Basic principles of antibiotic use

Michal Holub
Department of Infectious Diseases
First Faculty of Medicine
Charles University in Prague and Military University Hospital

1. Is antibiotical treatment indicated based on clinical findings?

Obvious bacterial infection
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- Localized infections: pneumonia, pyelonefritis etc.
- Infections with characteristic clinical findings: celullitis, 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 untill the diagnosis is not established
- Urgent situation: the patient with suspected severe infection:

  Febrile neutropenia
  Bacterial meningitis
  Necrotizing celullitis
  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
- Antibiotical 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, uretritis 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%**

Antibiotical 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 -** aminoglykosides are much more effective in an alkaline medium
- **Potential side effects -** chloramphenicol – occurrence of aplasia
- **Bactericidal (bc) vs. bacteriostatic agents -** in lifetheatening infections or in immunocompromised patients bc 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
- **Infection due to multiple organisms** – intraabdominal sepsis or pelvic abscess

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

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**

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, tubercolosis, Legionnaire´s disease or opportunistic infection in immunocompromised host etc.**

10. What is the appropriate dose?

Generic name	Pediatric regimen	Adult regimen
phenoxymethylpenicillin	50,000 IU/kg/d q4h	800,000 IU q6h
amoxicillin	50-60 mg/kg/d q8h	500-1000 mg q8h
cephalexin	25-50 mg/kg/d q6h	250-500 mg q6h
doxycycline	4 mg/kg/d q12h	100 mg q12h
clarithromycin	7,5 mg/kg/d q12h	500-1000 mg q12h
cotrimoxazole	30(6) mg/kg/d q12h	960 mg q12h

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