

AVAILABILITY AND USE OF ANTIMICROBIALS FROM 1928 TO TODAY

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When did it all begin?

- Used by the ancients
 - Egypt: Garlic, willow, sycamore, acacia
 - India: Asafoetida (hing) which is sulpha-rich root
 - China
- 1600's
 - Fungus used in topical wounds (Penicillium spp)
 - Herbal remedies (rich in flavonoids, condensed tannins)



Modern use

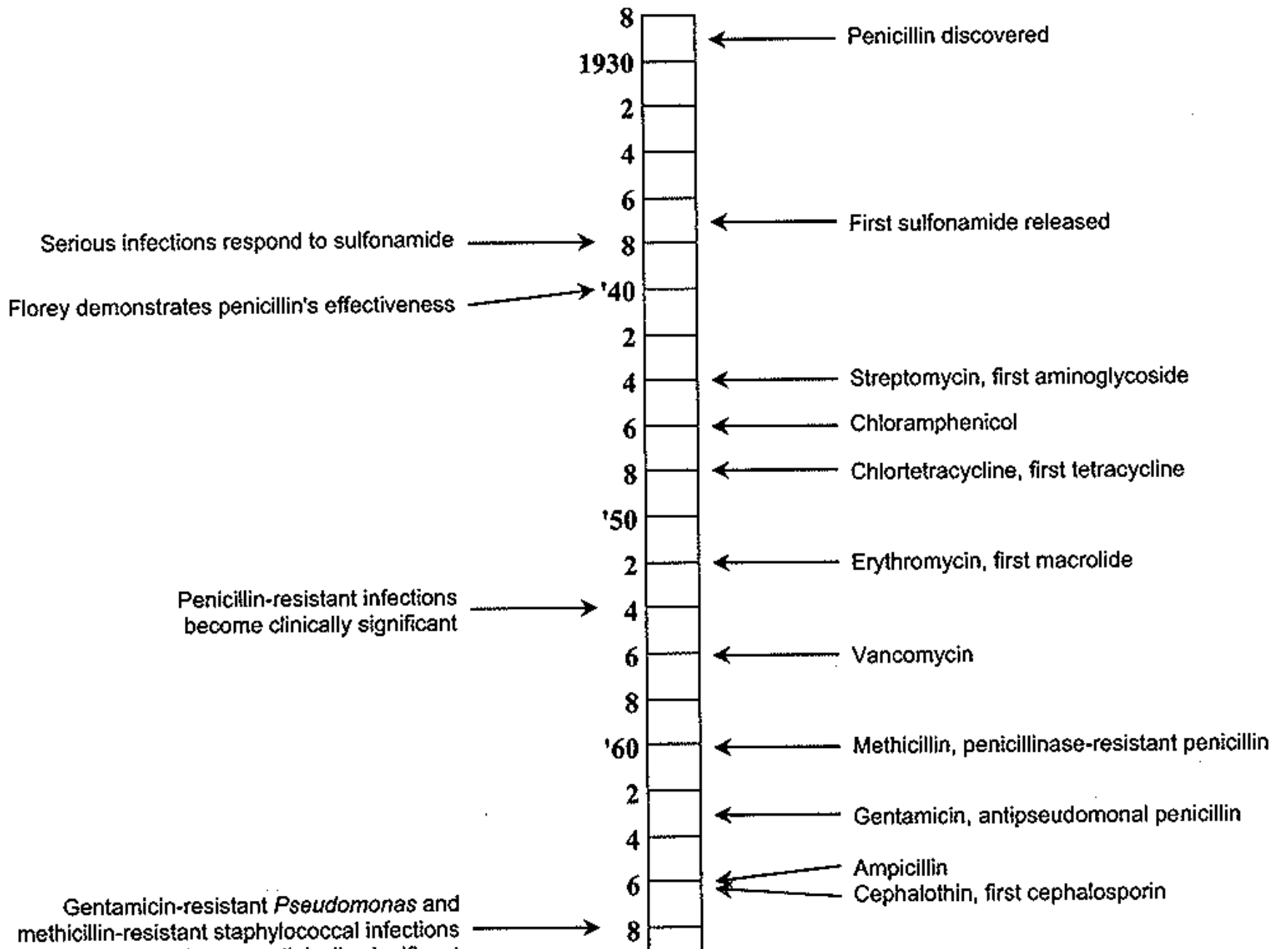


Modern Antimicrobial Age

- 1928
 - Flemming describes inhibitory properties of penicillin.
 - Unable to isolate the compound
- 1940
 - Florey's team mass produces penicillin
 - Effective in rodent model
- 1944
 - Pfizer manufactures penicillin in deep tanks
 - Streptomycin and terramycin follow

Human Infectious Diseases

Antibacterial Agents



OVERLAPPING IN VITRO ACTION OF ANTIBIOTICS

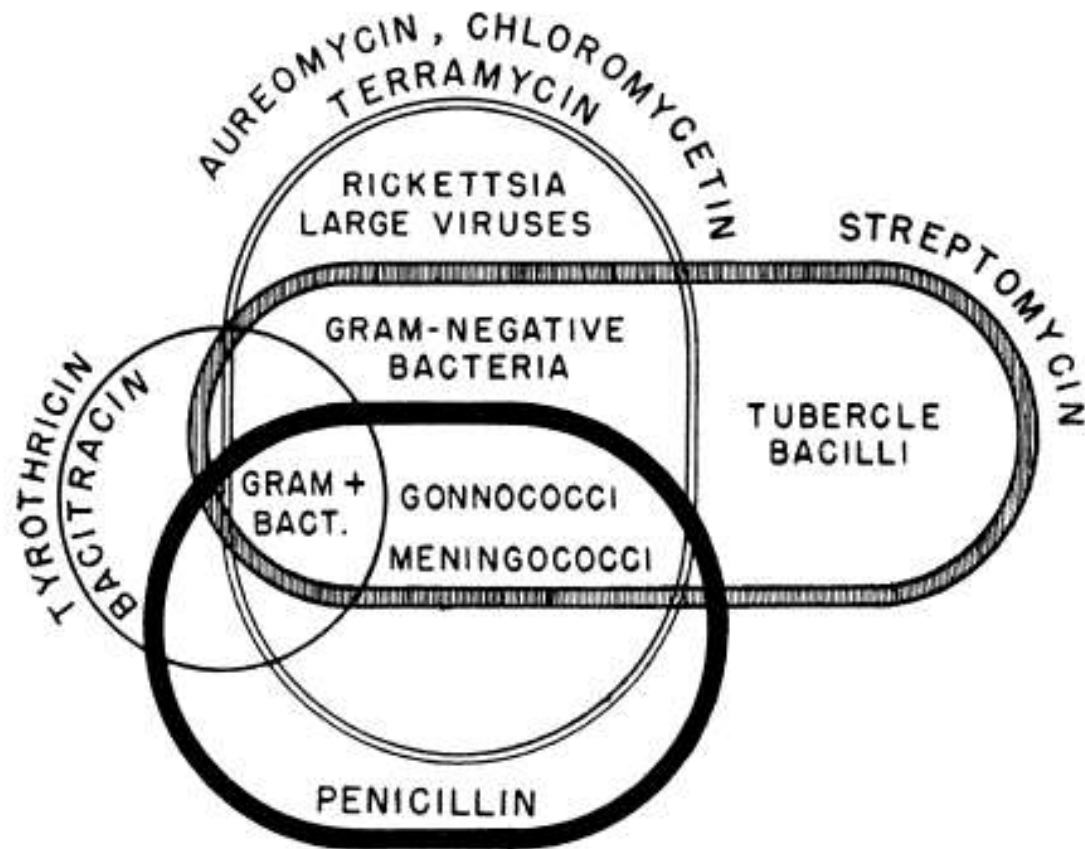
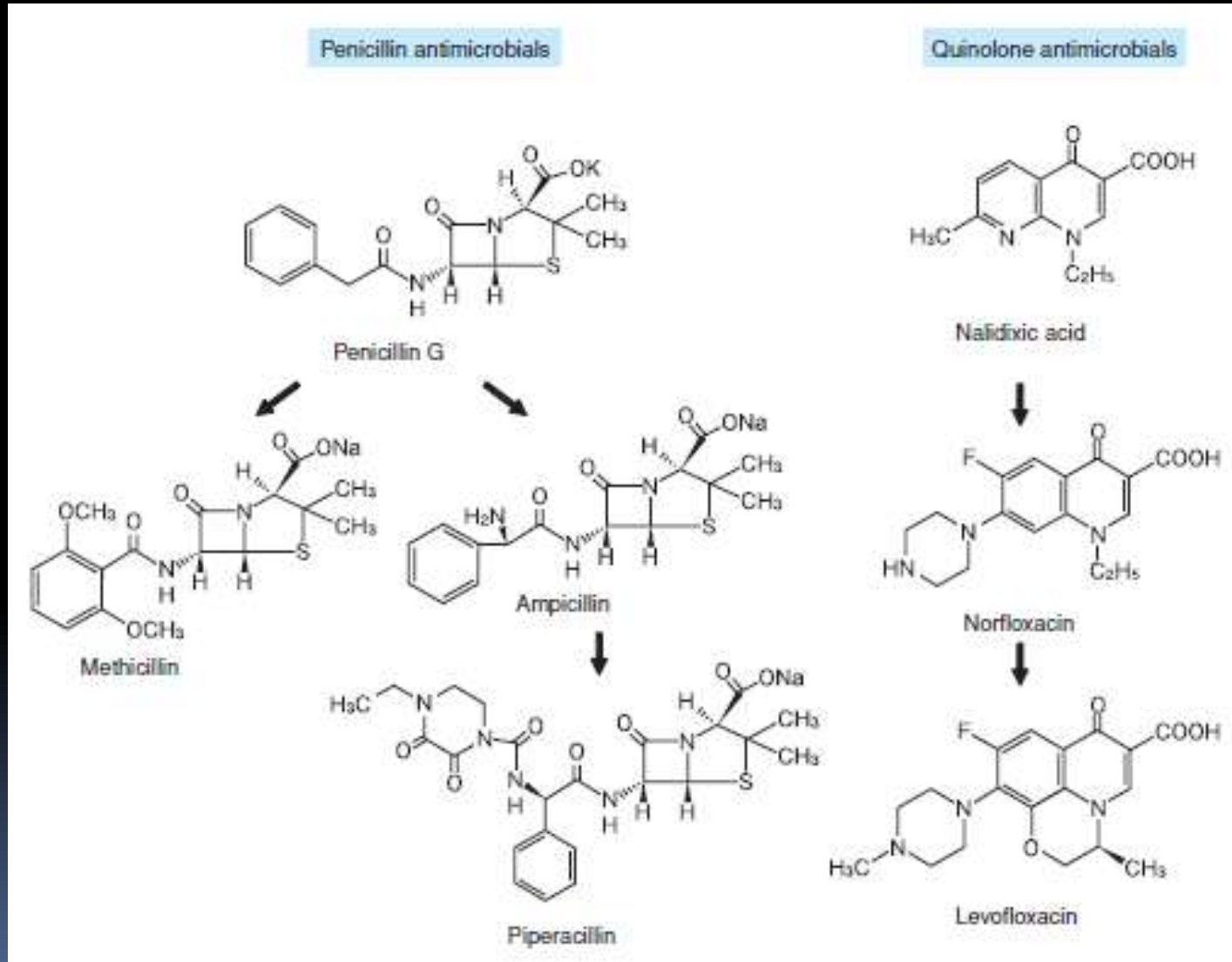


FIG. 1. Diagram showing the types of infections in which the different antibiotics are most effective. (After Pulaski, Ann. N. Y. Acad. Sci. 53: 348. 1950.)

Antimicrobial Production

- Thousands of new antibiotics/antimicrobials
 - Difference in spectrum, safety and efficacy
- From millions of different soil samples
- Majority of fungal origin
- Has only left us with 20 major classes
 - Similar skeletons, similar mechanisms,
- All characterised by development of resistance

Modification around a skeleton



Veterinary Use: Food Animals

- Penicillin: reconstituted in water used for mastitis in latter part of war.
- Streptomycin was shown to be a growth promoter in chicks in 1946.
- 1949, chlortetracycline fermentation mash improved growth in poultry.
- Later as became cheaper, therapeutic use began
- 1950-1960: Food safety concerns were given consideration.

Veterinary Use: Small Animals

- Not surprisingly that use in small animal began soon after discovery
- Latter 1940's: Dogs were being treated with streptomycin, sulphonamide, penicillins and/or aureomycin for pneumonias
- Also urolithiasis treated with surgical intervention and direct penicillin infusion

Food Safety concerns

- 1980's and 1990's
- Food safety based on MRL
 - Based on toxicity
 - Allergy potential?? (rare in food)
- More recently
 - Safety based on bacterial endpoints

Current Use of Antimicrobial

Companion Animals

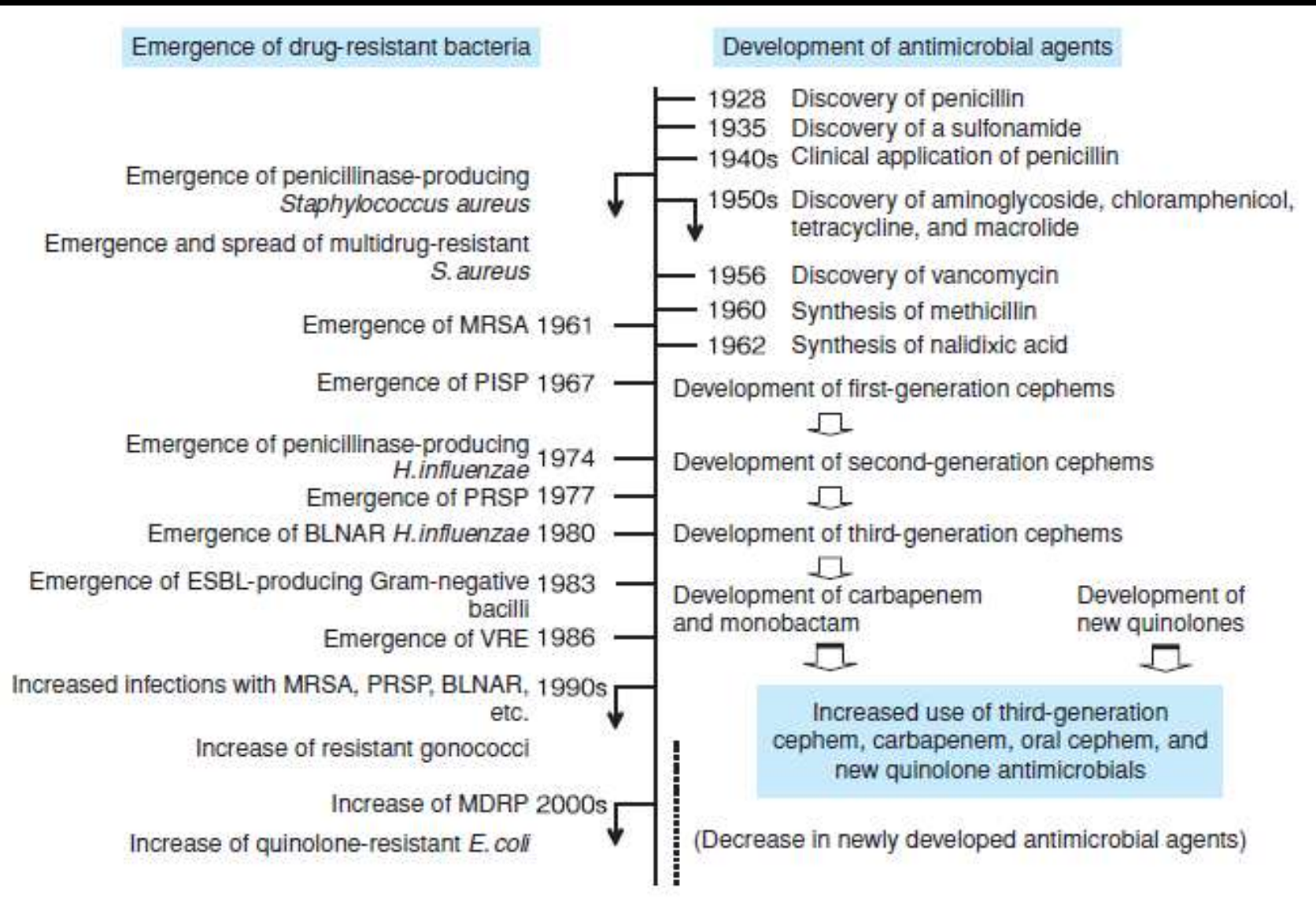
- Therapeutic
- Prophylactic

Productions Animals

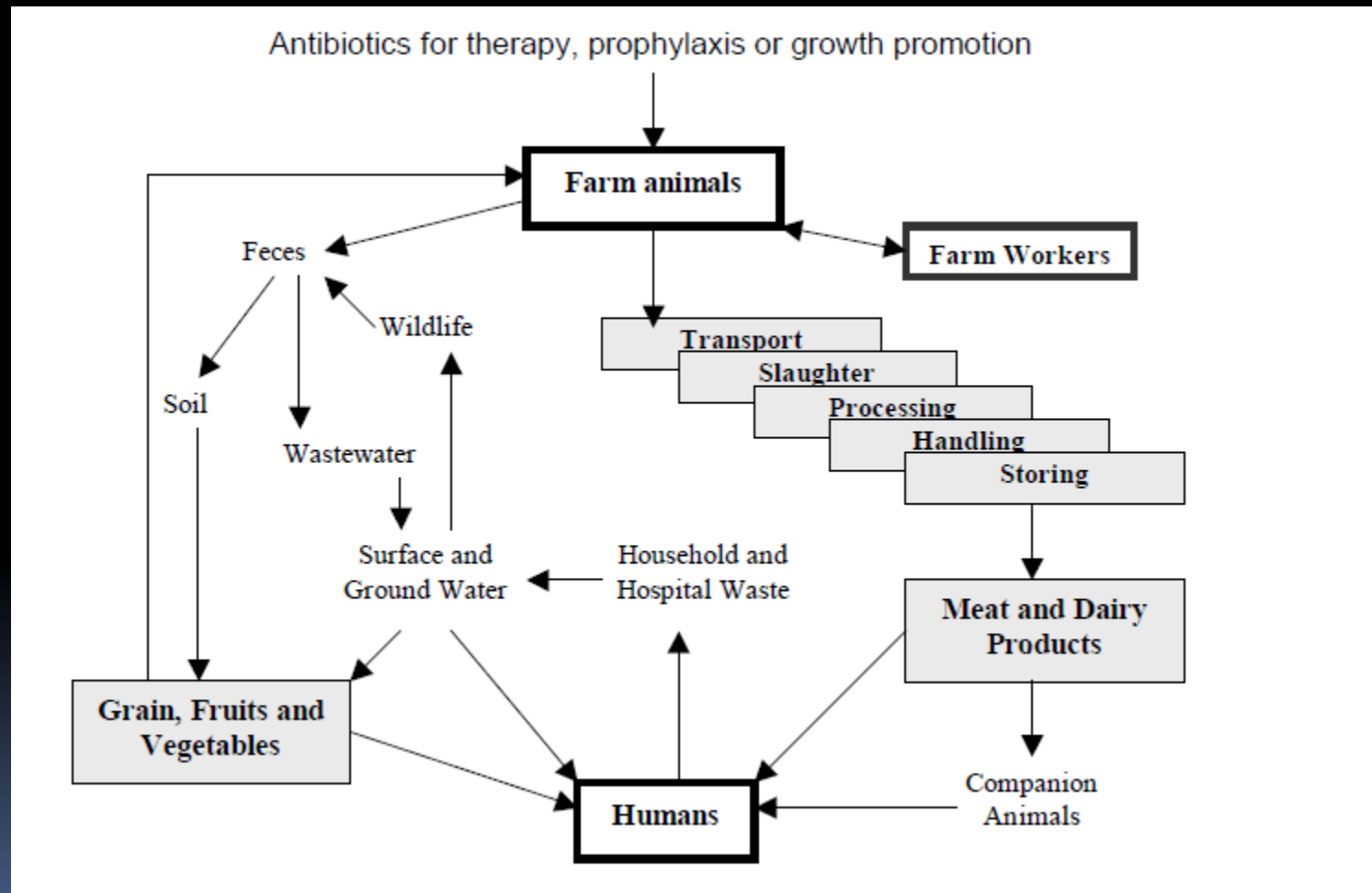
- Therapeutic
- Prophylactic
- Metaphylactic
- Growth Promotion (GP)

- Animal health uses 50% to 60% of all produced antimicrobials
- In the US, 33.33% used to enhance production (includes the ionophores)

Resistance



Development of resistance in food producing animals



Consequences of in-food antibiotics

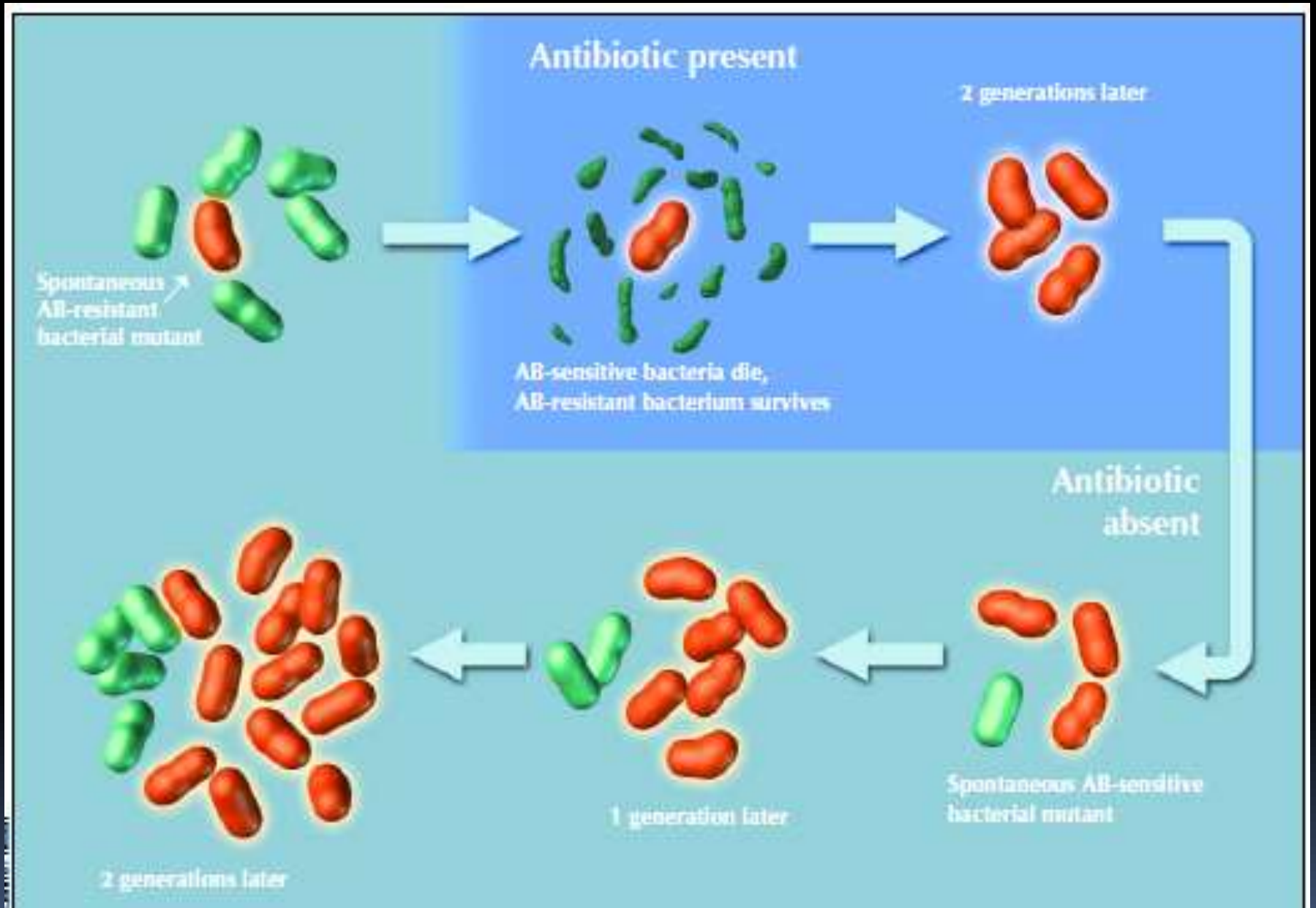
- Low chance of human toxicity – low absorption
- Possibility of transferable resistance
 - *Salmonella Typhimurium*
 - Vancomycin resistant enterococci
 - Erythromycin resistant staphylococci
 - *Campylobacter jejuni*
 - *Escherichia coli*
- Different regulatory approach: EU, FDA, etc
 - EU: prevent use
 - FDA: stringent control of use and availability (separate vet/medical therapeutic from AGP)

Growth Promoting Antibiotic: EU

- In the EU states
- 1971 – UK restricts use of compounds of human therapeutic value as growth promoter
- 1986-Sweden prevents antimicrobial use for growth promotion
- 95 to 99 (EU states) Avoparcin, Spiramycin, virginiamycin, Zn bacitracin banned
- 2006 – EU stops all in-food growth promoters based on 'precautionary principle'. Follows WHO recommendation

Life after the EU ban

- Benefits
 - Slight decrease in production in calves, pigs and fattening pigs
 - Increased investment in alternates (ZnO, enzymes)
 - Decrease in overall antibiotic utilisation
 - No increase in therapeutic use (except for Denmark).
 - Decrease in resistance in enterococci
 - Change in production practices of countries exporting to EU
- Pitfalls
 - Decrease in production in weaning pigs
 - Increased use in ionophors (necrotic enteritis in broilers)
 - Pastures contaminated with Zn
 - Increase in cost of production (\$0.12/kg)
 - Costs of a trace-back system (\$0.40/lb)
 - No decrease in human disease



Recent Trends

- Focus on good hygiene practices in production
- Antibiotics controlled by veterinarians
 - Focus on diagnosis
 - Therapeutic use promoted
- Follow prudent selection guidelines
 - Numerous guidelines available
 - Prophylactic/Metaphylactic should be avoided

Conclusion

- Antimicrobial been used since discovery
- Has been increased concerns in use
 - Divergence in veterinary and medical use
 - Increase precautions in food safety
 - Attenuated use in certain area
- Continues to be of clinical importance
 - Increasing need for quality protein production