Antibiotic Prescription Rules

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Post antibiotic era

- Antibiotic resistance is an increasing global threat
- In some countries more than 95% of the bacteria are resistant to greater than 90% of the antibiotics
- CDC and WHO estimated the year of 2050 as the start of post antibiotic era which is similar to pre antibiotic era
- Logic antibiotic use can postpone resistance of the bacteria

Antibiotic prescription

- Targeted :
  - Based on culture results
- Empiric:
  - Before culture results
  - In culture negative suspected infections
  - In infections which sampling is difficult(pneumonia, sinusitis, ..)

Principles of antibiotic selection

1. Respect Microbiology Lab results
2. Attention to contamination of microbiological results
3. 50-90 rules
4. Selection of the best antibiotic
5. The most determinant in empiric therapy is severity of the infection

Principle 1- Respect microbiology lab data

- Rule 1- Before antibiotic prescription culture specimen should be requested as much as possible
- Rule 2- Before any change in antibiotic therapy culture specimen should be requested as much as possible
- Rule 3- Antibiotics should be started after report of culture results if possible
- Rule 4- If antibiotic was started empirically it should be modified after report of culture results

Rule 1- Before antibiotic prescription culture specimen should be requested as much as possible

- In a patient with fever, chills, back pain and frequency: U/A and U/C and B/C × 2
- In a patient with wound infection: wound culture
- In young infants with high fever: B/C × 2, U/A , U/C, CSF/C
- Tip of all excised devices: culture
- All abscesses: cultures

Rule 2- Before any change in antibiotic therapy culture specimen should be requested as much as possible

- In patient with VAP and negative culture results, before change of antibiotics: BAL/C, B/C × 2, U/A , U/C
- In patient under treatment with cefepime in ICU who developed fever and thrombocytopenia before change of antibiotics: B/C × 2, U/A , U/C, BAL/C , ….

Rule 3- Antibiotics should be started after report of culture results if possible(mild symptom)

- In a child with FTT and pyuria
- In a patient with chronic ulcer
- In a child with enuresis and pyuria
- In a patient with chronic osteomyelitis
- In patient with suspected endocarditis
- In suspected indwelling catheter infection

Case 1

- In a patient with urosepsis, Meropenem was empirically started.
- After 3 days the results of U/C and B/C revealed growth of E.coli sensitive to Ampicillin, Meropenem, and Ceftriaxone.
- What's the best recommendation?

Case 1

- Meropenem should be discontinued and Ampicillin started regardless of improve or not improving of the patient.

Case 2

- In a patient with septic shock, Meropenem+ Vancomycin was started.
- After 3 days B/C showed growth of S.aureus sensitive to Cloxacillin, Clindamycin, Erythromycin, Linezolid, and Imipenem.
- What's the best recommendation?

Case 2

- Meropenem and Vancomycin should be discontinued and Cloxacillin be started

Case 3

- In a patient with septic shock, Ceftriaxon+ Vancomycin was started.
- After 3 days B/C showed growth of E.coli resistant to Ceftriaxone, Ampicillin, Piperacillin Tazobactam and sensitive only to Meropenem.
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- The condition of the patient not improved.
- What's the best recommendation?

Case 3

- Ceftriaxone and Vancomycin should be discontinued and Meropenem be started.

Principle 2. Attention to contamination of microbiological results

- Rule 5- If a positive culture result reported from a site with no evidence of the infection, contamination should be suspected
- Rule 6 - In most cases skin flora should be considered as contamination(CONS, Micrococcus spp., Diphtheroids, Bacillus spp., …) except in indwelling devices(CVC, VP shunt, …)
- Rule 7 - Growth of a bacteria in Bactec after 18-24 hours and in conventional B/C after 24-48 hours usually indicates contamination results

Rule 5- If a positive culture result reported from a site with no evidence of the infection, contamination should be suspected

- Growth of E.coli in U/C of a patient without pyuria and lower urinary symptom
- Growth of Enterococcus spp. in B/C of a patient without fever or hypotension
- Growth of S.aureus in CSF/C of a patient with NL CSF analysis

Rule 6 - In most cases skin flora should be considered as contamination (CONS, Micrococcus spp., Diphtheroids, Bacillus spp., ...) except in indwelling devices(CVC, VP shunt, ...)

- Growth of CONS in B/C of a patient with sepsis
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- Growth of Diphtheroids in CSF/C of a patient with meningitis

Rule 7 - Growth of a bacteria in Bactec after 18-24 hours and in conventional B/C after 24-48 hours usually indicates contamination results

- Growth of E.coli in Bactec after 96 hours should be suspected as contamination
- Growth of CONS in B/C after 72 hours usually indicates contamination

Principle 3- 50-90 rules

- Rule 8- 50 rule: If a patient was treated with an antibiotic that the causative agent is resistant to that antibiotic, 50% chance of good response is present

- Rule 9- 90 rule: If a patient was treated with an antibiotic that the causative agent is sensitive to that antibiotic, 90% chance of good response is present

Case 4

- A patient with sepsis was treated with Ceftriaxone + Vancomycin.
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- After 3 days the condition of the child significantly improved.
- B/C and U/C revealed Klebsiella pneumonia resistant to Ceftriaxone, Piperacillin Tazobactam and only sensitive to Meropenem.
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- What's the best advice?

Case 4

- B/C and U/C repeated.
- CSF culture requested.
- Ceftriaxone continued.
- Vancomycin discontinued.

Case 5

- A patient with febrile UTI was treated with Cefixime.
- After 3 days the condition of the child improved.
- U/C revealed growth of Klebsiella pneumonia resistant to Cefixime and only sensitive to Meropenem.
- What's the best advice?

Case 5

- U/C repeated.
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- Cefixime continued.

Case 6

- A patient with fever, vomiting and pyuria was treated with Ceftriaxone.
- After 3 days the condition of the child was not improved.
- U/C revealed growth of E.coli sensitive to Ceftriaxone, Piperacillin Tazobactam, Co-Trimoxazole, Meropenem.
- What's the best recommendation?

Case 6

- U/C repeated.
- Ceftriaxone discontinued.
- Co-Trimoxazole be started.

Principle 4- Rule 10- Selection of the best antibiotic

1. Good efficacy (sensitive, bactericide vs. bacteriostatic)
2. Low adverse effects
3. Competent with specific condition of the patient(G6PD, Renal failure, hepatic failure, previous allergy)
4. Narrow spectrum
5. Old
6. Cheap
7. Available
8. Tolerable(good taste, low infusion adverse events)
9. Wide interval
10. Per Oral

Case 7

- A 3 years old patient with severe febrile UTI.
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- U/C revealed growth of E.coli sensitive to Meropenem, Ceftriaxone, Piperacillin Tazobactam, Ampicillin, Nitrofurantoin and Co-Trimoxazole.
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- A) What's the order of the best antibiotic?
- B) The child had allergy to Penicillin. What's the best antibiotic?

Case 7

- A)
  - No Nitrofurantoin;
  - Ampicillin, Co- Trimoxazole, Ceftriaxone= Piperacillin Tazobactam, Meropenem
- B)
  - Co- Trimoxazole, Ceftriaxone, Meropenem

Case 8

- A 5 year child with cyanotic heart disease and endocarditis admitted to hospital.
- Blood cultures showed growth of staphylococcus aureus sensitive to cefazolin, Cloxacillin, Clindamycin, Co-Trimoxazole, Vancomycin, Linezolid, Teicopelanin, and Meropenem.
- What's the order of the best antibiotics?

Case 8

- No Clindamycin, Cefazolin= Cloxacillin, Co-Trimoxazole, Teicopelanin, Vancomycin, Meropenem, Linezolid.

Principle 5. Empiric therapy should be started in accordance to severity of the infection

- Rule 11- In mild to moderate infections probable sensitivity of 60% is adequate.

- Rule 12- In mild to moderate infection escalation therapy (step up) should be considered.

Case 9

- In a case of outpatient shigellosis.
- We suspect efficacy of 10% for Ampicillin, 30% for Trimethoprim Sulfamethoxazole, 50-60% for Cefixime, 70% for Ciprofloxacin.
- What's the best advise?

Case 9

- S/C.
- Cefixime.
- If no response Ciprofloxacin.

Case 10

- In a case of subacute sinusitis,
- We suspect efficacy of 30% for Erythromycin, 60% for Amoxicillin, 90% for Amoxicillin-Clavulanate, and 97% for Ceftriaxone.
- What's the best advice?

Case 10

- Amoxicillin.
- If no response Amoxicillin- Clavulanat.
- If no response Ceftriaxone.

Principle 5. Empiric therapy should be started in accordance to severity of the infection

- Rule 13- In severe and life threatening infections advising the most effective antibiotic, combinational antibacterial therapy and high doses of antibiotics should be considered

- Rule 14- In severe and life threatening infections de-escalation (step down) therapy should be considered after obtain of culture results

Severe and life threatening infections

- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)
- Severe sepsis
- Severe community-acquired pneumonia
- Meningitis
- Severe fever and neutropenia in hematologic malignancies

Rules of de-escalation therapy after 72-96 hours in severe infections

- Rule 15- If the cultures were positive and the patient is improving, modifying antibiotics to the best antibiotic in accordance to microbiological results is necessary.

- Rule 16- If the cultures were positive and the patient is not improving, modifying antibiotics to the best antibiotic in accordance to microbiological results is necessary.

Case 11

- In a patient with empyema , Ceftriaxone+ Vancomycin was started.
- After 3 days the condition of the child is not improved.
- The pleural culture showed growth of Streptococcus pneumoniae sensitive to penicillin, Clindamycin, Ceftriaxone, and Vancomycin.
- What's the best advice?

Case 11

- Discontinue Ceftriaxone+ Vancomycin.
- Start of Penicillin G.

Case 12

- In a patient with empyema , Ceftriaxone+ Vancomycin was started.
- After 3 days the condition of the child improved and the pleural culture showed growth of Streptococcus pneumoniae sensitive to penicillin, Clindamycin, Ceftriaxone, and Vancomycin.
- What's the best advice?

Case 12

- Discontinue Ceftriaxone+ Vancomycin.
- Start of Penicillin G.

Case 13

- In a case of bacterial meningitis Ceftriaxone+ Vancomycin was started.
- The result of CSF culture revealed growth of Neisseria meningitides sensitive to Penicillin and Ceftriaxone.
- The condition of the patient significantly improved.
- What's the best recommendation?

Case 13

- D/C Ceftriaxone+ Vancomycin.
- Start of Penicillin G.

Case 14

- In a case of premature neonate with sepsis Meropenem+ Vancomycin was started.
- After 3 days the results of Peripheral and Central line cultures showed growth of candida spp.
- The neonate is not improved. what's the best recommendation?

Case 14

- D/C Meropenem+ Vancomycin.
- Start of antifungal.
- Excise of central catheter.

Rules of de-escalation therapy after 72-96 hours in severe infections

- Rule 17- If the cultures were negative and the patient is improving, continuing antibiotics for 7-10 days is recommended.

Rules of de-escalation therapy after 72-96 hours in severe infections

- Rule 18- If the cultures were negative and the patient is not improving:
  - ✓ Consider nonbacterial causes (emboli, ARDS, viral, fungal …) and D/C antibiotics if possible
  - ✓ Request more cultures(blood, BAL, site of infection)
  - ✓ Request more investigations(history/ physical exam, Sonography, CT, MRI, procalcitonin,.)
  - ✓ Change antibiotics to second line antibiotics

Examples of Changing antibiotics to second line in culture negative, not improving cases

- D/C vancomycin
- D/C carbapenems, flouroquinolons, aminoglycosides, colistin, tigecycline, antipseudomonas cephalosporins
- Start a narrower spectrum antibiotic(s) for gram negatives(positives) such as cefepime, ceftazidime, piperacillin-tazobactam, Ceftriaxone, Cefotaxime, if possible
- Start of anti-fungal or antiviral if indicated(fever+ neutropenia, influenza season, HSV stomatitis)

Case 15

- A 3 Mo. old infant with septic shock treated with Meropenem and Vancomycin.
- After 3 days the infant is improving.
- The results of B/C, U/C, CSF/C were negatives.
- What's the appropriate advice?

Case 15

- Continue Meropenem+ Vancomycin for 7-10 days.

Case 16

- A 3 Mo. old infant with septic shock treated with Meropenem and Vancomycin.
- After 4 days the infant is not improving.
- The results of B/C, U/C were negatives.
- What's the appropriate advice?

Case 16

- D/C Meropenem+ Vancomycin.
- Request B/C × 2, U/A, U/C, CXR, Abdominal sono, CSF analysis and Culture if possible.
- Start of Cefepime or Piperacillin Tazobactam.
- Evaluation of non-infectious causes (Cardiology consult, ...).

Home to message

- Antibiotic resistance is an increasing global threat
- Logic antibiotic use can postpone resistance of the bacteria and saves the lives.
- 5 principles of antibiotic prescription includes:
  - Prescribe based on Microbiology Lab results
  - Avoid treatment of contamination cases
  - Attention to 50-90 rules
  - Selection of the best antibiotic in each condition
  - In empiric therapy potent new ABs for severe infections and old less potent for mild infections