Principles of antimicrobial therapy

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1. The definition of: antimicrobial agents, antibiotics, chemotherapeutics.

2. The effects of antibacterial drugs and basic terms MIC

synergism - inhibition of growth with a combination of drugs when their concentration are less than or equal to 25% of the MIC of each drug acting alone

additive result - 50% of the MIC of each drug is required to produce inhibition

antagonism - more than 50% of the MIC of each drug is necessary to produce inhibitory effect

3.Selection of an antibiotic – what is important?

- Type of therapy: empiric or definitive
- Identification of microbe responsible for infection
- Duration, density of inoculum

4.Empiric therapy - type of infectious microbe is expected on the base of site of infection, clinical characteristics of infection and infection origin (community acquired or hospital-acquired).

No microbiological confirmation.

Definitive therapy - type of infectious microbe is expected - based on microbiological test

5.Odontogenic infections

•Causes: dental caries, deep restorations,pulpitis, periapical abscess, periodontitis, periodontal abscess, pericoronitis

•Results: osteoperiosteitis of the jaw, osteomyelitis, deep fascial space infections

•Predisposing conditions: periodontal accumulations, necrotic pulp tissue, tissue damage

•Young children

•Endogenous flora of the mouth: anaerobes >aerobes, synergism

Etiology:

- Bacteroides, anaerobic Streptococcus, Fusobacterium, Peptococcus, Peptostreptococcus, Eubacterium, alpha-hemolytic streptococci, Actinomyces, Veilonella, Lactobacillus
- Staphylococci (trauma), Gram-negative aerobic rods (elderly, hospital-aquired)

6. The resistance to antibiotics

- Primary
- Secondary

Mutation (one-step, multi-step)

Migration of genetic material (transduction, transformation, conjugation, transposition)

The biochemical mechanisms of the resistance to antibiotics:

- enzymatic barrier
- modification of target sites
- the permeability barrier
- omitting mechanism
- mechanism of increased excretion

7.Postantibiotic effect - antimicrobial activity, even when antibiotic concentration in serum is below MIC

aminoglycosides

fluorinated quinolones

macrolides

8.Antibiotic selection and adverse effects;

Kidneys dysfunction – avoid: aminoglycosides, vancomycin, polipeptides, amphotericin B

Liver dysfunction - avoid: doxycyclin, clindamycin, erythromycin, ketokonazole, isoniasid

Neurologic diseases

Attention: high doses of natural penicillins, nitrofurantoin, quinolones

Hypersensitivity

Attention: beta-lactams, sulfonamides, macrolides

Genetic problems

Sulfonamides, nitrofurantoin – glucose-6-phosphate dehydrogenase deficiency

Neutropenia

Attention: metronidazole, aminopenicillins, cefalosporins

Anemia

Attention: zidovudine, amphotericin B

Older persons: attention!!!

tetracyclines, aminoglycosides, vancomycin, quinolones

Neonates and infants
tetracyclines, quinolones, sulfonamides!!!
Pregnancy and lactation: acceptable –natural penicillins, aminopenicillins, 1st generation cephalosporins, erythromycin, contraindicated: quinolones, tetracyclines, sulfonamides

9.Antibiotic selection and distribution

- Proteins in plasma: hipoalbuminemia (hepatic failure, nephrotic syndrome) – Sulfonamides? Aminoglycosides?
- Leukocytosis (leukemia), anemia – Aminoglycosides?
- Bones infection. Clindamycin? Aminoglycosides?
- Antibiotic selection and topical factors- ematoma, abscessus, gastic acid pH

10.Antibiotics combinations
Bactericidal+bactericidal = synergism or indifference, rare antagonism
Bacteriastatic+bacteriastatic = additive result, rare antagonism or synergism
Bactericidal+bacteristatic = additive result
or antagonizm (higher susceptablity to bacteriacidal) or synergism (higher susceptability to bacteriastatic)

synergism:
$MIC_{A+B} \leq 25\%MIC_A$ i $MIC_{A+B} \leq 25\%MIC_B$
Drug A increases susceptablity of microbes to drug B
Additive effect:
$MIC_{A+B} = 50\%MIC_A$ i $MIC_{A+B} = 50\%MIC_B$
Drug A and B act independent each on other
Antagonism:
$MIC_{A+B} > 50\%MIC_A$ i $MIC_{A+B} > 50\%MIC_B$
Drugs A and B act independent each on other

Indications for the clinical use of
antibiotics combinations
When?

- treatment of mixed infections , long-term antibiotic therapy, empiric therapy

Why?

- resistance prevention, synergism achievement, doses reduction

11.Principles for prescribing antimicrobials:
•Use only when there is an indication
•Use only when the risk/benefit balance is favorable
•It is not a substitute for establishing adequate drainage
•Choose the narrowest spectrum drug that will be effective
•Adequate dose
•Appropriate duration
•Choose the drug with the fewest side effects
•Choose the least expensive agent
•Laboratory identification if necessary
•Avoid resistance: too long use and/or use of sub-optimal doses

12. Prophylaxis against sytemic infections according to ADA 2019

Patient Selection

The current infective endocarditis/valvular heart disease guidelines state that use of preventive antibiotics before certain dental procedures is reasonable for patients with:

- prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts;
- prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords;
- a history of infective endocarditis;
- a cardiac transplant[a] with valve regurgitation due to a structurally abnormal valve;
- the following congenital (present from birth) heart disease:[b]
- unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
- any repaired congenital heart defect with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or a prosthetic device

[a] *According to limited data, infective endocarditis appears to be more common in heart transplant recipients than in the general population; the risk of infective endocarditis is highest in the first 6 months after transplant because of endothelial disruption, high-intensity immunosuppressive therapy, frequent central venous catheter access, and frequent endomyocardial biopsies.*[9]

[b] *Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease.*

Pediatric Patients
Congenital heart disease can indicate that prescription of prophylactic antibiotics may be appropriate for children. It is important to note, however, that when antibiotic prophylaxis is called for due to congenital heart concerns, they should only be considered when the patient has:

- Cyanotic congenital heart disease (birth defects with oxygen levels lower than normal), that has not been fully repaired, including children who have had a surgical shunts and conduits.
- A congenital heart defect that's been completely repaired with prosthetic material or a device for the first six months after the repair procedure.
- Repaired congenital heart disease with residual defects, such as persisting leaks or abnormal flow at or adjacent to a prosthetic patch or prosthetic device.

Antibiotic prophylaxis is not recommended for any other form of congenital heart disease.

Dental Procedures
Prophylaxis is recommended for the patients identified in the previous section for all dental procedures that involve manipulation of gingival tissue or the periapical region of the teeth, or perforation of the oral mucosa.

13.Superinfections
The appearance of bacteriological and clinical evidence of a
new infection during chemotherapy of a primary one.

- changes in the normal microbial population of the intestinal, upper respiratory and genitourinary tract
- when broad-spectrum agents are used