Microbiology Nuts & Bolts
Antibiotics Part 2

Dr David Garner
Consultant Microbiologist
Frimley Park Hospital NHS Foundation Trust

Part 1

- How antibiotics work
- How resistance occurs
- How to choose and antibiotic
- Empirical vs. targeted therapy
- Broad vs. narrow spectrum
- The implications of prescribing an antibiotic

Aims & Objectives

- To understand how to review an antibiotic on a daily basis
- To know when it is safe to switch from IV to oral antibiotics
- To know how to investigate the reasons for a failing antibiotic regimen
- To have a working knowledge of therapeutic drug monitoring
- To understand the difficulties of prescribing in particular patient groups: renal failure & obesity

Requirements

- Table of bacterial causes of infection
- Table of antibiotic spectrum of activity
- Table of antibiotic tissue penetration

Causes of infection

Spectrum of activity
How to review an antibiotic?

- Is the patient getting better?
- Can the antibiotic be converted from IV to oral?
- Can the antibiotic be narrowed down to a specific treatment?
- Are antibiotic levels required?
- Is the patient’s renal and liver function stable?
- Is the patient experiencing side effects?
- Have any other drugs been started that might interfere with the antibiotics?
- Can the antibiotics be stopped?

When is an oral switch safe?

If YES to ALL consider changing to oral

- Is the patient able to swallow and tolerate oral fluids?
- Is the patient’s temperature settled and <38°C for 24-48 hours?
- Has the patient’s white blood cell count settled and <10 x 10^9/L for 48 hours?
- Is the patient’s blood pressure stable?
- Is the patient’s respiratory rate <20 bpm?
- Is the patient’s CRP falling?
- Are oral antibiotic formulations available?

- If YES to ANY continue IV
- Does the patient have an infection that specifically indicates the need for IV antibiotics, because there is no oral treatment?
  - Meningitis
  - Infective endocarditis
  - Encephalitis
  - Osteomyelitis
  - Febrile neutropaenia

How to review an antibiotic?

- Is the patient getting better?
- Can the antibiotic be converted from IV to oral?
- Can the antibiotic be narrowed down to a specific treatment?
- Are antibiotic levels required?
- Is the patient’s renal and liver function stable?
- Is the patient experiencing side effects?
- Have any other drugs been started that might interfere with the antibiotics?
- Can the antibiotics be stopped?

Therapeutic Drug Monitoring

- Required for:
  - Aminoglycosides e.g. Gentamicin, Amikacin, Tobramycin
  - Glycopeptides e.g. Vancomycin, Teicoplanin
  - Chloramphenicol
- Peak and trough levels
  - Peak – 1 hour post dose
  - Trough – immediately pre dose
Therapeutic Drug Monitoring

What is wrong?

- Dose too low
  - Increase dose

- Dose too high
  - Decrease dose

What is wrong?

- Elimination too slow
  - Give less frequently

- Elimination too fast
  - Give more frequently

What is wrong?

- Dose too infrequent
  - Give more frequently

- Dose too frequent
  - Give less frequently

How to review an antibiotic?

- Is the patient getting better?
- Can the antibiotic be converted from IV to oral?
- Can the antibiotic be narrowed down to a specific treatment?
- Are antibiotic levels required?
- Is the patient's renal and liver function stable?
- Is the patient experiencing side effects?
- Have any other drugs been started that might interfere with the antibiotics?
- Can the antibiotics be stopped?

Antibiotic dosing in renal failure

- Many antibiotics require dose reduction in renal failure
- eGFR is not an accurate predictor of renal function
- Use Cockcroft Gault equation
  - Actual body weight or Ideal Body Weight (IBW) if weight > 20% above IBW
  - Also use IBW for patients with oedema & ascites
How might weight effect GFR?

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>eGFR</th>
<th>Calculated GFR</th>
<th>Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>63</td>
<td>33</td>
<td>-30</td>
</tr>
<tr>
<td>50</td>
<td>63</td>
<td>37</td>
<td>-26</td>
</tr>
<tr>
<td>55</td>
<td>63</td>
<td>40</td>
<td>-23</td>
</tr>
<tr>
<td>60</td>
<td>63</td>
<td>44</td>
<td>-19</td>
</tr>
<tr>
<td>65</td>
<td>63</td>
<td>47</td>
<td>-16</td>
</tr>
<tr>
<td>70</td>
<td>63</td>
<td>51</td>
<td>-12</td>
</tr>
<tr>
<td>75</td>
<td>63</td>
<td>55</td>
<td>-8</td>
</tr>
<tr>
<td>80</td>
<td>63</td>
<td>59</td>
<td>-4</td>
</tr>
</tbody>
</table>

www.microbiologynutsandbolts.co.uk

How to review an antibiotic?

- Is the patient getting better?
- Can the antibiotic be converted from IV to oral?
- Can the antibiotic be narrowed down to a specific treatment?
- Are antibiotic levels required?
- Is the patient experiencing side effects?
- Have any other drugs been started that might interfere with the antibiotics?
- Can the antibiotics be stopped?

www.microbiologynutsandbolts.co.uk

Common side effects

- **Objective**
  - Fever
  - Renal failure
  - Hyperkalaemia
  - Cholestasis
  - Hepatitis
  - Neutropenia
  - Thrombocytopenia
  - Prolonged QT interval
  - Ototoxicity

- **Subjective**
  - GI disturbance
  - Rashes
  - Pain at cannula site
  - Altered mood
  - Headaches
  - Joint pain
  - Muscle pain
  - Taste disturbance
  - Numbness & tingling

www.microbiologynutsandbolts.co.uk

Common drug interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Antibiotic(s)</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins e.g. Simvastatin</td>
<td>Macrolides &amp; Rifampicin</td>
<td>Altered levels</td>
</tr>
<tr>
<td></td>
<td>Statins, Cephalosporins, Tetracyclines &amp; Aminoglycosides</td>
<td>Myopathy</td>
</tr>
<tr>
<td>ACE Inhibitors e.g. Ramipril</td>
<td>Ramipril</td>
<td>Reduced levels</td>
</tr>
<tr>
<td></td>
<td>Antagonists &amp; Angiotensin Converting Enzymes</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Diuretics e.g. Furosemide</td>
<td>Aminoglycosides, Glycopeptides &amp; Polymyxins</td>
<td>Ototoxicity</td>
</tr>
<tr>
<td></td>
<td>Thiazides &amp; Loop diuretics</td>
<td>Hyperkalaemia</td>
</tr>
<tr>
<td>PPIs e.g. Omeprazole</td>
<td>Macrolides &amp; Aminoglycosides</td>
<td>Altered levels</td>
</tr>
<tr>
<td>Immunosuppressors e.g. Methotrexate</td>
<td>Ciprofloxacin, Tetracyclines &amp; Penicillins</td>
<td>Decreased levels</td>
</tr>
<tr>
<td></td>
<td>Thiazides &amp; Antimalarials</td>
<td>Bone marrow toxicity</td>
</tr>
</tbody>
</table>

www.microbiologynutsandbolts.co.uk
How to review an antibiotic?

- Is the patient getting better?
- Can the antibiotic be converted from IV to oral?
- Can the antibiotic be narrowed down to a specific treatment?
- Are antibiotic levels required?
- Is the patient's renal and liver function stable?
- Is the patient experiencing side effects?
- Have any other drugs been started that might interfere with the antibiotics?
- Can the antibiotics be stopped?

Duration of therapy

Remember: patients are not necessarily back to normal when antibiotics can be stopped

<table>
<thead>
<tr>
<th>Condition</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia &amp; exacerbation of COPD</td>
<td>7 days</td>
</tr>
<tr>
<td>Simple UTI</td>
<td>3 days women 7 days man</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>7 days</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Septic arthritis &amp; septicemia</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Cholecystitis, cholangitis &amp; peritonitis</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Sepsis &amp; meningitis</td>
<td>10-14 days</td>
</tr>
</tbody>
</table>
**Duration of therapy**

*Remember: patients are not necessarily back to normal when antibiotics can be stopped*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia &amp; exacerbation of COPD</td>
<td>7 days</td>
</tr>
<tr>
<td>Simple UTI</td>
<td>3 days women, 7 days men</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>7 days</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Septic arthritis &amp; osteomyelitis</td>
<td>6-8 weeks</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td></td>
</tr>
<tr>
<td>Cholecystitis, cholangitis &amp; peritonitis</td>
<td>7 days</td>
</tr>
<tr>
<td>Septic &amp; meningitis</td>
<td></td>
</tr>
</tbody>
</table>

### Reasons for failing antibiotics

- Has the antibiotic been given for long enough?
- Is the diagnosis correct?
- Is the antibiotic correct for the diagnosis and the common causative microorganisms?
- Does the patient have a new problem or secondary infection?
- Is the patient compliant with treatment?
- Is the patient actually being given the antibiotic?
Reasons for failing antibiotics

- If on oral antibiotics is the patient able to swallow or absorb them?
- Is the dose appropriate?
- Is the patient on any drugs that might interact with the antibiotics?
- Does the patient have prosthetic material that needs removing?
- Does the patient have a resistant microorganism?

Antibiotic dosing

- Infections requiring high-dose therapy:
  - Meningitis & encephalitis
  - Infective endocarditis
  - Septic arthritis & osteomyelitis

Antibiotics in obesity

- Most antibiotics discovered before 1960
- Doses based on weights of 60-70kg
- Current population:
  - 66% over-weight
  - 33% obese
  - 4% morbidly obese

Biofilms - slime cities

- Biofilms form on prosthetic material
- Collection of multiple microorganisms surrounded by glycocalyx “slime”
- Bacteria change “behaviour” and become much more resistant to antibiotics

Types of IV Device

- Peripheral Venous Catheter
- Peripheral Arterial Catheter
- Short-term Central Venous Catheter (CVC)
- Peripherally Inserted Central Catheter (PICC)
- Long-term Central Venous Catheter (CVC) e.g. Broviac, Groshong, Hickman catheters
- Totally Implanted Catheter
- Pacemaker, cardioverter defibrillator
- IVC filters
- Prosthetic vascular grafts
Intravenous catheter infections

- IV lines breach the body’s main barrier to infection, the skin.
- The most common causes of infection are skin bacteria e.g. Staphylococci.
- Gram-negative bacteria are unusual and normally occur in immunosuppressed patients or those on antibiotics that cause changes in skin flora.
- The main treatment of an IV line infection is to remove the line.
- Essential with Staphylococcus aureus, Pseudomonas sp. and Klebsiella sp.

Reasons for failing antibiotics

- If on oral antibiotics is the patient able to swallow or absorb them?
- Is the dose appropriate?
- Is the patient on any drugs that might interact with the antibiotics?
- Does the patient have prosthetic material that needs removing?
- Does the patient have a resistant microorganism?

How antibiotics work

Antibiotic resistance
**Conclusions**

- Reviewing patients safely and effectively with antibiotics requires making sure they are receiving:
  - The right antibiotic
  - ...at the right dose
  - ...by the right route
  - ...and the right duration
  - ...for the right infection
  - ...at the right time!

Any Questions?