Microbiology Nuts & Bolts Antibiotics Part 2

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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

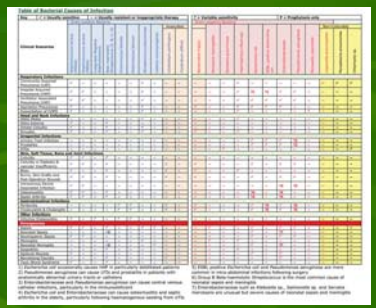
Aims & Objectives

- 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

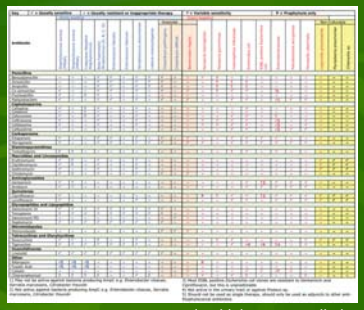
Requirements

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

Causes of infection



Spectrum of activity



Tissue penetration

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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 patients renal and liver function stable?
- Is the patient experiencing side effects?
- Have any other drugs been started that might interfere with the antibiotics?
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When is an oral switch safe?

If YES to ALL consider changing to oral	If YES to ANY continue IV
Is the patient able to swallow and tolerate oral fluids?	Is the patient's swallow unsafe?
Is the patient's temperature settling and <38°C for 24-48 hours?	Does the patient have continuing sepsis?
Has the patient's heart rate been <100 bpm for 12 hours?	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
Is the patient's peripheral white blood cell count 4-12 x10^9/L?	
Is patient's blood pressure stable?	
Is the patient's respiratory rate <20bpm?	
Is the patient's CRP falling?	
Are oral antibiotic formulations available?	

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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

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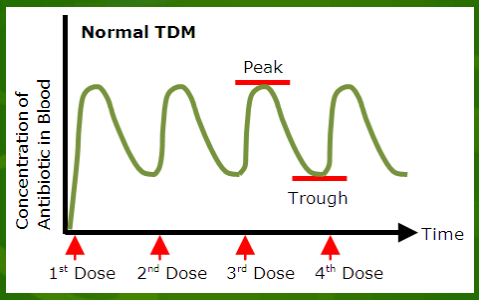
Therapeutic Drug Monitoring



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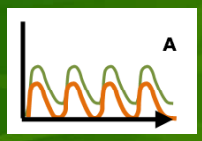
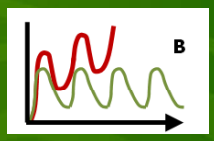
What is wrong?



Dose too low
Increase dose



Dose too high
Decrease dose

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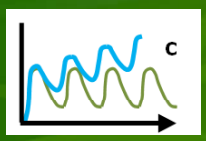
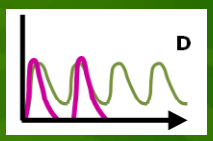


Elimination too slow
Give less frequently



Elimination too fast
Give more frequently

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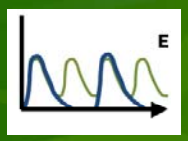
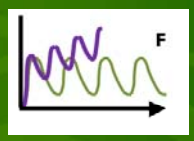
What is wrong?



Dose too infrequent
Give more frequently



Dose too frequent
Give less frequently

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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

Male: CrCl = $\frac{1.23 \times (140 - \text{age in years}) \times \text{weight in kg}^{*}}{\text{Serum creatinine } (\mu\text{mol/L})}$

Female: CrCl = $\frac{1.04 \times (140 - \text{age in years}) \times \text{weight in kg}^{*}}{\text{Serum creatinine } (\mu\text{mol/L})}$

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How might weight effect GFR?

Female, Age 87, Creatinine 75

Weight (kg)	eGFR	Calculated GFR	Variance
45	63	33	-30
50	63	37	-26
55	63	40	-23
60	63	44	-19
65	63	47	-16
70	63	51	-12
75	63	55	-8
80	63	59	-4

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Common side effects

- Subjective
  - GI disturbance
  - Flushing
  - Pain at cannula site
  - Altered mood
  - Headaches
  - Joint pain
  - Muscle pain
  - Taste disturbance
  - Numbness & tingling
- Objective
  - Fever
  - Renal failure
  - Hyperkalaemia
  - Cholestasis
  - Hepatitis
  - Neutropaenia
  - Thrombocytopaenia
  - Prolonged QT interval
  - Ototoxicity

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Common drug interactions

Drug	Antibiotic (s)	Interaction
Statins e.g. Simvastatin	Macrolides & Rifampicin	Altered levels
	Macrolides, Daptomycin, Fusidic acid & Azole antifungals	Myopathy
ACE Inhibitors e.g. Ramipril	Rifampicin	Reduced levels
	Trimethoprim	Hyperkalaemia
Diuretics e.g. Furosemide	Aminoglycosides, Glycopeptides & Polymyxins	Ototoxicity
	Trimethoprim	Hyperkalaemia
PPIs e.g. Omeprazole	Macrolides & Azole antifungals	Altered levels
Immunomodulators e.g. Methotrexate	Ciprofloxacin, Tetracyclines & Penicillins	Increased levels
	Trimethoprim & Antimalarials	Bone marrow toxicity

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Duration of therapy

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

Condition	Duration of treatment
Pneumonia & exacerbation of COPD	
Simple UTI	
Pyelonephritis	
Cellulitis	
Septic arthritis & osteomyelitis	
Clostridium difficile	
Cholecystitis, cholangitis & peritonitis	
Sepsis & meningitis	

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Cholecystitis, cholangitis & peritonitis	7 days
Sepsis & meningitis	Depends on cause!

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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?

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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?

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Antibiotic dosing

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

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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

Antibiotic Dosing

Antibiotic	Weight	Dose
IV Aciclovir	IBW	10mg/kg TDS
IV AmBisome	Actual	3-5mg/kg OD
IV Amikacin	ABW	7.5mg/kg TDS
IV Benzylpenicillin	-	2.4g 4 hourly
IV Ceftriaxone	-	2g BD
IV Ciprofloxacin	-	600mg BD
IV Clindamycin	-	1.2g QDS
IV Daptomycin	Actual	4-6mg/kg OD
IV Gentamicin	ABW	5mg/kg OD
IV Meropenem	-	2g TDS
IV Metronidazole	-	500mg QDS
IV Piptazobactam	-	4.5g QDS
IV Teicoplanin	Actual	6mg/kg BD for 3 doses then OD
IV Vancomycin	Actual	15mg/kg BD

Ideal Body Weight (IBW)
Male IBW = 50 + (2.3 x height in inches above 60 inches)
Female IBW = 45 + (2.3 x height in inches above 60 inches)

Adjusted Body Weight (ABW)
ABW = 0.4 x (Actual Body Weight – IBW) + IBW

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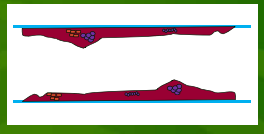
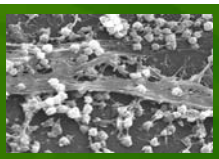
Biofilms- slime cities

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





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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

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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.

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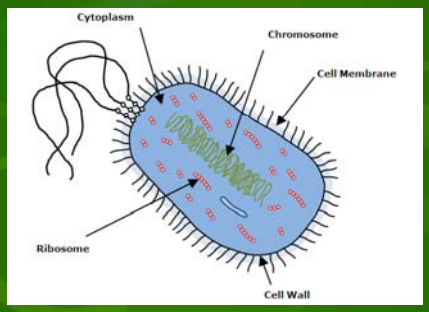
How antibiotics work



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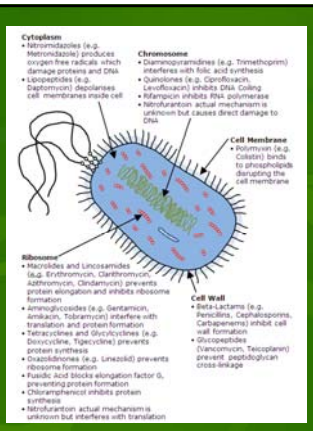

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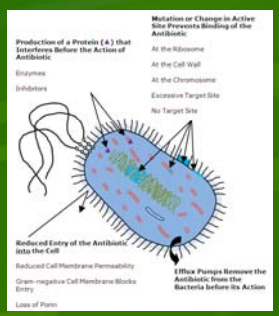
Antibiotic resistance



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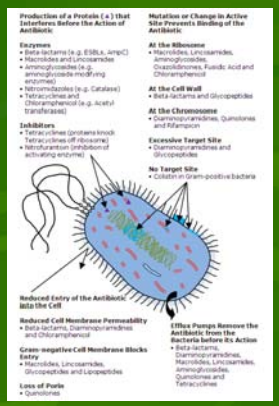

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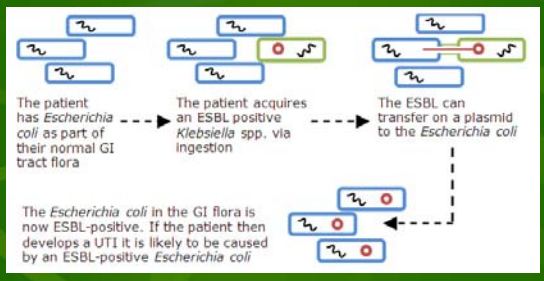
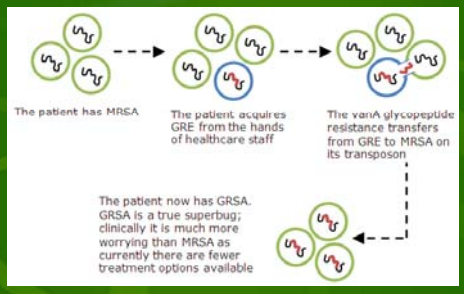
Plasmids



Transposons



Absolute resistance

Microorganism	Absolute Resistance
MRSA	• Beta-lactams
Enterococcus spp.	• Cephalosporins • Ciprofloxacin • Erythromycin, Clarithromycin, Azithromycin, Clindamycin
Pseudomonas spp.	• Ampicillin, Amoxicillin • Cefuroxime, Cefotaxime, Ceftriaxone
Klebsiella spp.	• Ampicillin, Amoxicillin
Proteus spp.	• Nitrofurantoin
Gram-negative bacilli	• Teicoplanin, Vancomycin • Linezolid
AmpC producing bacteria e.g. *Enterobacter cloacae, Citrobacter freundii, Serratia marcescens* and *Morganella morganii*	• Ampicillin, Amoxicillin • Cefuroxime, Cefotaxime, Ceftriaxone, Ceftazidime
Listeria monocytogenes	• Cefotaxime, Ceftriaxone
Non-Culturable bacteria e.g. *Mycoplasma* spp. and *Chlamydia* spp.	• Beta-lactams • Teicoplanin, Vancomycin
Aerobes	• Metronidazole

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?