Principles of antibiotic therapy

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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 bactercidal conc. (MBC)
- Specialized testing for: fastidious organisms (obligate anaerobes), *Haemophilus spp*, pneumococci, MRSA
- Resistance mechanism of the bacteria:

  eg: *Staph. aureus, E. coli, Enterbacter* …..

Disc diffusion test

E - test

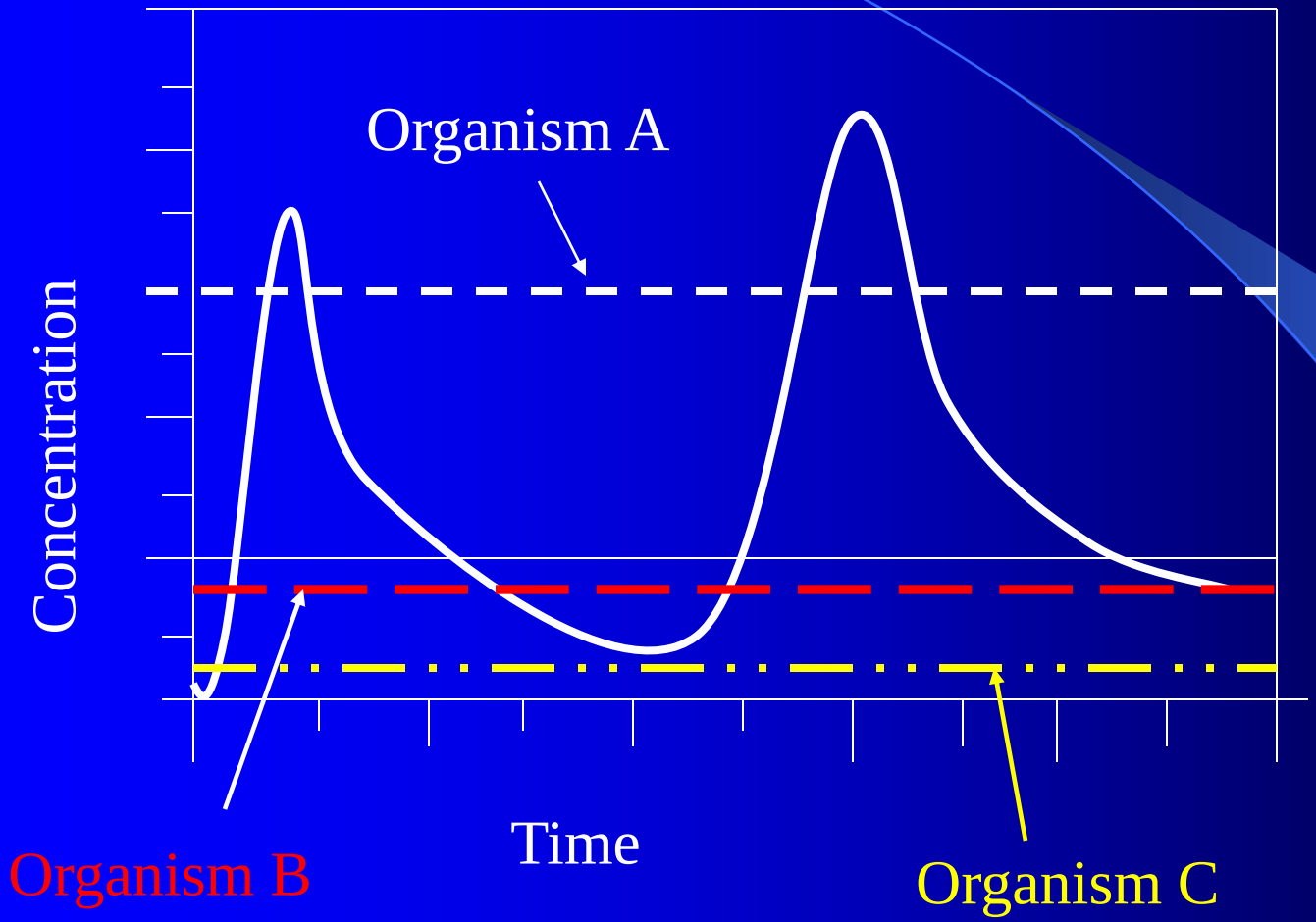
Pharmacodynamic profile

- 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

- Mobile applications
- 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 → Contrindicated**
- ?? rifampin, Ag, azithromyccin, 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

  Osteomylitis

  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 → 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

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