

The background is a solid blue color with a gradient. A thin, light blue curved line starts from the top left and curves downwards towards the center. A larger, semi-transparent blue triangular shape is positioned in the lower right quadrant, pointing towards the center.

Principles of antibiotic therapy

Key points

- Introduction
- Choice of the proper antibiotic
- Antimicrobial combinations
- Choice of the route and efficacy assessment

Sir A. Fleming: discoverer of Penicillin



Noble prize 1945

Choice of the proper agent

- 1) Identification of the organism
- 2) Antimicrobial susceptibility
- 3) The narrowest effective spectrum
- 4) Host factors (Allergy, Age, renal and liver, site of infection, pregnancy, metabolic abnormalities)

Identification of the organism

- Gram stain (CSF, Pleural, synovial, peritoneal, urine, sputum)
- ELISA / latex agglutination
- PCR
- **CULTURE** (best if before Abx)
- Bacteriologic statistics (the application of knowledge of the organisms most likely to cause infection in a given clinical sitting)

Antimicrobial susceptibility

- Disk diffusion method
- Epsilometer (E-test)
- Minimum inhibitory conc. (MIC)
- Minimum bactericidal conc. (MBC)
- Specialized testing for: fastidious organisms (obligate anaerobes), *Haemophilus spp*, pneumococci, MRSA
- Resistance mechanism of the bacteria:
eg: *Staph. aureus*, *E. coli*, *Enterbacter*



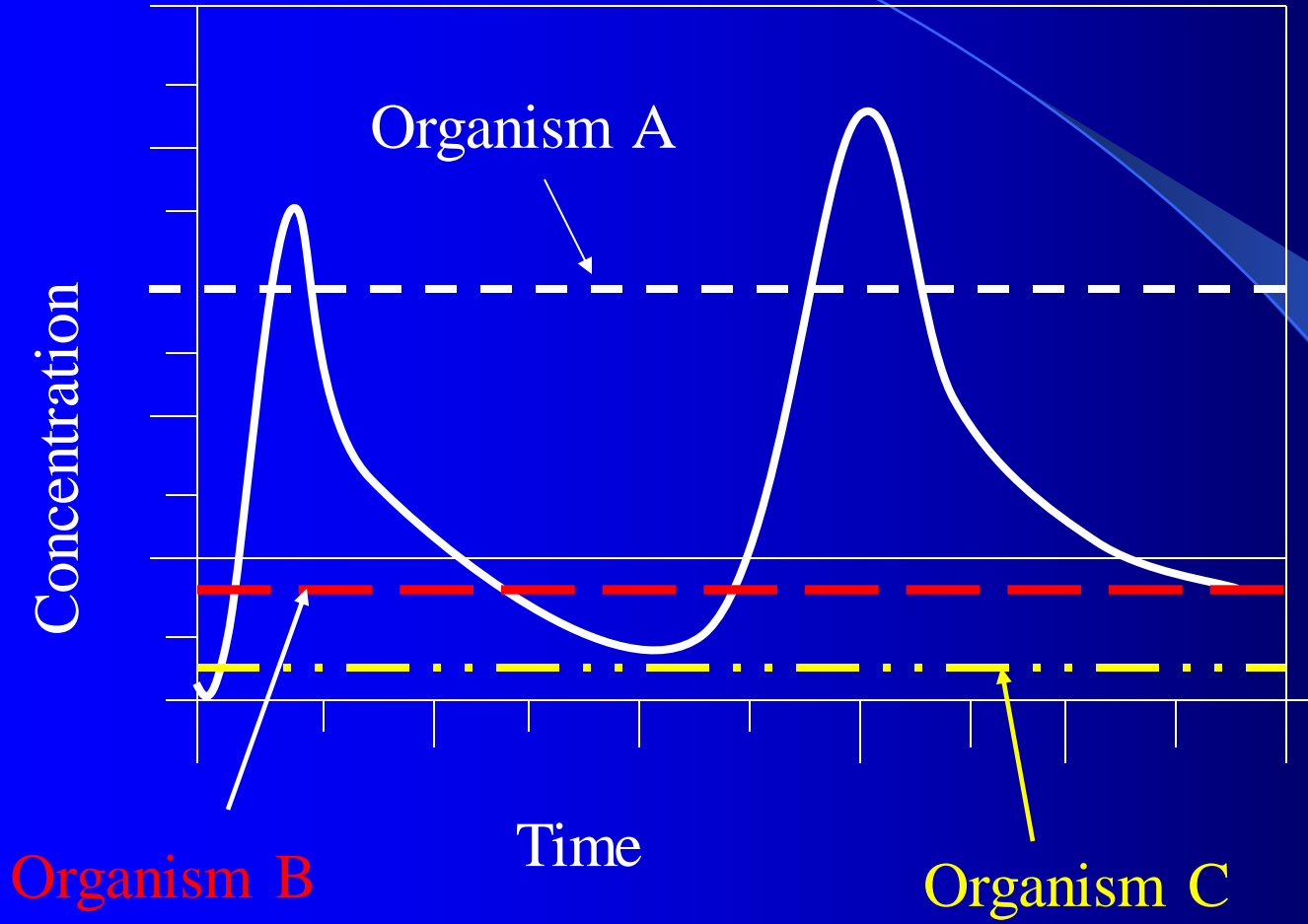


Pharmacodynamic profile

- Area under the curve / time curve to MIC (AUC / MIC)
- Maximal serum conc. / MIC (C_{\max} / MIC)
- Time during dosing interval that plasma conc. exceed the MIC (t / MIC)

Conc. & Time dependent dosing

- **Conc. dependent** (FQ, Ag) → increase in conc leads to a more rapid rate of bacterial death (i.e. large dose at long intervals)
- **Time dependent** (β -lactams, vancomycin)
→ reduction in bacterial density is proportional to the time that the conc. exceeds MIC (i.e. sufficient dose at appropriate intervals to keep conc. above MIC)



A : resistant; B : moderately susceptible; C very susceptible

Published data

- Manuals

eg: Sanford's

Medical letter on drugs and therapeutics

(nb: use this information within its context)

Host factors

- Previous history of adverse reactions
- Neutrophil function → neutropenic are treated aggressively
- CLL, MM, asplenia → treated empirically

Age

- Renal function (impaired physiologic function)
- Absorption
- Tetracyclines
- INH hepatotoxicity
- Nephrotoxicity
- Ag and cochlear toxicity

Genetic / metabolic

- Hemolysis in G6PD deficiency
- DM : sulfa drugs can potentiate the sulfonylurea hypoglycemic agents
 - Dextrose load
 - Poor IM absorption (use IV route)

Pregnancy

- Safe : PCN, cephalosporin, erythromycin base
- Dangerous: tetracyclines (hepatic toxicity, dental discoloration)
- ? Teratogenic: metronidazole
- FQ, clarithromycin, erythromycin →
Contraindicated
- ?? rifampin, Ag, azithromycin, clindamycin, imipenem, vancomycin, TMP

Renal and liver fx

- Vancomycin & Aminoglycosides
(gentamicin, amikacin)

Site of infection

- Optimal therapy requires concentrations $>$ MIC at the site of infection
- Meningitis
 - Endocarditis
 - Osteomyelitis
 - Chronic prostatitis
 - Intraocular infections
 - Abscesses
 - Foreign body
 - UTI

Immune system

- Abx can cause immune suppression esp. in the immunosuppressed patients
- Suppress monocyte transformation, phagocytosis, chemotaxis, antibody production

Combinations

- Some physicians use combinations for the sense of security → deleterious effects
- **Indications:** 1) prevention of emergence of resistant bacteria : TB, *staph* endocarditis
2) polymicrobial infections : abd. sepsis
3) initial therapy: eg: Ag + piperacillin
4) Synergism:...

Synergism

- For resistant organisms
- Limited data to support their benefit
- e.g.: PCN + Ag → Enterococcal endocarditis
- Oxacillin + Ag → Staph. endocarditis
- Anti-pseudomonal β -lactam + Ag → Pseudomonas bacteremia
- Impaired host

Antagonism

- Too many in vitro reports
- Clinically was seen in : PCN + tetracyclines
- 2 β -lactams \rightarrow induce β lactamases
- More important in immunosuppressed pts

Adverse effects

- 5% of pts will have a side effect
- Combinations → more cost, more adverse effects

Route

- Oral → stable , mild infection (reliable pts)
- IV → serious infections (sepsis) + DM

Monitoring the response

- Clinically
- Drug levels
- Lab tests

Cost

- If all other factors are equal, the least expensive drug should be chosen

Wrong uses

- Abx for simple gastroenteritis
- Routine use of Flagyl to clean bowel
- Abx for common cold and simple bronchitis