Principles of antibiotic treatment; betalactams

Principles of antibiotic treatment - HIGHLIGHTS

***** Antimicrobials are drugs used to treat infectious diseases. Antimicrobial therapy can be **definitive (specific)**, **empirical**, or **prophylactic**.

* Main focus of antimicrobial therapy is selective targeted therapy in order to avoid toxicity to the host and to avoid emergence of resistance.

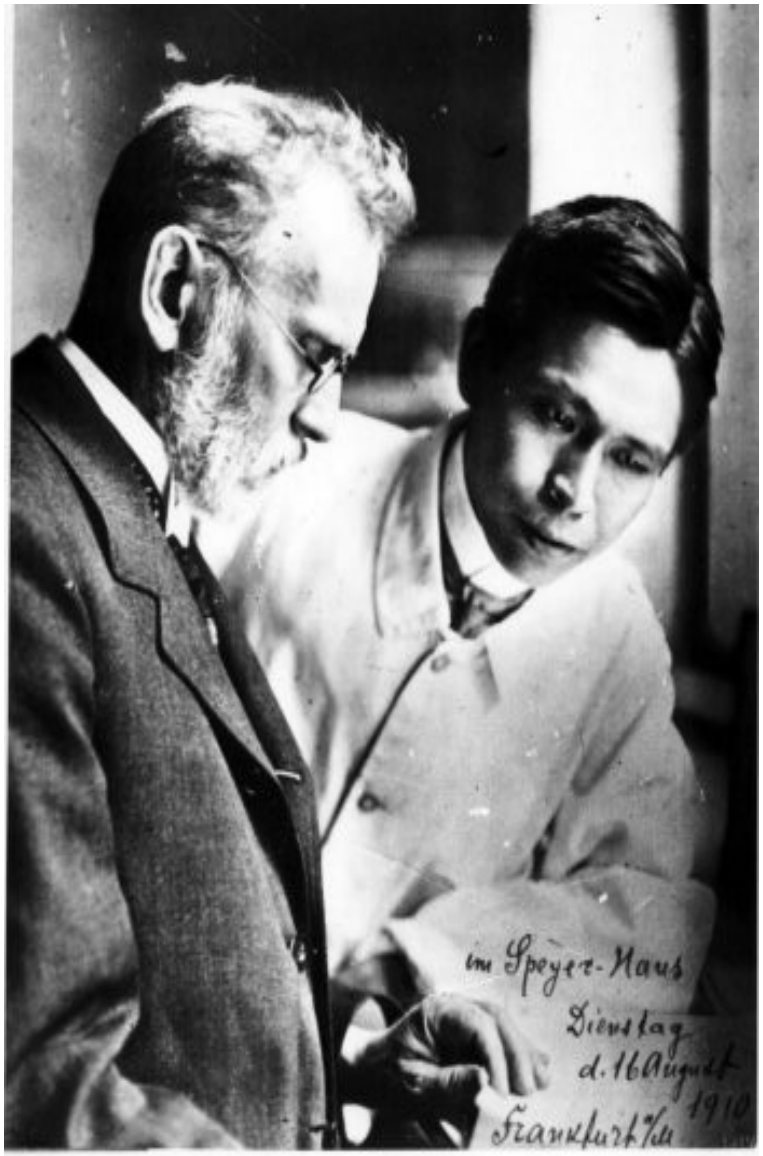
Principles of antibiotic treatment - HIGHLIGHTS

* This is achieved by understanding the pharmacokinetic/paharmacodynamic parameters of antimicrobials such as **bactericidal** and **static nature**, **spectrum of activity**, **host factors**, and **biology of the organism**.

What is important ?

- Antibiotics have drastically reduced the number of deaths due to infection.
- They have changed the face of health care.
- Currently lose efficacy.
- The threat of a return to the period before the discovery of antibiotics !
- If we want to maintain their effectiveness must be used correctly !!!

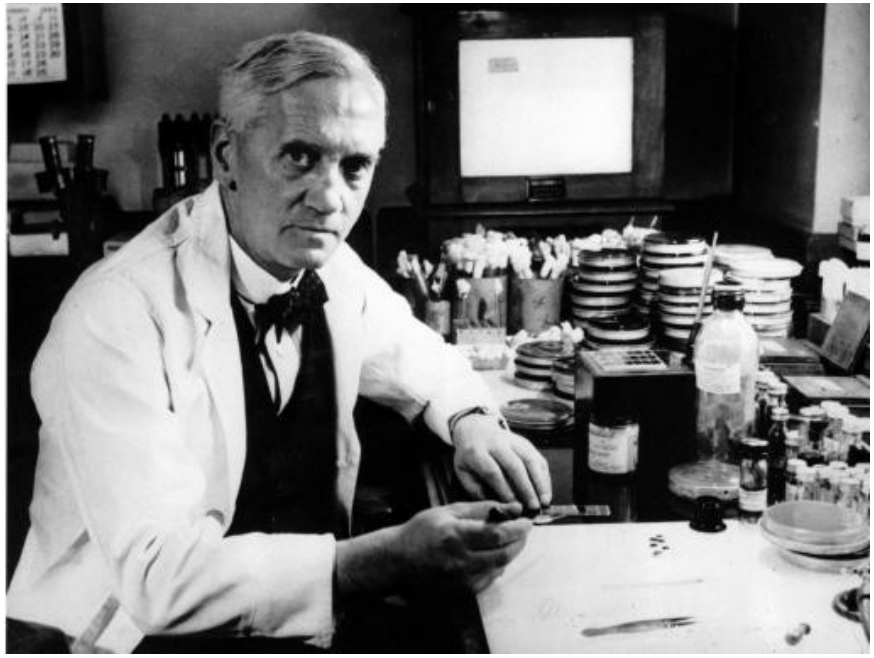
The History of Chemotherapy

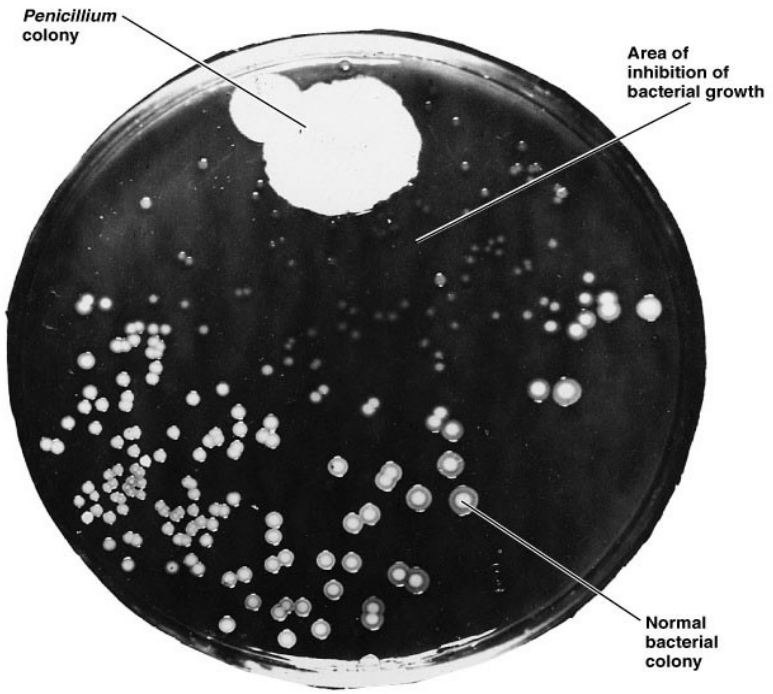


- **Paul Ehrlich** and Sahachiro Hata developed **Salvarsan** (Arsphenamine) against syphilis in 1910: The concept of **chemotherapy** to treat microbial diseases was born.
- Ehrlich´s Magic bullets.. - **Selective toxicity**: A drug that kills harmful microbes without damaging the host
- **Gerhard Domagk´-** Sulfa drugs (**sulfanilamide**) discovered in 1932 → against Gram+ bacteria

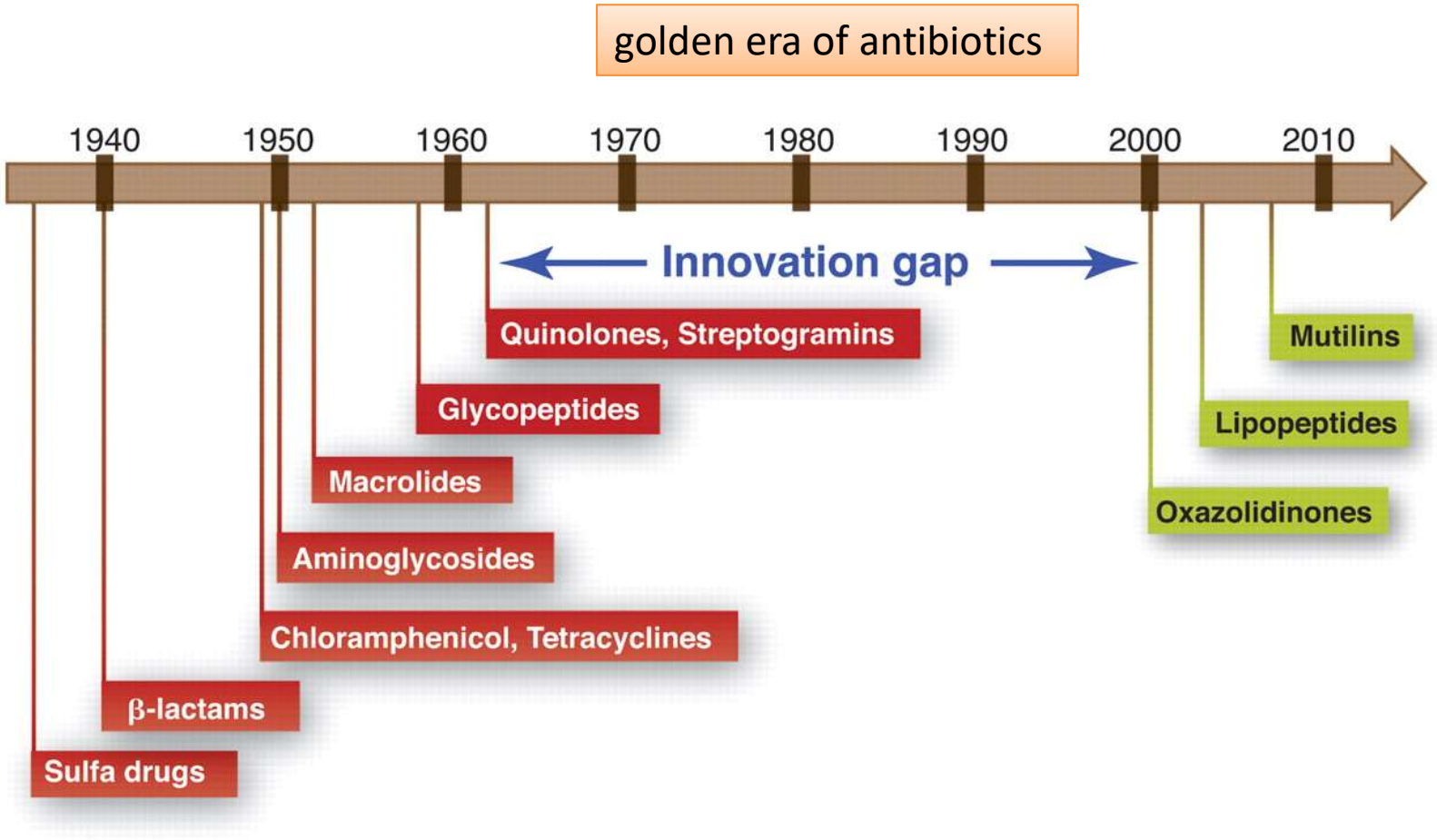
The History of Antibiotic

- **1928 – Fleming discovered penicillin, produced by *Penicillium*.**





History of and Innovation Gap in Antibiotics…



Definitions – ANTIBIOTIC x CHEMOTHETAPEUTIC AGENT

Antibiotic: Drug produced by a microorganism that kills or inhibits (in small amounts) the growth of another microorganism

Chemotherapeutic agent: (fluoroquinolones, sulfonamides): Synthetic chemical that kills or inhibits the growth of microorganisms

Antibiotic: in a broader sense – all drugs with antibacterial activity

Microbial Sources of Antibiotics…

TABLE 20.1 **Representative Sources of Antibiotics**

Microorganism	Antibiotic
Gram-Positive Rods	
Bacillus subtilis	Bacitracin
Bacillus polymyxa	Polymyxin
Actinomycetes	
Streptomyces nodosus	Amphotericin B
Streptomyces venezuelae	Chloramphenicol
Streptomyces aureofaciens	Chlortetracycline and tetracycline
Streptomyces erythraeus	Erythromycin
Streptomyces fradiae	Neomycin
Streptomyces griseus	Streptomycin
Micromonospora purpureae	Gentamicin
Fungi	
Cephalosporium spp.	Cephalothin
Penicillium griseofulvum	Griseofulvin
Penicillium notatum	Penicillin

Antibiotics are part of bacterial self protection…

*** Competition with other microorganisms – „produced by a microbe, inhibits other microbes“**

*** Microorganisms that produce these substances have molecular mechanisms to control production and prevent self-destruction – naturally resistant bacteria - (origin of acquired resistance)**

Definitions

- Chemotherapy — The use of drugs (antibacterial) to a treat disease
- Antimicrobial drugs — Interfere with the growth of microbes within a host
- Antibiotic — Substance produced by a microbe that, in small amounts, inhibits another microbe
- **Selective toxicity — A drug that kills harmful microbes without damaging the host**
- Bacteriostatic/ or bacteriocidal — Modes of action that either kill inhibit growth
- Spectrum of activity between narrow vs. — Range of effect within or groups of microbes; broad-spectrum

Intensity and speed of action of antibiotics

Bactericidal: kill bacteria

Bacteriostatic: inhibit growth of susceptible bacteria, rather than killing them immediately; will eventually lead to bacterial death

Antibiotic spectra

- **Range of effect within or between groups of microbes; narrow vs. broad-spectrum**

- **The original natural molecules used by humans as antibiotics have a very narrow spectrum.**
  - **Penicillin activity is restricted to Gram-positive bacteria.**
- **Natural molecules can be chemically modified making it possible to broaden their spectrum.**
- **Antibiotics are classified as either broad-spectrum or narrow-spectrum**

Antibiotic Spectrum of Activity

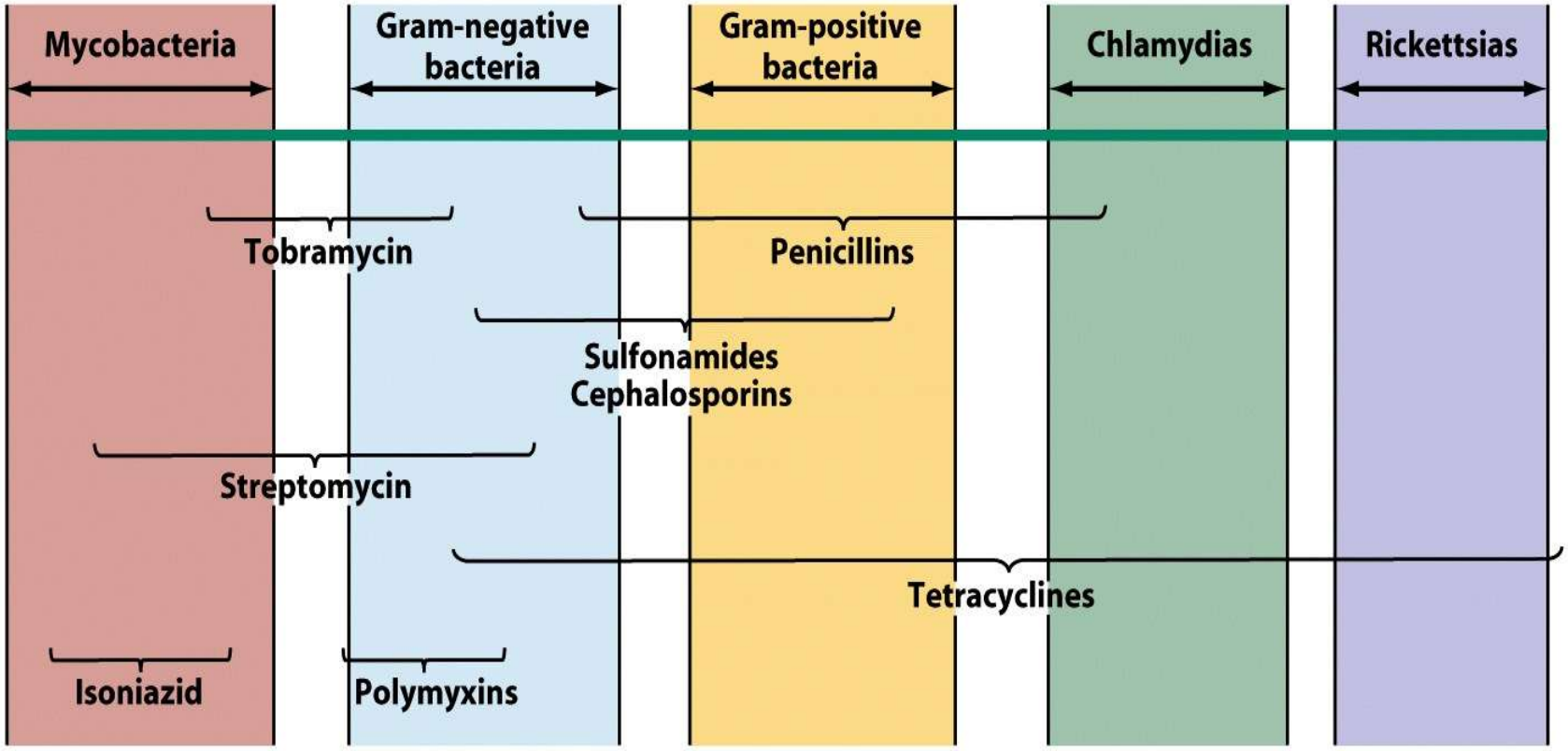


Figure 13-1 Microbiology, 7/e

Spectrum of activity in clinical practice

- broad spectrum - the higher probability of kill pathogens (if unknown)
- broad spectrum - higher probability dysmicrobia, side effects and the emergence of resistance
- prefer targeted therapy - we know the pathogen, its sensitivity to antibiotics and may choose antibiotics with narrow spectrum

IDEAL ANTIBIOTICS CRITERIA

1. Most selective, most effective to infected microorganisms
2. More bactericidal effect in the site of action
3. Antibacterial effect is not interfered by body fluid, exudate, plasma protein or enzymes and persist for a long duration in the blood
4. Minimal toxicity
5. Resistance develops slowly
6. Given by any route
7. Reachable cost

ANTIBIOTIC TARGETS

* The cell wall is the most appealing target for antibiotics.
* It is found in both Gram-positive and Gram-negative bacteria.

* The plasma membrane is involved with important physiological functions.

  - It is a prime target for antibiotics.
  - Any disruption of the membrane destroys the bacteria.

* Ribosomes are sites for protein synthesis.

* Antibiotics act at different sites on bacterial ribosomes – inhibiotion of protein synthesis

* DNA and RNA are universal components which can be attacked by antibiotics.

Modes of Antimicrobial Action