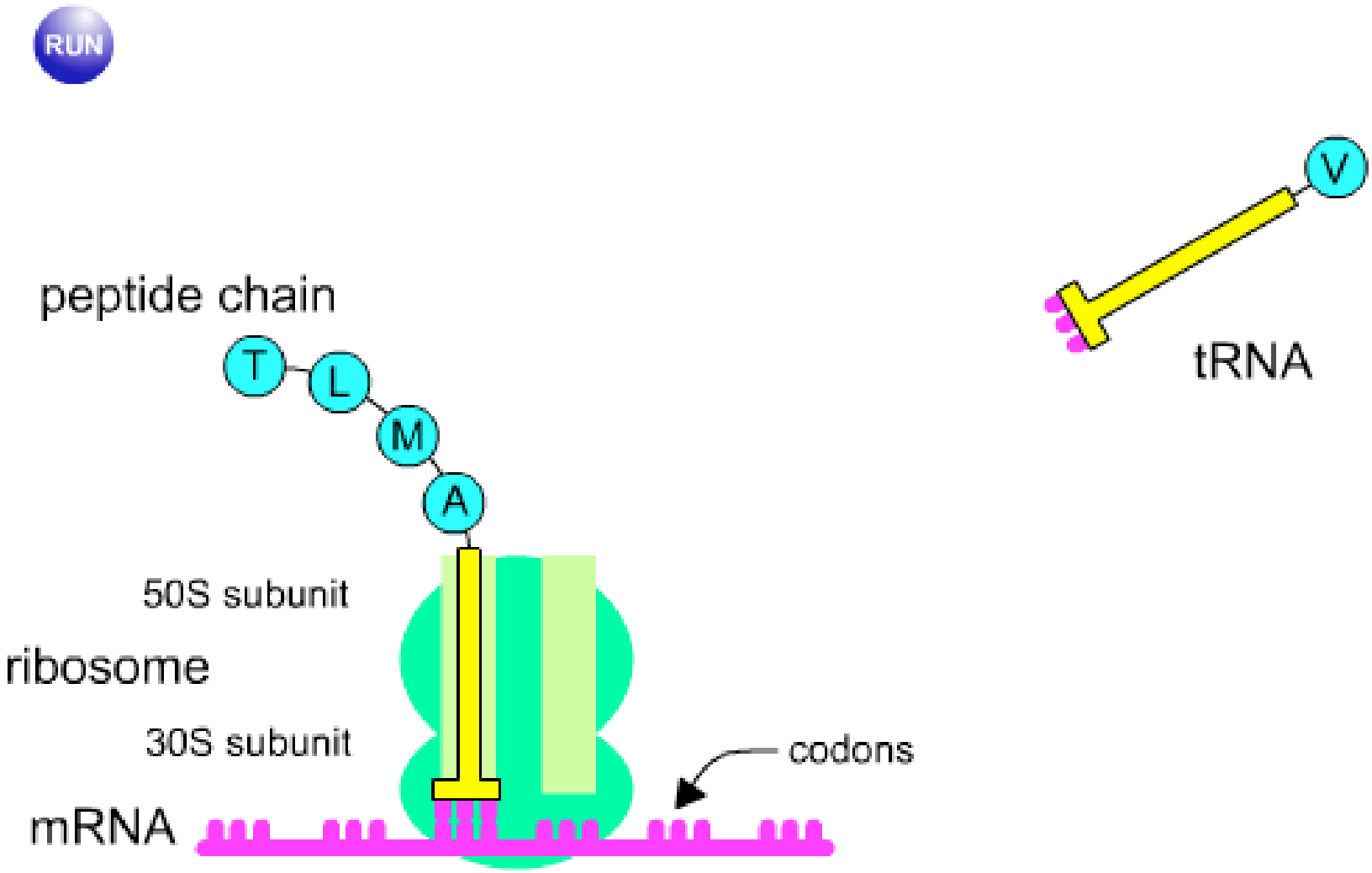
Aminoglycosides

drugs

- **old drugs**
  - streptomycin / dihydrostreptomycin
  - neomycin (Framycetin)
- **newer drugs**
  - gentamicin
  - amikacin
  - tobramycin
  - netilmicin
- **aminocyclitols**
  - apramycin
  - spectinomycin

mechanism

- block peptide synthesis
- rapidly bacteriocidal
- effect concentration dependent
- post antibiotic effect

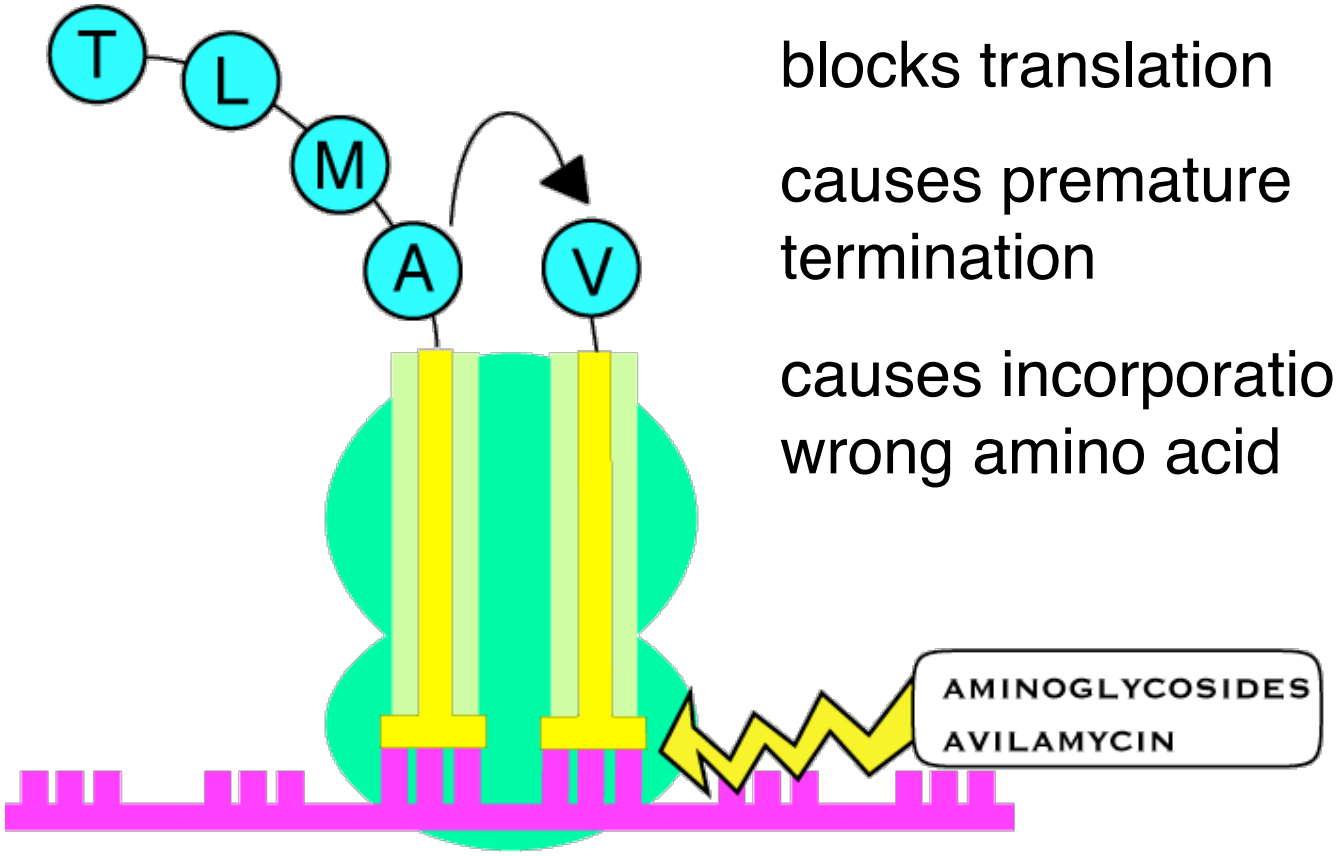

RUN
peptide chain
T
L
M
A
V
tRNA
50S subunit
ribosome
30S subunit
codons
mRNA

blocks initiation of protein synthesis

blocks translation

causes premature termination

causes incorporation of wrong amino acid



mechanism

- **must get into cell to act**
  - oxygen dependent polyamine carrier
  - not present in anaerobes
  - blocked by low pH, Ca^{++}, Mg^{++}, hyperosmolar conditions

resistance

- **develops quickly**
  - especially Staphs
- **cross resistance not complete**
  - amikacin not easily broken down

resistance

- **inactivation**
  - at least 9 enzymes
  - plasmid transmitted
- **failure to get into cells**
  - cell wall damaging drugs
  - chloramphenicol
- **alterations in binding site**
  - chromosomal mutation

spectrum of activity

- **aerobic Gram negatives**
  - Pseudomonas
- **(Staphs)**
- **(Mycobacteria)**
- **not Streps**

side effects

- **ears**
  - deafness
  - loss of balance
- **kidneys**
  - failure
- **(neuromuscular blockade)**

ears

- **deafness**
  - dihydrostreptomycin
  - neomycin
  - amikacin
  - people & cats most sensitive
- **loss of balance**
  - streptomycin
  - gentamicin

kidneys

- **all aminoglycosides**
- **potentiated by**
  - dehydration
  - frusemide
  - low blood pressure
  - NSAIDs?

pharmacokinetics absorption

- **highly polar**
  - not absorbed from gut
  - do not penetrate CNS / eye / secretions
  - useful concentrations in synovial fluid

administration

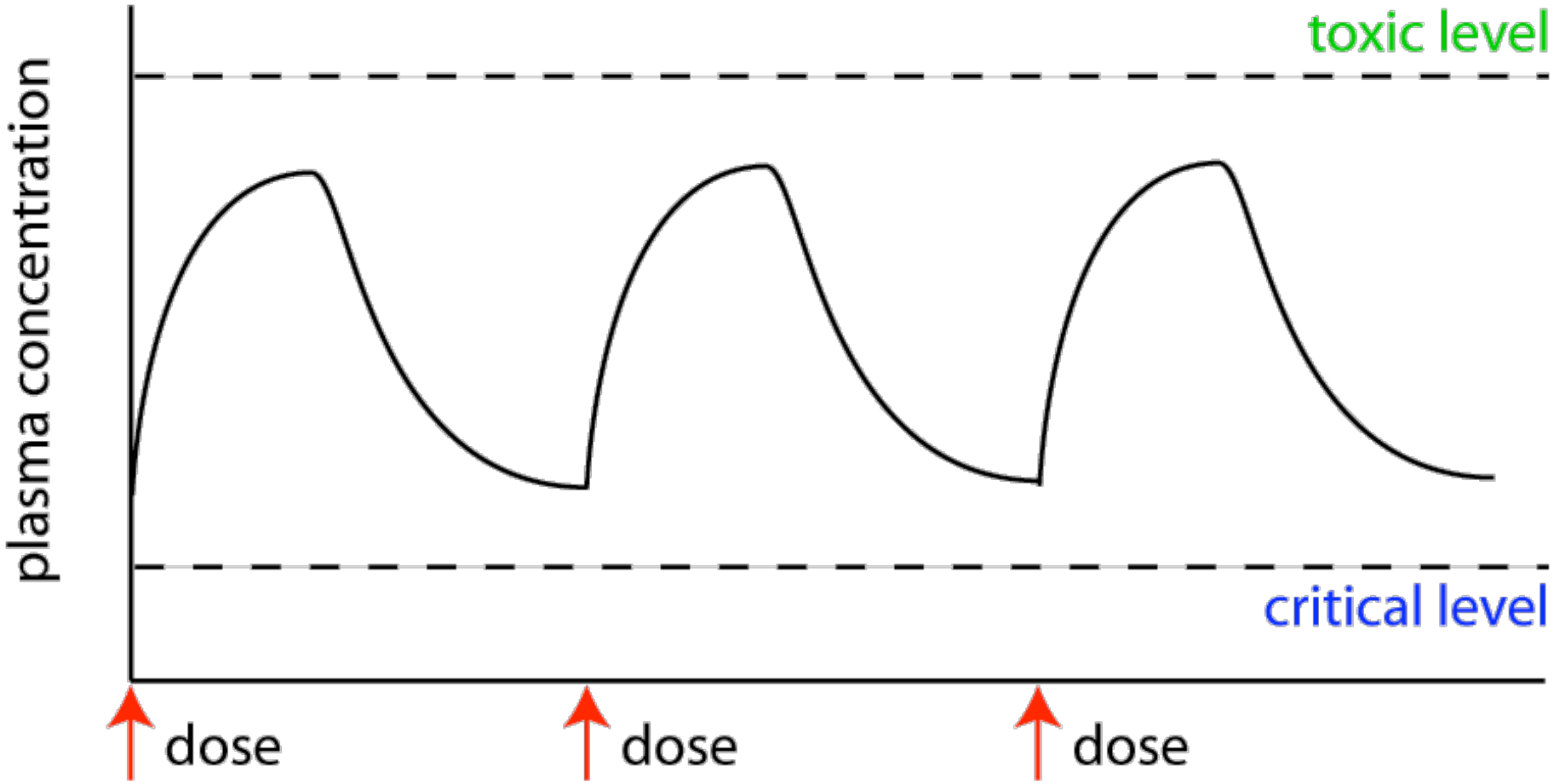
- **usually given parenterally**
  - im or sc 90% bioavailable
  - im injections painful
- **other preparations**
  - intramammary
  - oral

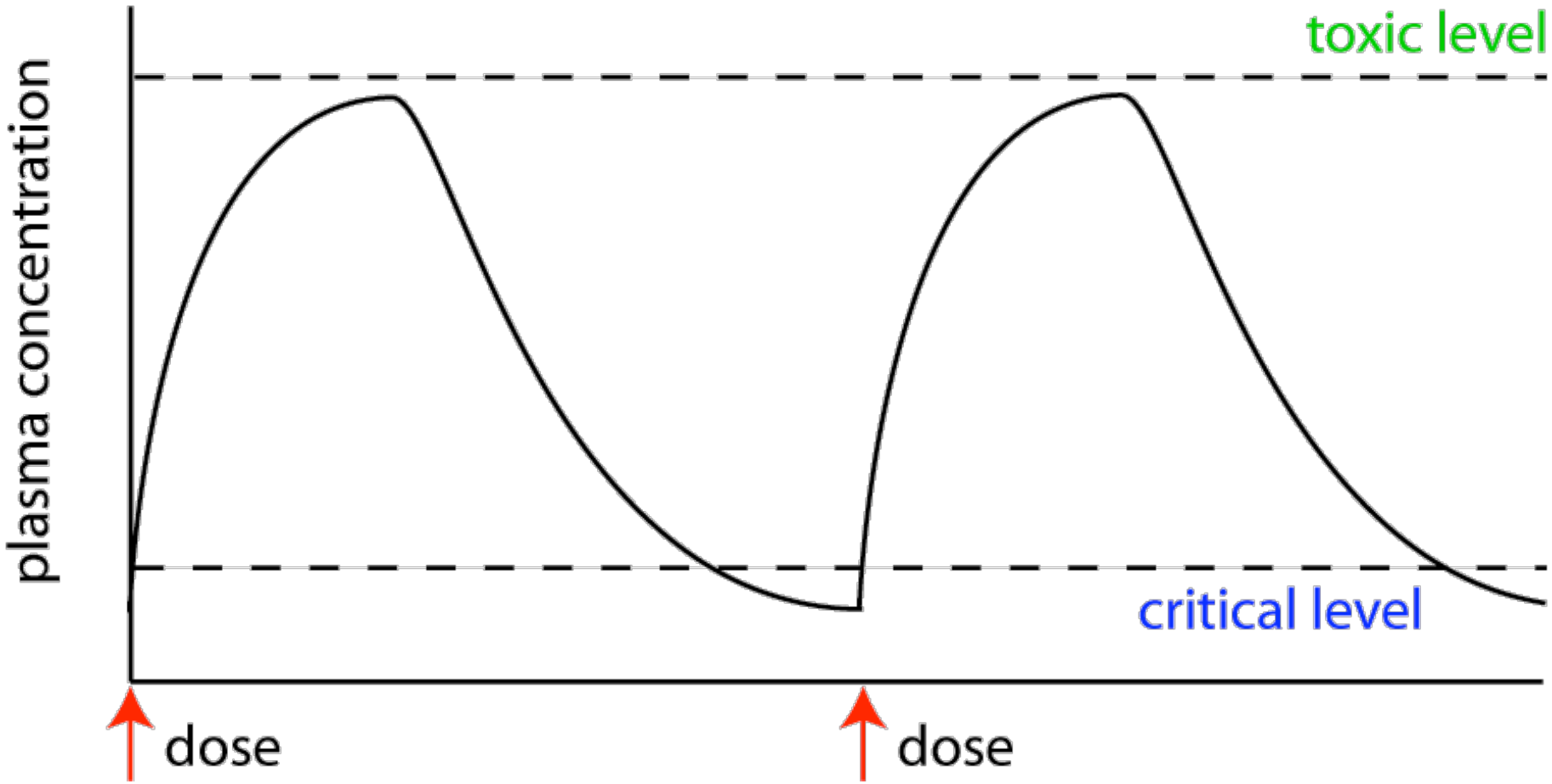
distribution

- **to extracellular fluid**
  - not into cells
- **rapid**
- **not protein bound**

elimination

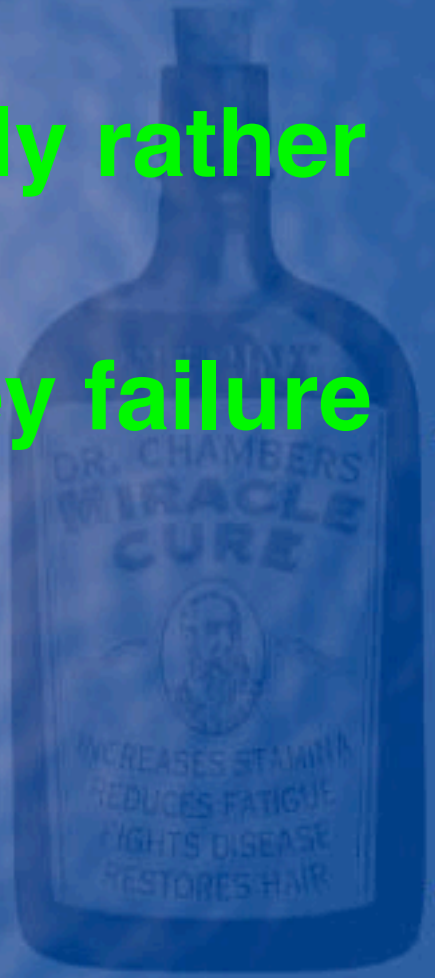
- **parenteral**
  - glomerular filtration
- **oral**
  - faeces
- **short half lives - 2 - 3 hours**
- **inactivated by pus**


toxic level
plasma concentration
critical level
dose
dose
dose


toxic level
plasma concentration
critical level
dose
dose

administration

- give a big dose once daily rather than small doses often
- reduce the dose in kidney failure
- monitor creatinine

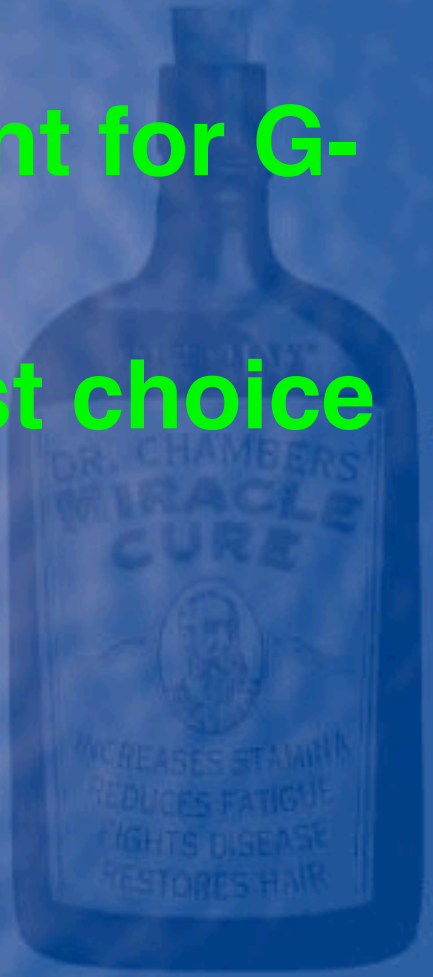


residues

- hangs around in kidneys for years
- long witholding times

use

- **used to be main treatment for G- aerobes**
- **fluoroquinolones now 1st choice**
  - less toxic in most species
  - horses?

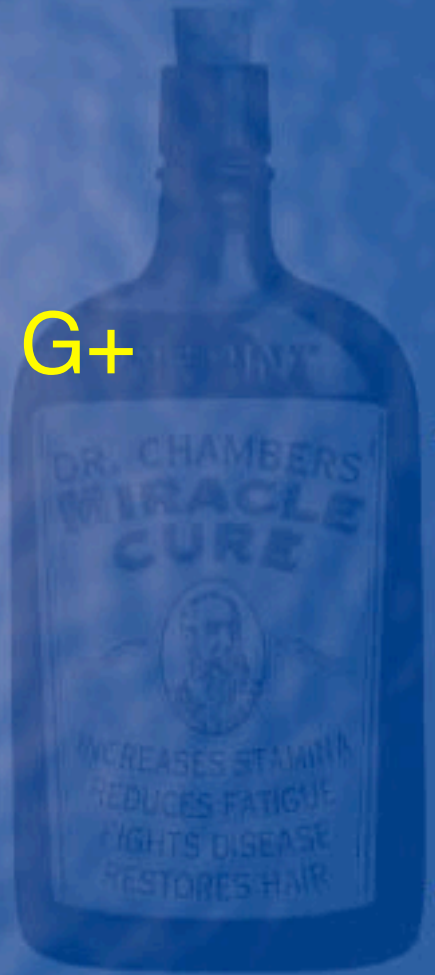


indications

- **streptomycin**
  - leptospirosis
  - (TB in people)
- **gentamicin etc**
  - serious G- infections
  - *Pseudomonas* infections
  - mainly horses

combinations

- **penicillin & gentamicin**
  - broad spectrum
  - sometimes used for difficult G+
- **penicillin, gentamicin & metronidazole**
  - covers most bacteria
  - peritonitis etc



abuse

- **mastitis**
  - no evidence of efficacy in NZ
- **neonatal diarrhoea**
  - use fluids instead
- **horticulture**
  - fireblight
  - use declining

precautions

- **fluid balance**
  - ensure animal is not dehydrated
  - watch blood pressure
  - avoid nephrotoxic drugs
- **working dogs**

interactions

- **penicillins**
  - synergy?
  - chemically incompatible
- **some cephalosporins**
- **frusemide**
  - nephrotoxicity

3 yr old thoroughbred

- injured knee 3 days ago
- knee now swollen, hot & painful
- TPR normal

diagnosis

- **septic arthritis**
  - bacteria unknown

treatment

- flush joint
- intra-articular penicillin & gentamicin
- systemic penicillin & gentamicin

aminoglycosides

- G- aerobes
- toxic to kidneys and ears
- give a big dose once daily rather than small doses often
- may be synergistic with penicillins under some conditions