Basic principles of antibiotic use

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1. Is antibiотical treatment indicated based on clinical findings?
   - Obvious bacterial infection
   - Localized infections: pneumonia, pyelonephritis etc.
   - Infections with characteristic clinical findings: cellulitis, streptococcal tonsillitis etc.
   - Inflammatory markers: leukocytosis, neutrophilia, lymphocytopenia, left shift, presence of bands, elevated C-reactive protein (CRP) and procalcitonin (PCT)

2. Urgency of the situation?
   - Non-urgent situation: mild infection, which does not require treatment until the diagnosis is not established
   - Urgent situation: the patient with suspected severe infection:
     - Febrile neutropenia
     - Bacterial meningitis
     - Necrotizing cellulitis
     - Septic shock

3. Have appropriate clinical specimens been obtained, examined and cultured?
   - Standard cultivation
   - Gram stain
   - Latex agglutination (Strep test®)
   - Appropriate cultures – anaerobic and aerobic cultures
   - Antibiotic treatment can be modified when the pretreatment cultures become available
   - Follow up cultures are less reliable than initial pretreatment cultures

4. What organisms are most likely to be causing the infection?
   - Type of focal infection
   - Age: bacterial meningitis of newborns – group B streptococci, Gram-negative bacteria
   - Epidemiologic features: hospital vs. community acquired infections, prior antibiotic use, etc.
   - Prior culture data: surveillance cultures in critically ill patients, immunocompromised patients, etc.

Diagnosis of community acquired pneumonia

- Pneumonia due to mycoplasma and chlamydia - procalcitonin (PCT) < 0,5 ng/mL
- S. pneumoniae, L. pneumophila serotype 1 - detection of antigens in urine
- L. pneumophila - signs of disseminated infection, diarrhea and confusion
- Infection due to mycoplasma and chlamydia - multiform erythema, conjunctivitis, urethritis and reactive arthritis
Managing community acquired pneumonia

Major symptoms (CURB-65)
- C - confusion
- U - urea >7 mmol/L
- R - respiratory rate >30 breaths/min.
- B - blood pressure <90 mm Hg, diastolic BP <60 mm Hg
- Age >65 yrs.

Minor symptoms
- Immunosuppression or severe underlying diseases (IHD, DM, CRF etc.), bilateral pneumonia, oxygen saturation <92%

Antibiotic treatment
- Only one major symptom of CURB-65 classification = β-lactam p.o., i.m. nebo i.v. or 1st generation cephalosporin
- CURB-65 ≥2 = β-lactam + advanced macrolide
- CAP due to M. pneumoniae, C. pneumoniae or L. pneumophila = advanced macrolide (azithromycin, clarithromycin) or doxycycline (adults)

5. If multiple antibiotics are available to treat pathogen, which agent would be the best?

- Prior antibiotic allergies
- Antibiotic penetration - CNS infection, abscesses etc.
- PH - aminoglycosides are much more effective in an alkaline medium
- Potential side effects - chloramphenicol – occurrence of aplasia
- Bactericidal (β) vs. bacteriostatic agents - in lifethreatening infections or in immunocompromised patients β antibiotics are necessary

6. Is an antibiotic combination appropriate?

- Synergism - one antibiotic enhances the activity of another (measured by time killing curves)
- - serial inhibition of microbial growth
- - one antibiotic enhances the penetration of another (penicillin and aminoglycoside)
- Broad spectrum of activity – in severe sepsis and septic shock of unclear etiology and febrile neutropenia
- Infecction due to multiple organisms – intraabdominal sepsis or pelvic abscess

7. Are there special considerations related to host factors?

- Genetic factors
- Pregnancy and lactation: A. antibiotics considered safe - penicillins, cephalosporins, erytromycin base and aztreonam. B. antibiotics to be used with caution - aminoglykosides, vancomycin, clindamycin, imipenem-cilastatin and cotrimoxazole
- Renal and liver functions

Disadvantage of multiple antibiotics

- Risk of drug sensitivity or toxicity
- Risk of colonization with resistant organism
- Possibility of antagonism (i.e. penicillin and tetracyclin)
- High cost
- False sense of security: the use of multiple agents to cover all organisms is not possible and may be associated with complications
8. How to assess effectiveness of antibiotic therapy?

- Clinical assessment - decreased temperature - 48 hrs. for bactericidal antibiotics, 3 to 4 days for bacteriostatic drugs
- Inflammatory markers - significant decrease of CRP >25% from the baseline within 24 hrs.
- Contagiousness of patient - bactericidal antibiotics 24 hrs., bacteriostatic antibiotics - 5 days

9. Will initial therapy need modification after culture data are available?

- The antibiotic treatment should be modified if necessary based on clinical course (i.e. relief of symptoms) and findings on cultivation
- Narrow spectrum of antibiotics should be used (to decrease risk of colonization)
- Negative cultures in the patient with pneumonia and no prior antibiotics: mycoplasmal pneumonia, flu, tuberculosis, Legionnaire’s disease or opportunistic infection in immunocompromised host etc.

10. What is the appropriate dose?

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Pediatric regimen</th>
<th>Adult regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>phenoxymethylpenicillin</td>
<td>50,000 IU/kg/d q4h</td>
<td>800,000 IU q6h</td>
</tr>
<tr>
<td>amoxicillin</td>
<td>50-60 mg/kg/d q8h</td>
<td>500-1000 mg q8h</td>
</tr>
<tr>
<td>cephalaxin</td>
<td>25-50 mg/kg/d q8h</td>
<td>250-500 mg q6h</td>
</tr>
<tr>
<td>doxycycline</td>
<td>4 mg/kg/d q12h</td>
<td>100 mg q12h</td>
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<tr>
<td>clarithromycin</td>
<td>7,5 mg/kg/d q12h</td>
<td>500-1000 mg q12h</td>
</tr>
<tr>
<td>cotrimoxazole</td>
<td>30(6) mg/kg/d q12h</td>
<td>960 mg q12h</td>
</tr>
</tbody>
</table>

References

- Suchopár J, Šimek R, Valentová Š et al., eds. Remedia compendium. 3.vydání. Praha, Panax Co, spol. s.r.o. 1999