

# Antibiotics

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# Topics to be covered

- How to decide?
- Mechanisms of resistance
- Antibiotics as per class including spectrum of cover

# How to decide

- Prophylaxis vs Rx
- CA vs HCA
- Source
- Allergies
- Know your local epidemiology/policy
- Loading dose

# Prophylaxis

- Type of surgery
- Clean vs clean contaminated
- Colonisers/pathogens
- Timing of dosing
- Repeat dosing
- Duration

# Treatment

- Empiric vs definitive
- Duration
- Extended courses – staph pneumonia
- Staph BSI
- Grafts/mesh
- Osteomyelitis
- Infective endocarditis

# Understanding the microbiology

| Gram-positive cocci  | Gram-negative cocci   |
|--|---|
| <b>Aerobic</b><br>In clusters <ul style="list-style-type: none"><li>• Coagulase (+): <i>Staphylococcus aureus</i></li><li>• Coagulase (-): <i>Staphylococcus lugdunensis</i> and other coagulase-negative staphylococci</li></ul> In pairs/chains <ul style="list-style-type: none"><li>• Optochin sensitive: <i>Streptococcus pneumoniae</i></li><li>• Alpha-hemolytic: Viridans group <i>Streptococcus</i>, <i>Enterococcus</i></li><li>• Beta-hemolytic:<ul style="list-style-type: none"><li>○ Group A Strep (<i>Streptococcus pyogenes</i>)</li><li>○ Group B Strep (<i>Streptococcus agalactiae</i>)</li><li>○ Group C, D, G Strep</li></ul></li></ul><br><b>Anaerobic:</b> <i>Peptostreptococcus</i> spp. and many others | <b>Aerobic</b> <ul style="list-style-type: none"><li>• Diplococcus: <i>Neisseria meningitidis</i>, <i>N. gonorrhoeae</i>, <i>Moraxella catarrhalis</i></li><li>• Cocco-bacillus: <i>Haemophilus influenzae</i>, <i>Acinetobacter</i></li></ul><br><b>Anaerobic:</b> <i>Veillonella</i> spp. |

| Gram-positive rods   | Gram-negative rods   |
|--|--|
| <p><b>Aerobic</b></p> <ul style="list-style-type: none"> <li>• Large: <i>Bacillus spp</i></li> <li>• Cocco-bacillus: <i>Listeria monocytogenes</i>, <i>Lactobacillus spp</i></li> <li>• Small, pleomorphic: <i>Corynebacterium spp</i></li> <li>• Branching filaments: <i>Nocardia spp</i>, <i>Streptomyces spp</i></li> </ul> <p><b>Anaerobic</b></p> <ul style="list-style-type: none"> <li>• Large: <i>Clostridium spp</i></li> </ul> | <p><b>Aerobic</b></p> <p>Lactose fermenting (Lactose positive):</p> <ul style="list-style-type: none"> <li>• <i>Enterobacter spp</i>, <i>Escherichia coli</i>, <i>Klebsiella spp</i></li> <li>• <i>Citrobacter spp*</i>, <i>Serratia spp*</i></li> </ul> <p>Non lactose-fermenting (Lactose negative):</p> <ul style="list-style-type: none"> <li>• Oxidase (-): <i>Acinetobacter spp</i>, <i>Burkholderia spp</i>, <i>E. coli</i>, <i>Proteus spp</i>, <i>Salmonella spp</i>, <i>Shigella spp</i>, <i>Serratia spp*</i>, <i>Stenotrophomonas maltophilia</i></li> <li>• Oxidase (+): <i>P. aeruginosa</i>, <i>Aeromonas spp.</i></li> </ul> <p><b>Anaerobic:</b> <i>Bacteroides spp</i>, <i>Fusobacterium spp</i>, <i>Prevotella spp.</i></p> |

| SOURCE     | COMMUNITY ACQUIRED  |  |                                 | HEALTH CARE ASSOCIATED  |
|------------|---|--|---------------------------------|---|
| SKIN, BONE | STREP PNEUMONIA, MSSA<br>GRAM NEG ANEAROBES   |  |                                 | E – Entorobacteriaceae<br>S – MRSA/VRSA<br>- Stenotrophomonas<br>K – Klebsiella Producing Carbapenamases<br>A – Acinetobacter<br>P – Pseudomonas<br>E – Enterococcus Faecium<br>(D) – Clostridium Difficile |
| RESP TRACT | STREP PNEUMONIA<br>H INFLUENZAE<br>KLEBSIELLA PNEUMONIA<br>MORAXHELLA CATTARHALIS<br>CORYNEBACTERIUM<br>ATYPICALS – LEGIONELLA, CHLYMIDIA, MYCOPLASMA |  |                                 |   |
| GIT        |   | GRAM +   | GRAM -                          |   |
|            | STOMACH   | PEPTOSTREPTOCOCCUS<br>G+ COCCI IN CHAINS                             | E COLI<br>KLEBSIELLA<br>PROTEUS |   |
|            | SMALL BOWEL<br>(APPENDIX)   | STREP CIA *  |                                 |   |
|            | COLON   | ENTEROCOCCUS –<br>FEACALIS (S); FEACIUM<br>(R)<br>G+ COCCI IN CHAINS |                                 |   |
| GYNEA      | N GONNORHEA<br>GROUP B HEAMOLYTIC STREP<br>ANEAROBES<br>ATYPICAL - CHLYMIDIA  |  |                                 |   |

\* STREPTOCOCCUS CONSTELLATIS, INTERMEDIUS, ANGINOSIS

PENNICILIN SENSITIVE, PRONE TO MULTIPLE INTRA ABDOMINAL ABCESES

HCA – 48-72HRS POST ADMISSION; READMISSION WITHIN 3MONTHS; OLD AGE HOMES;PRISON;PSYCH FACILITY; LONG STANDING INDWELLING CATHETERS



## Pharmacokinetics

What does the body do to the drug ?

- **A**bsorption
- **D**istribution
- **M**etabolism
- **E**xcretion

### PK-PD

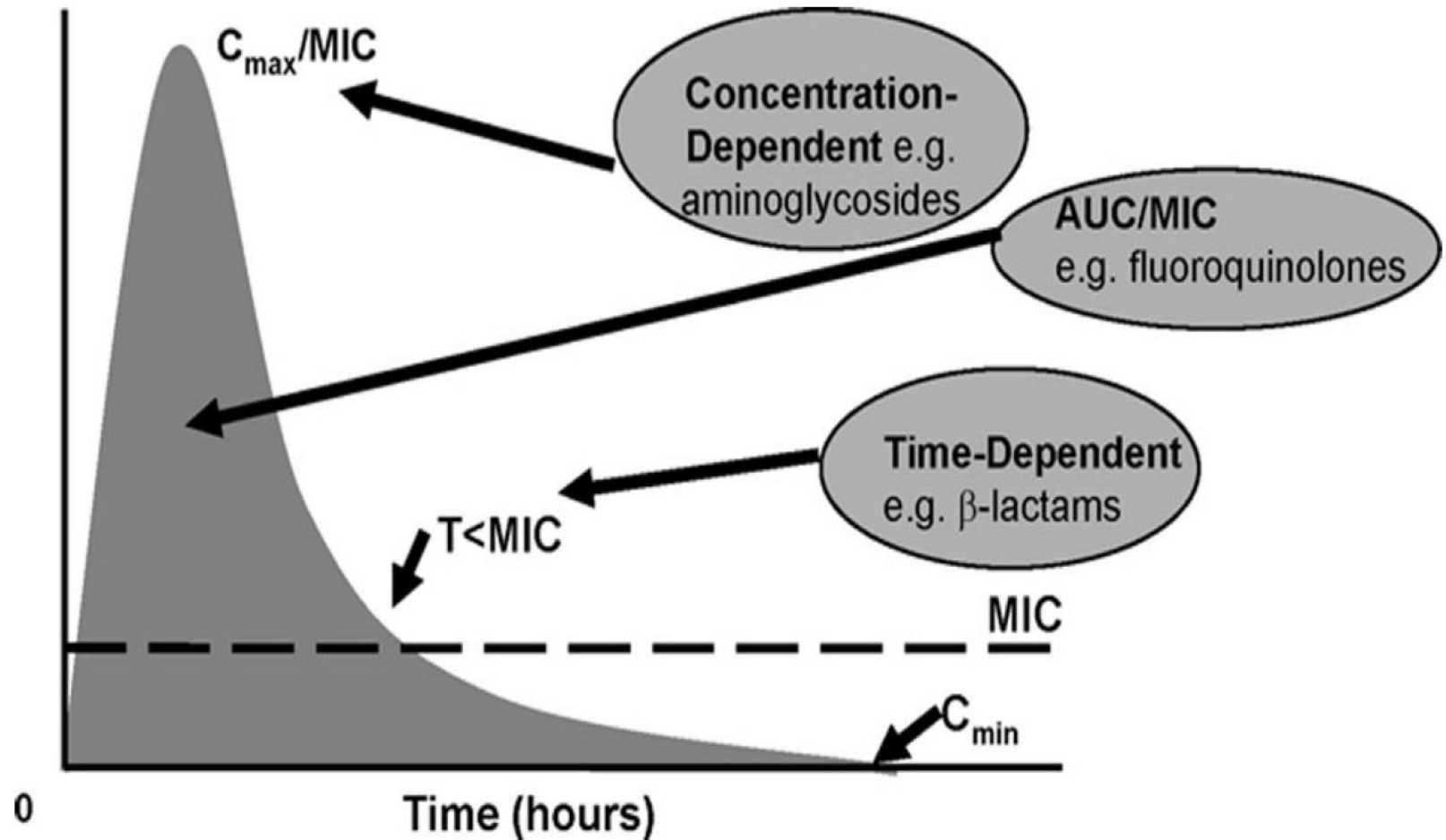
Drug  
concentrations  
and  
effect

## Pharmacodynamics

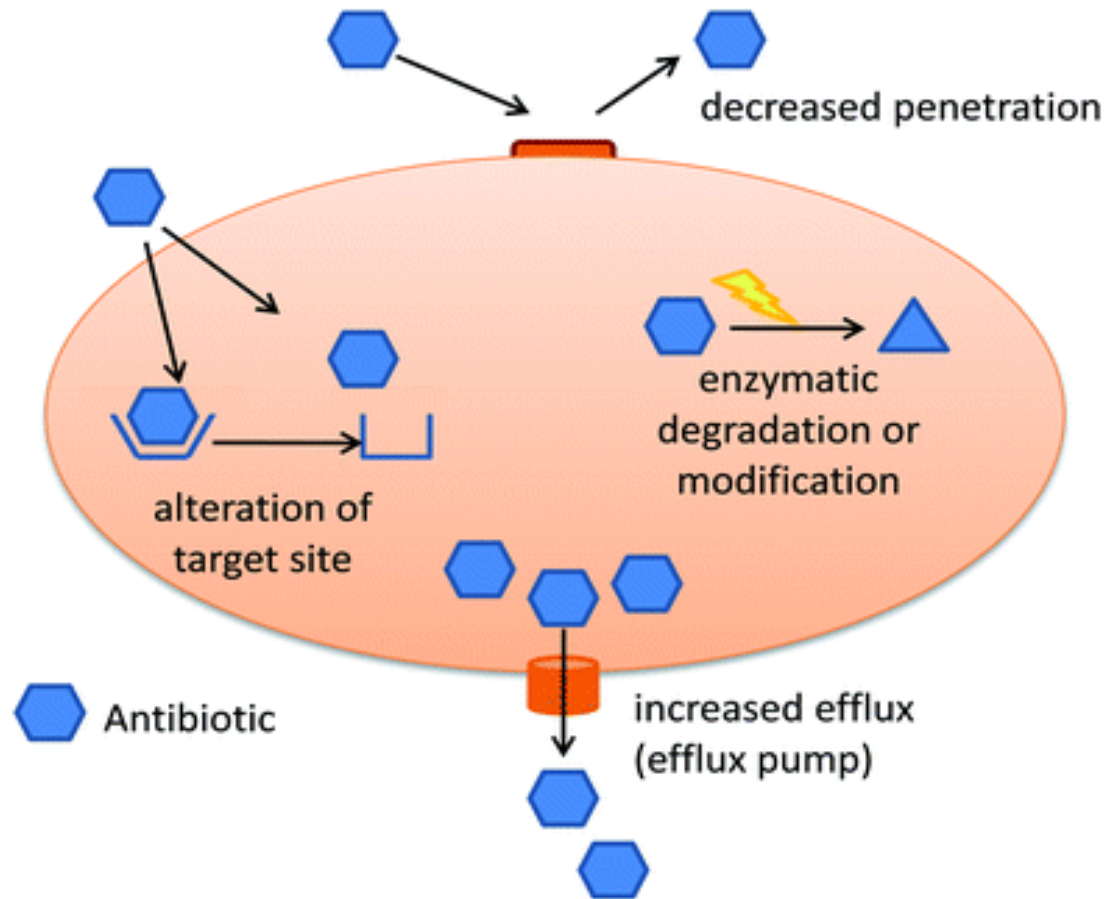
What does the drug do to the organisms ?

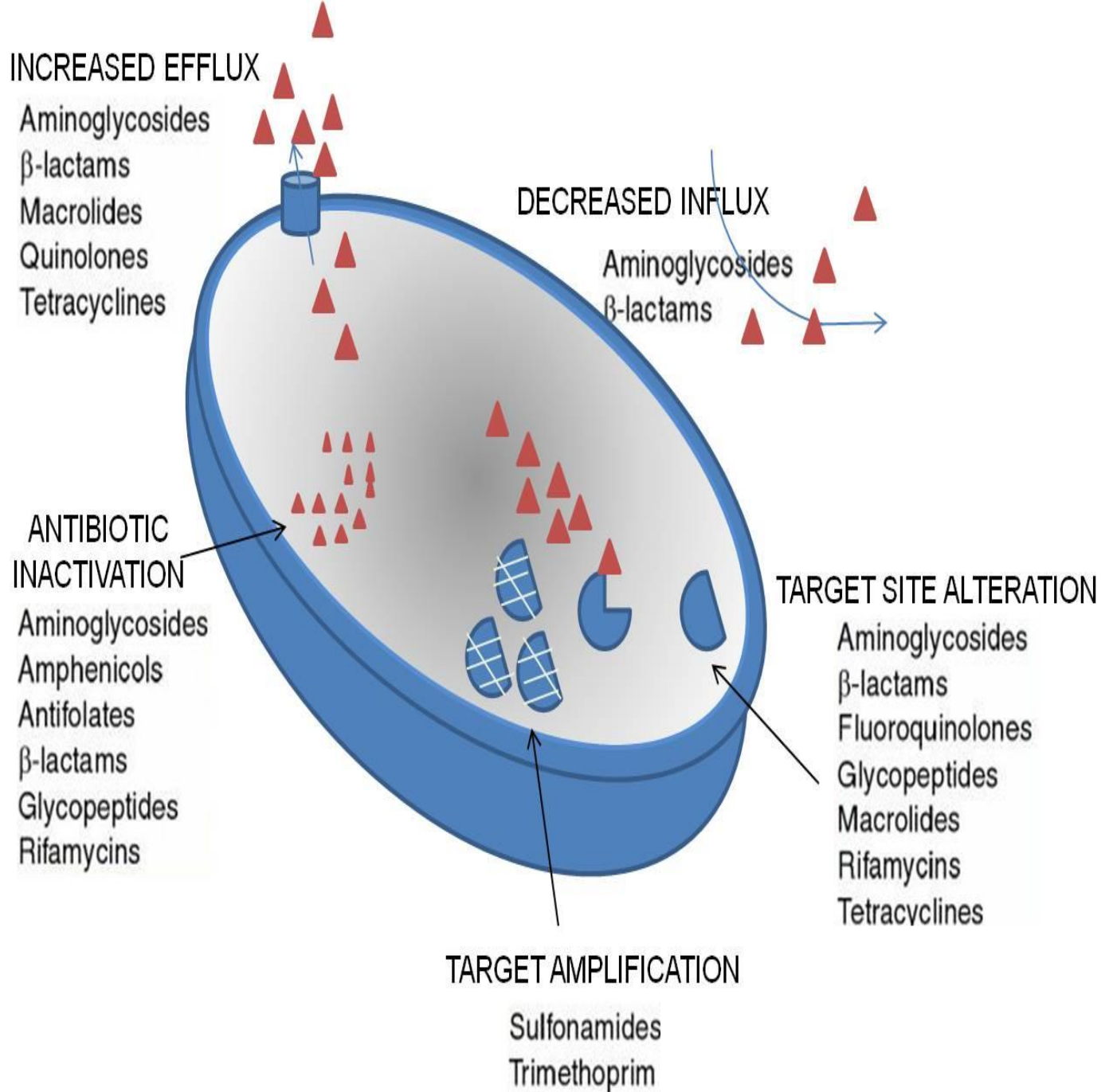
- Effect = antimicrobial activity
  - Desirable
    - ✓ inhibition and killing
  - Undesirable
    - ⊗ adverse effects

# Dosing

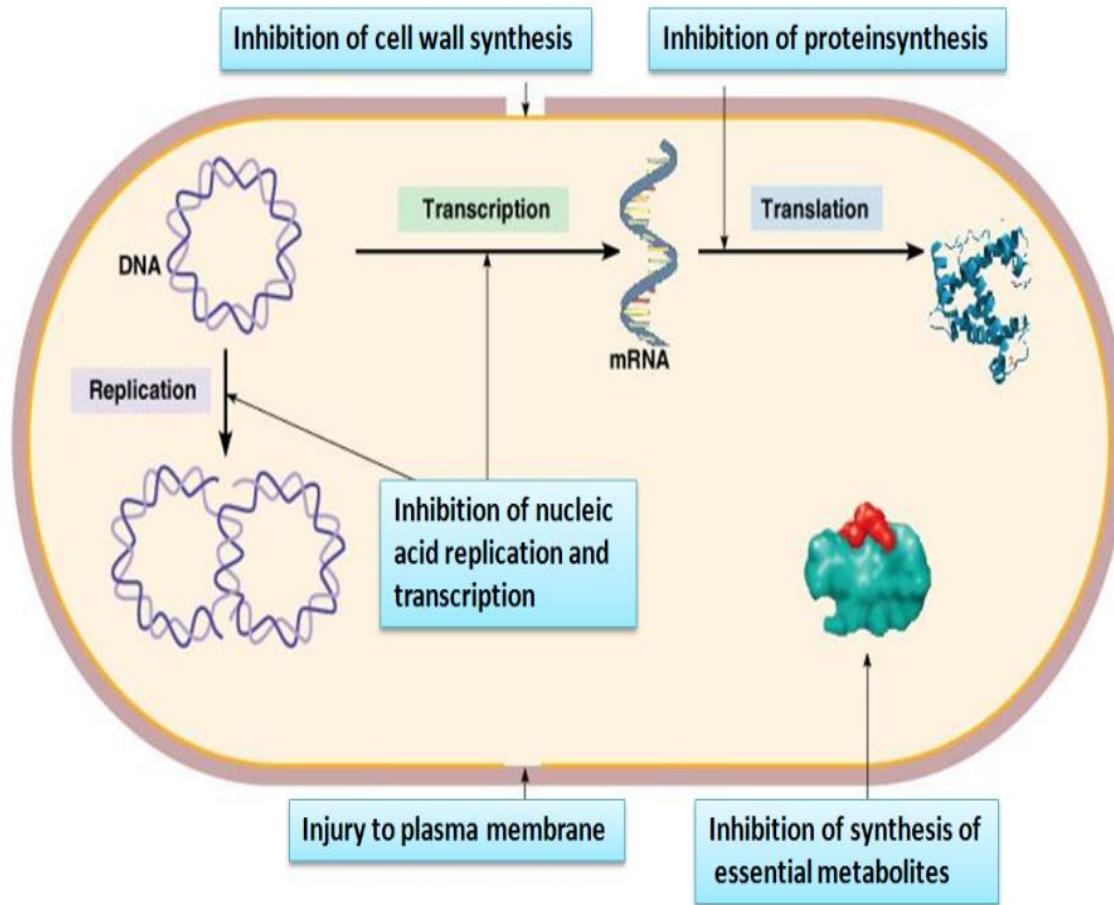


# Mechanism of resistance

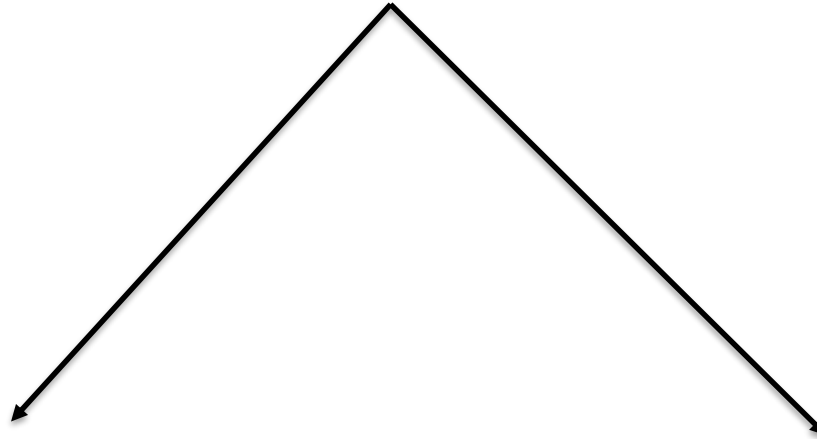




# Mechanisms of action



# 1. Inhibitors of cell wall synthesis



## 1.1 Beta Lactams

- Penicillins
- Co-drugs
- Cephalosporins
- Monobactams
- Carbapenems

## 1.2 Glycopeptides

| Penicillins                                   | Cover  |
|---|--|
| Natural – Penicillin G, Penicillin V          | Gram + & - cocci<br>Gram + bacilli<br>Spirochaetes |
| Synthetic – Penicillin VK                     | Same as above                                      |
| Antistaphylococcal – cloxacillin, methicillin | Treats penicillinase producing staph               |

| Co - drugs                    | Cover  |
|-------------------------------|--|
| Amoxicillin – clavulanic acid | Gram + (penicillinase producing<br>eg. Strep pyogenes, MSSA)<br>Gram – (penicillinase producing<br>eg. E coli, Klebs Pneum))<br>Anerobes (eg. Bacteroides) |
| Piperacillin - tazobactam     | Same as above<br><br><b><u>HOWEVER!</u></b><br><br>Also antipseudomonal<br>May cover ESBL producers<br>(depends on local ecology)                          |



| Cephalosporins  |  | Cover  |
|---|--|--|
| <u>1<sup>st</sup> generation</u><br>eg. Cefazolin         |  | (for Strep & MSSA)   |
| <u>2<sup>nd</sup> generation</u><br>eg. Cefuroxime        |  | (required)   |
| <u>3<sup>rd</sup> generation</u><br>eg. Ceftriaxone       |  | high   |
| <u>4<sup>th</sup> generation</u><br>eg. Cefepime          |  | high   |
| <u>5<sup>th</sup> (new) generation</u><br>eg. Ceftaroline |  | in high<br>nal and<br>ation but gram +<br>ow includes MRSA |

**NO ANAEROBIC  
COVER**

# Monobactam

- Eg. Aztreonam
- Historic
- Limited gram neg cover
- Pseudomonas
- High S/E profile, expensive

| Drug                         | Gram +<br>(MSSA,<br>Strep) | Gram -<br>Enterobacte<br>ricia | Pseudomo<br>nas | Anaerob<br>es | Special<br>considerations   |
|------------------------------|----------------------------|--------------------------------|-----------------|---------------|---|
| 1 <sup>st</sup><br>Ertapenem | +                          | +                              |                 | +             | No<br>enterococcal<br>cover   |
| 2 <sup>nd</sup><br>Imipenem  | +                          | +                              | +               | +             | Enterococcal<br>cover   |
| 2 <sup>nd</sup><br>Meropenem | +                          | +                              | +               | +             | High dose<br>crosses BBB<br>No<br>enterococcal<br>cover                                     |
| 2 <sup>nd</sup><br>Doripenem | +                          | +                              | +               | +             | Stable in<br>solution for 12<br>hours (constant<br>infusion)<br>No<br>enterococcal<br>cover |

## 1.2 Glycopeptides

- *Vancomycin*
- extended spectrum gram positive cover only
- 30mg/kg loading and the 30mg/kg/day
- Nephrotoxic, red man syndrome
  
- *Lipoglycopeptide* – Teicoplanin
- Less nephrotoxic
- CANNOT be monitored

## 2. Inhibitors protein synthesis

### TETRACYCLINES

- Doxycycline
- Minocycline
- *Glycylcline – Tigecycline*
- Gram +, - & anaerobes

### MACROLIDES

- Erythromycin
- Azithromycin
- Clarithromycin
- *Ketolide – Telithromycin*
- Gram +, gram – cocci, anaerobes

### LINCOSAMIDES

Clindamycin

**Gram + & anaerobes only**

### AMINOGLYCOSIDES

- Amikacin
- Gentamycin
- Tobramycin
- Gram - only (kills on peak, toxic on trough)

### OXAZOLIDINONES

Linezolid

Extended gram + cover including MRSA, VRSA, Enterococci

### 3. Inhibitors cell membrane function

- **Lipopeptides**
- *Polymixins – Colistin*
- Narrow spectrum gram neg cover  
(Pseudomonas, Acinetobacter, CRE)
- Inherent resistance – Proteus, Serratia
- *Cyclic lipopeptide – Daptomycin*: Extended gram positive cover (not for lung)

# 4. Anti-metabolites



## Sulfonamides

---

- Bactericidal/Bacteriostatic (depends on organism)
- Sulfamethoxazole/Trimethoprim (Co-trimoxazole)
- Spectrum of Activity:
  - Gram-positives: Streptococci (+/-), Staphylococci (including some MRSA), but **NOT** enterococci
  - Gram-negatives: limited to respiratory pathogens and select other organisms (e.g., E. coli, Enterobacter, Proteus)
  - Pneumocystis carinii ("PCP") – in HIV/AIDS patients
  - Poor against anaerobes and atypical bacteria

## 5. Inhibitors nucleic acid synthesis

| Generation | Drug Names                                   | Spectrum   |
|------------|--|--|
| 1st        | nalidixic acid                               | Gram(-) but not Pseudomonas species  |
| 2nd        | norfloxacin<br>ciprofloxacin<br>ofloxacin    | Gram(-) (including Pseudomonas species), some Gram(+) (S. aureus) and some atypicals |
| 3rd        | levofloxacin<br>sparfloxacin<br>gemifloxacin | Same as 2 <sup>nd</sup> generation with extended Gram(+) and atypical coverage       |
| 4th        | moxifloxacin                                 | Same as 3 <sup>rd</sup> generation with broad anaerobic coverage                     |



**A POCKET GUIDE TO ANTIBIOTIC PRESCRIBING  
FOR ADULTS IN SOUTH AFRICA, 2015**

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**TOM BOYLES**

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**ON BEHALF OF THE SOUTH AFRICAN ANTIBIOTIC STEWARDSHIP  
PROGRAMME (SAASP)**



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## GLOSSARY

| Term                                    | Definition   |
|---|--|
| Antibiogram                             | A list of antibiotics to which a cultured bacterium is susceptible, intermediate or resistant  |
| BC                                      | Blood culture  |
| BD                                      | Twice daily  |
| Beta-lactam antibiotic                  | Antibiotic class containing a beta-lactam ring that inhibits bacterial cell wall synthesis. Includes penicillins, cephalosporins and carbapenems   |
| CA                                      | Community-acquired   |
| CAP                                     | Community acquired pneumonia   |
| Cleaning solution                       | Antiseptic for hand hygiene, including 0.5% chlorhexidine in 70% alcohol and iodine-based solutions  |
| Community-acquired (CA) infection       | Illness starts prior to, or within 48 hours of admission   |
| CRB-65 score                            | <p>A clinical prediction rule for mortality in community-acquired pneumonia. The score is an acronym for individual risk factors as follows:</p> <p><b>C</b>onfusion of new onset<br/> <b>R</b>espiratory rate <math>\geq 30</math> breaths per minute<br/> <b>B</b>lood pressure <math>&lt; 90</math> mmHg systolic or <math>&lt; 60</math> diastolic<br/> <b>65</b> years or older</p> <p>A single point is assigned to each risk factor.</p>  |
| CRE                                     | Carbapenem resistant Enterobacteriaceae  |
| CXR                                     | Chest X-ray  |
| eGFR                                    | Estimated glomerular filtration rate   |
| ESBL                                    | Extended spectrum beta lactamase producing organism  |
| Health care associated infection (HCAI) | <p>Any patient with a new infection starting <math>\geq 48</math> hours after admission and was not apparent at the time of admission, or any catheter or line-associated infection irrespective of time of insertion.</p> <p>The following factors increase risk:</p> <ul style="list-style-type: none"> <li>• Admission to an acute care hospital within 90 days of the current presentation</li> <li>• Resident of a nursing home or long-term care facility</li> <li>• Recent intravenous antibiotic therapy, chemotherapy or wound care within the past 30 days of the current presentation</li> <li>• Patients attending a haemodialysis clinic</li> </ul> |
| HCAP                                    | Health care associated pneumonia   |
| IPC                                     | Infection prevention and control   |
| im                                      | Intramuscular injection  |
| iv                                      | Intravenous  |
| MRSA                                    | Methicillin resistant <i>Staphylococcus aureus</i>   |
| MSSA                                    | Methicillin sensitive <i>Staphylococcus aureus</i>   |
| po                                      | Per os (oral)  |
| Rx                                      | Treatment/therapy  |
| TOE                                     | Trans-oesophageal echocardiogram   |
| TTE                                     | Trans-thoracic echocardiogram  |
| VRE                                     | Vancomycin resistant enterococci   |

## **Disclaimer**

This document is provided as an information resource for all health care workers to assist in the appropriate prescribing of antibiotics. It attempts to summarise relevant information for clinicians from South African and International guidelines as well as reference to textbooks, key publications and expert opinion.

Recommendations change rapidly and opinion can be controversial. The authors do not warrant that the information contained in this booklet is complete and shall not be liable for any damages incurred as a result of its use.

## **Acknowledgements**

We would like to acknowledge the following colleagues who provided input during the editing phase of this book:

Dr Adrian Brink, Prof Alan Karstaedt, Prof Andrew Whitelaw, Prof Andries Gous, Ms Andriette van Jaarsveld, Prof Andy Parish, Dr Cloete van Vuuren, Dr Colleen Bamford, Dr Dena van den Bergh, Prof Guy Richards, Prof Gary Maartens, Dr Ivan Joubert, Dr James Nuttall, Sr Lesley Devenish, Prof Olga Perovic.

# Chapter 1

## Why do we need this guide?

The international community sits at the tipping point of a post-antibiotic era, where common bacterial infections are no longer treatable with the antibiotic armamentarium that exists. In South Africa, the identification of the first case of pan-resistant *Klebsiella pneumoniae* (Brink et al, J Clin Microbiol. 2013;51(1):369-72) marks a watershed moment and highlights our tip of the antibiotic resistance 'iceberg' in this country. Multi-drug resistant (MDR)-bacterial infections, predominantly in Gram-negative bacteria such as *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are now commonplace in South African hospitals. Whilst a number of expensive new antibiotics for Gram-positive bacterial infections have been manufactured recently (some of which are licenced for use in South Africa), no new antibiotics active against Gram-negative infections are expected in the next 10-15 years. Hence what we have now, needs conserving.

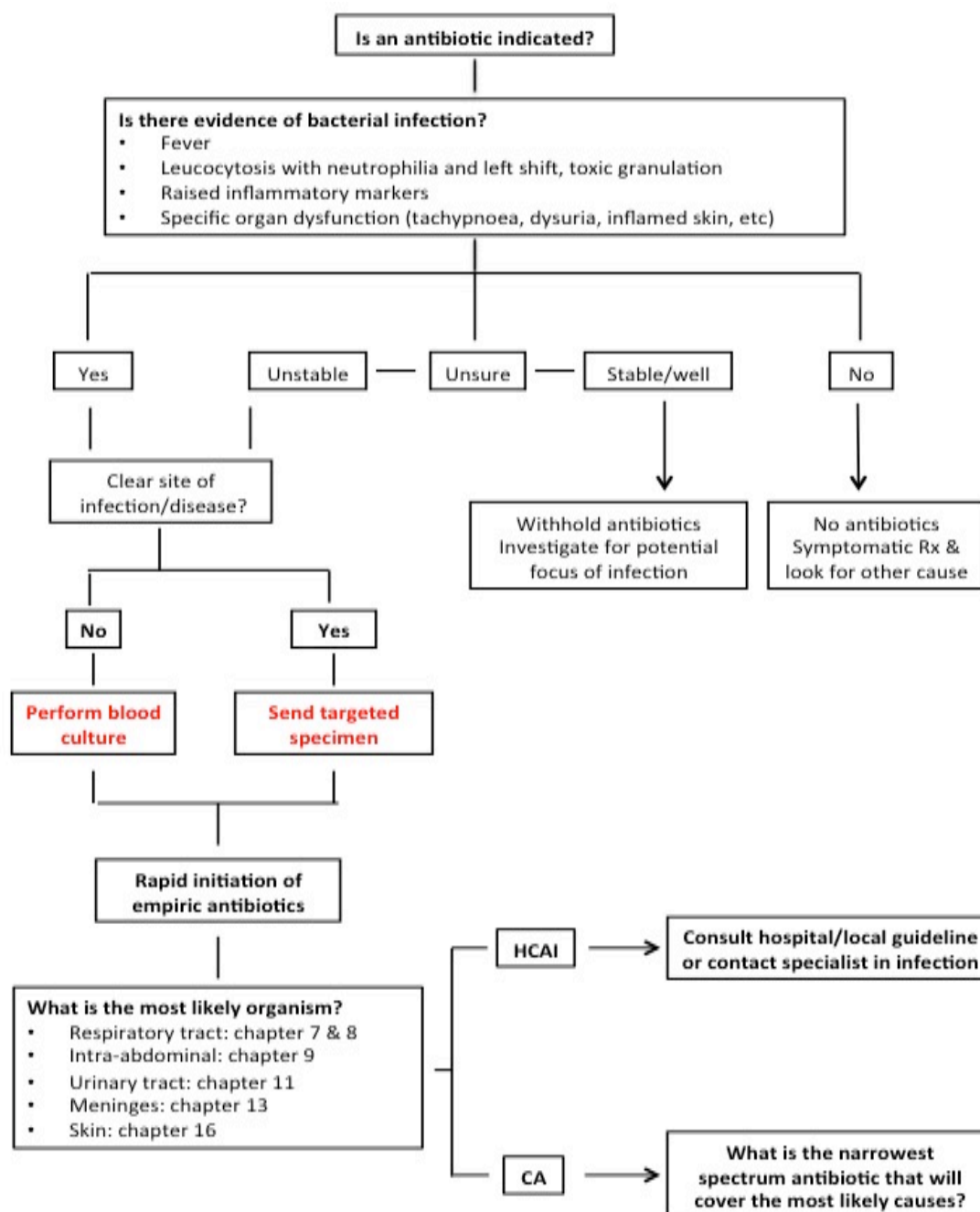
The development of antibiotic resistance is a natural phenomenon. Drug-resistance mutations have been found in 30,000-year old ice blocks. In addition, bacteria may acquire antibiotic resistance mechanisms by horizontal gene transfer. There are over 1000 different naturally occurring enzymes that are produced by different bacteria, which inactivate antibiotics. The overuse of antibiotics is driving the selection of antibiotic resistance. Given the right circumstances, the resistant bacteria that are selected out can either colonize a patient (be present, potentially transmissible, but not cause clinical disease i.e. infection) or cause infection. It follows that the more antibiotics are used, the greater the likelihood of selecting out antibiotic resistance, and the broader the spectrum of antibiotic that is used, the greater the number of different types of resistant bacteria will be selected out. The fact that it is estimated that half of all antibiotics prescribed in human health are unnecessary e.g. for viral upper respiratory tract infections, demands our renewed efforts to make antibiotic prescribing appropriate. When it is indicated, an antibiotic must be the right choice at the right dose, dosing interval and route, and for the right duration, and when it is not indicated, that antibiotic must not be prescribed.

Rather than be an exhaustive text on infectious diseases, microbiology or clinical pharmacology, the aim of this guide is to give you the practical information you need to perform antibiotic stewardship in an algorithmic manner, which mimics the day-to-day experience of the prescriber.

## Chapter 2

### Principles for rational antibiotic prescribing

#### 1. Decide if an antibiotic is indicated: does the patient have a bacterial infection?



Targeted refers to specimen from site of infection e.g. urine for cystitis

#### 2. Perform cultures before administering antibiotics in hospitalised patients or in outpatients with recurrent infections

This allows de-escalation to a narrow spectrum antibiotic once the antibiogram is available & is a cornerstone of antibiotic stewardship

### **3. Choose an appropriate empiric antibiotic:**

#### **a. Target the most likely pathogen(s) for the site of infection**

This can be predicted by understanding the broad groups of pathogens that most commonly cause infections at various sites:

- Skin and soft tissue: Gram positive cocci
- Urinary tract: Gram negative bacilli
- Intra-abdominal: Gram-negative, Gram-positive and anaerobic organisms
- See chapters on specific infections for more details

An appropriate empiric antibiotic can then be selected by matching the narrowest spectrum antibiotic with the likely pathogens. Spectrums of activity of commonly used antibiotics are shown below

|                        | Gram positive cocci |      |   |                    |                   |     |
|------------------------|---------------------|------|---|--------------------|-------------------|-----|
|                        | Clusters            |      | Pairs/chains                                    |                    |                   |     |
|                        | MSSA                | MRSA | <i>S. pneumoniae</i><br>Most other streptococci | <i>E. faecalis</i> | <i>E. faecium</i> | VRE |
| Amoxicillin/ampicillin | -                   | -    | +   | +                  | -                 | -   |
| Cloxacillin            | +                   | -    | +/-   | -                  | -                 | -   |
| Clindamycin            | +                   | +/-  | +   | -                  | -                 | -   |
| Ceftriaxone            | +                   | -    | +   | -                  | -                 | -   |
| Co-amoxiclav           | +                   | -    | +   | /                  | -                 | -   |
| Vancomycin             | /                   | +    | /   | /                  | +                 | -   |
| Ertapenem              | /                   | -    | /   | -                  | -                 | -   |
| Moxifloxacin           | /                   | +/-  | +   | /                  | +/-               | -   |
| Linezolid              | /                   | /    | /   | /                  | /                 | +   |
| Daptomycin             | /                   | /    | /   | /                  | /                 | /   |

|                        | Gram negative                               |                             |      |     |                           |                            |                               |
|------------------------|---|-----------------------------|------|-----|---------------------------|----------------------------|-------------------------------|
|                        | Bacilli                                     |                             |      |     |                           |                            | Cocci                         |
|                        | <i>E. coli</i><br><i>Klebsiella</i><br>spp. | <i>Enterobacter</i><br>spp. | ESBL | CRE | <i>Salmonella</i><br>spp. | <i>Pseudomonas</i><br>spp. | <i>Neisseria meningitidis</i> |
| Amoxicillin/ampicillin | -   | -                           | -    | -   | /                         | -                          | +/-                           |
| Penicillin             | -   | -                           | -    | -   | /                         | -                          | +/-                           |
| Cotrimoxazole*         | +/-   | +/-                         | +/-  | -   | +/-                       | -                          | -                             |
| Ceftriaxone            | +   | -                           | -    | -   | +                         | -                          | +                             |
| Co-amoxiclav           | +   | -                           | -    | -   | /                         | -                          | /                             |
| Ciprofloxacin          | +   | +                           | +/-  | +/- | +                         | +                          | /                             |
| Aminoglycosides        | +   | +                           | +/-  | +/- | -                         | +                          | -                             |
| Cefepime               | /   | +                           | -    | -   | /                         | +                          | /                             |
| Piptazobactam          | /   | +/-                         | -    | -   | /                         | +                          | /                             |
| Ertapenem              | /   | +                           | +    | -   | /                         | -                          | /                             |
| Imipenem               | /   | /                           | /    | +/- | /                         | +                          | /                             |
| Meropenem              | /   | /                           | /    | +/- | /                         | +                          | /                             |

\*Associated with much higher rates of toxicity than other antibiotics. Avoid using if a suitable alternative with a similarly narrow spectrum of activity is available

- + usually susceptible: recommended first line therapy while awaiting antibiogram
- frequent resistance or poor clinical efficacy: do not use
- +/- variable susceptibility: only use with antibiogram result
- / usually susceptible but not first choice: do not use unless there is a compelling reason (e.g. allergy, toxicity or resistance to first line drug or better outcomes for a particular site of infection)

## b. Assess likelihood of antibiotic resistance

Risk factors include known colonisation with a resistant pathogen, HCAI, recent antibiotic exposure. Local resistance patterns inform prescribing.

## c. Review potential contraindications

### Allergy:

Clinicians should differentiate an immediate type 1 IgE mediated hypersensitivity reaction from other less dangerous types of hypersensitivity. Classical signs of type 1 hypersensitivity are anaphylaxis, angioedema, urticarial rash, and bronchospasm. If a type 1



hypersensitivity reaction to penicillin has occurred, then all  $\beta$ -lactam antibiotics should be avoided, unless there is no alternative drug available when penicillin desensitisation can be attempted as an inpatient.

Patients with other types of hypersensitivity reactions, usually a maculopapular rash to amoxicillin, should avoid all penicillins but may tolerate other  $\beta$ -lactam antibiotics like cephalosporins. The 1<sup>st</sup> generation cephalosporins should be avoided as they have a higher risk of cross-reactivity with penicillin, but this risk is much lower for second- or third-generation cephalosporins reported to be only 0.1%.

If the previous reaction to penicillin was a maculopapular rash, it is relatively safe to use 2<sup>nd</sup>/3<sup>rd</sup> generation cephalosporins and use would depend on the patient's social circumstances and access to follow-up. However, in patients with a remote history of a rash on penicillin it is often difficult to differentiate a maculopapular rash from an urticarial rash – all  $\beta$ -lactam antibiotics should be avoided if urticaria occurred on penicillins as this is a type 1 reaction. In this setting, skin testing before using a cephalosporin is recommended, as a positive reaction to penicillin indicates type 1 hypersensitivity.

#### Toxicity:

Antibiotics can cause direct dose-dependent toxicity and should be avoided in patients at high risk of developing organ damage with a specific agent. For example, do not use aminoglycosides in patients with renal impairment or hearing loss.

#### d. Choose drug with adequate target tissue penetration

|                        | CSF                  | Lung    | Soft tissue | Urinary tract        |
|------------------------|----------------------|---------|-------------|----------------------|
| <b>Ampicillin</b>      | Good (in high doses) | Good    | Good        | Good                 |
| <b>Cloxacillin</b>     | Inadequate data      | Fair    | Good        | No data              |
| <b>Clindamycin</b>     | Poor                 | No data | Good        | No data              |
| <b>Co-amoxiclav</b>    | Poor                 | Good    | Good        | Fair                 |
| <b>Ceftriaxone</b>     | Good (in high doses) | Good    | Good        | Good                 |
| <b>Aminoglycosides</b> | Poor                 | Poor    | Fair        | Good (if normal GFR) |
| <b>Ciprofloxacin</b>   | Good (in high doses) | Good    | Good        | Good                 |
| <b>Co-trimoxazole</b>  | Good                 | Good    | Good        | Good                 |
| <b>Ertapenem</b>       | Poor                 | Good    | Good        | Good                 |
| <b>Meropenem</b>       | Good (in high doses) | Good    | Good        | Good                 |
| <b>Imipenem</b>        | Good*                | Good    | Good        | Good                 |
| <b>Vancomycin</b>      | Poor                 | Fair    | Poor        | Good                 |
| <b>Linezolid</b>       | Good                 | Good    | Good        | Good                 |
| <b>Daptomycin</b>      | Poor                 | Poor    | Good        | Good                 |

\*Associated with higher risk of seizures

#### e. Aim for a single drug with the desired spectrum of activity

Monotherapy is preferred unless combination therapy is required for synergy (e.g. endocarditis) or extended spectrum beyond what can be obtained with a single drug (e.g. atypical pathogens in severe CAP).

#### 4. Ensure correct dose and route of administration

The oral/enteral route is preferred whenever possible for patients with mild to moderate infections. Intravenous antibiotics should be reserved for severe infection or for certain sites such as the CSF, bacteraemia, endocarditis, bone and joint infections.

|                | Oral absorption (%) | Comments   |
|----------------|---------------------|--|
| Penicillin VK  | Moderate            | Take without food                                  |
| Amoxicillin    | Good                |  |
| Flucloxacillin | Good                | Take on empty stomach                              |
| Clindamycin    | Good                |  |
| Co-amoxiclav   | Good                |  |
| Ciprofloxacin  | Good                | Do not give via NGT or with antacids               |
| Doxycycline    | Excellent           | Take with food, do not co-administer with antacids |
| Azithromycin   | Poor                | Take without food                                  |
| Metronidazole  | Excellent           |  |
| Co-trimoxazole | Good                |  |
| Linezolid      | Excellent           |  |

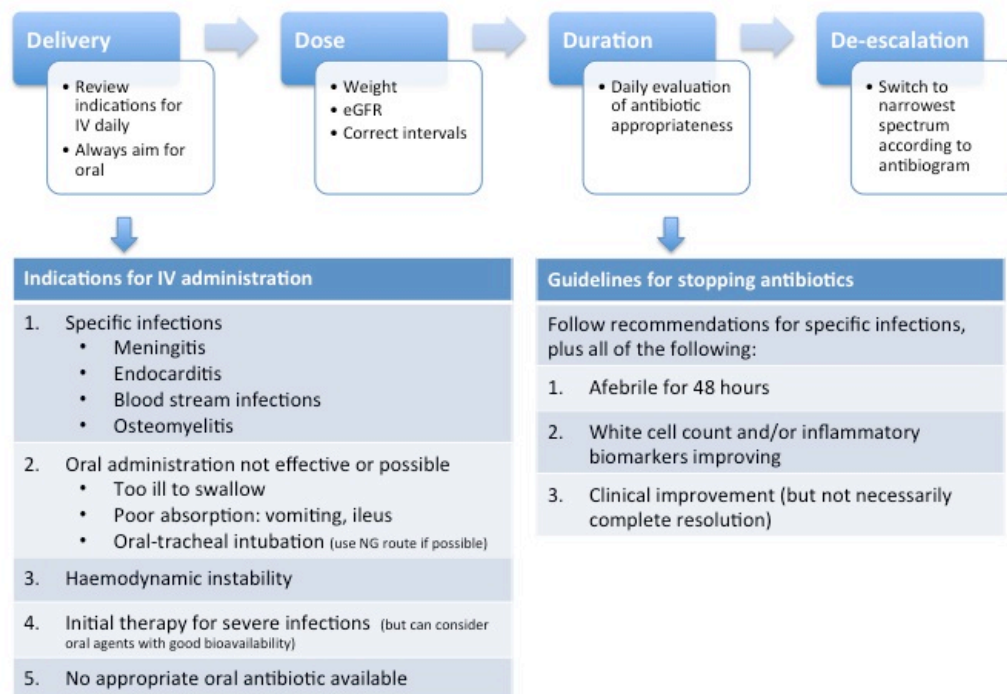
#### 5. Start the appropriate antibiotic rapidly in severe infections

Mortality increases by 8% for every hour antibiotic administration is delayed in septic shock<sup>1</sup>

#### 6. Practice early and effective source control

Search for and remove any persistent foci of infection

#### 7. Evaluate antibiotic appropriateness every day



<sup>1</sup> Kumar et al. Crit Care Med. 2006 Jun;34(6):1589-96.

## Chapter 3

### Interpreting test results

#### Non culture-based tests

Non culture-based tests such as urinary dipstick, peripheral white cell count (WCC), and C-reactive protein (CRP) confirm the presence of inflammation when positive but do not differentiate bacterial from non-bacterial causes. However, presence of nitrites on urine dipstick, high neutrophil count with left-shift and CRP >100 mg/ml all suggest bacterial infection. Negative results are generally good at excluding inflammation and therefore bacterial infection.

Procalcitonin (PCT) is more specific for bacterial infection than CRP or WCC but 10 times more expensive. There is high quality evidence for its use in a limited number of infections and its use should be limited to these indications. Specifically, low PCT safely excludes bacterial infection such that antibiotics can be withheld in meningitis, and acute exacerbations of chronic obstructive pulmonary disease (see later sections for details). PCT has no value in differentiating bacterial infection from tuberculosis and has very limited value in sepsis. Its price generally excludes its use in serial measurement to determine when to stop, although some evidence in ICU settings alone, exist.

#### Cultures

**Does this positive culture represent infection, colonisation or contamination?**

**Infection** = the presence of one or more microorganisms with an inflammatory response

**Colonisation** = the presence of microorganisms without significant inflammation.

**Contamination** = A culture that contains a microorganism(s) that did not originate from the intended anatomical site

#### Sterile sites

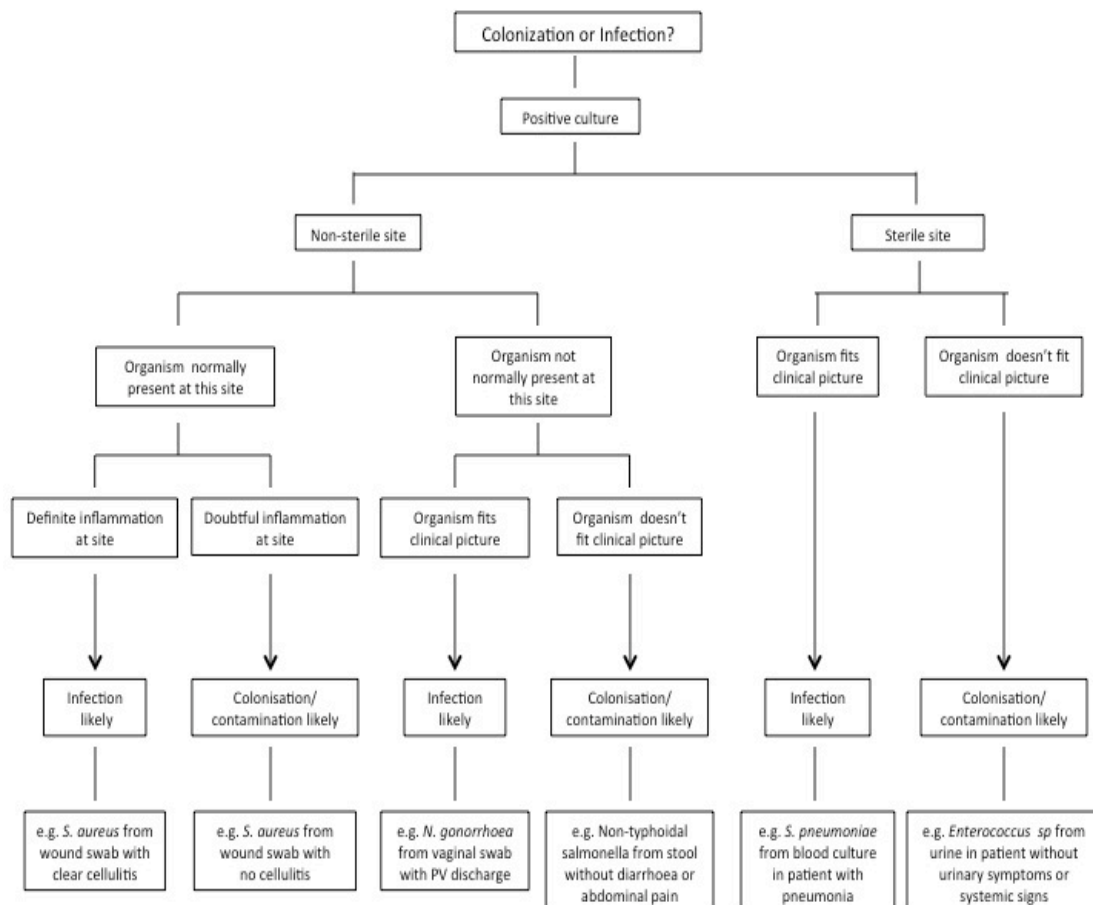
Normally sterile sites are CSF, lungs (below the glottis), urinary tract, biliary tract, and blood. Bacteria cultured from these sites are likely to be causing infection but still sometimes represent colonisation or contamination.

**Finding bacteria in a sterile site is abnormal but may represent infection, or contamination. Organisms colonizing skin such as coagulase-negative staphylococci may cause contamination of sterile sites. Colonisation of urinary tract can occur without causing infection. If the organism corresponds with the clinical scenario then this should be considered to be causing infection**

## Non-sterile sites

Non-sterile specimens include sputum (as it must pass through the mouth), pus swabs from skin, GI tract and vagina. Specimens from these sites are **expected to culture bacteria** (unless growth is inhibited by laboratory techniques). Interpretation therefore depends on the organism(s) being compatible with the clinical scenario.

**Cultures from non-sterile sites are often much harder to interpret and usually of less value.**



## Chapter 4

### Correct techniques of microbiological sampling

**Optimal sampling is very important to increase yields and decrease contamination rates (see boxes below).** Surgical specimens from abnormal structures such as abscesses should usually be collected at the time of operation. Once surgical drains are placed they quickly become colonised with skin and environmental bacteria and culture results are not interpretable. Pus swabs collected outside of theatre are discouraged, as it is extremely rare for them to yield information that will change patient management.

#### Box 1. Correct technique for collecting mid-stream urine specimens

Instructions for collection of urine specimens

##### Females

- Wash your hands
- Clean the vulva front to back with sterile gauze and sterile water
- Spread labia with fingers
- Void and collect urine mid-flow

##### Males

- Wash your hands
- Retract foreskin and wash glans with sterile gauze and sterile water
- Void and collect urine mid-flow

#### Box 2. Correct technique for collecting urine specimens from a catheter

- Use aseptic technique with sterile gloves and apron
- Clamp tubing just distal to sampling port
- Wait for urine to collect above clamp
- Wipe sampling port with cleaning solution
- Remove urine with a small gauge sterile needle and syringe
- Transfer urine to sterile container
- Clean port again
- Unclamp tubing

### Box 3. Correct technique for performing a pus swab

1. Wounds with slough, necrotic tissue, or dried exudate should first be debrided
2. Wash the wound with sterile saline
3. If the wound is dry moisten the tip of the swab with sterile saline
4. Move swab tip across the wound surface in a zig-zag motion at the same time as being rotated between the fingers
5. Apply gentle pressure to release fluid from the base of the wound
6. Aim to include as much of the area of the wound as possible but avoid intact skin around the wound
7. Document clinical information on laboratory request form
8. Transfer to laboratory as soon as possible

### Box 4. Correct technique for performing a blood culture

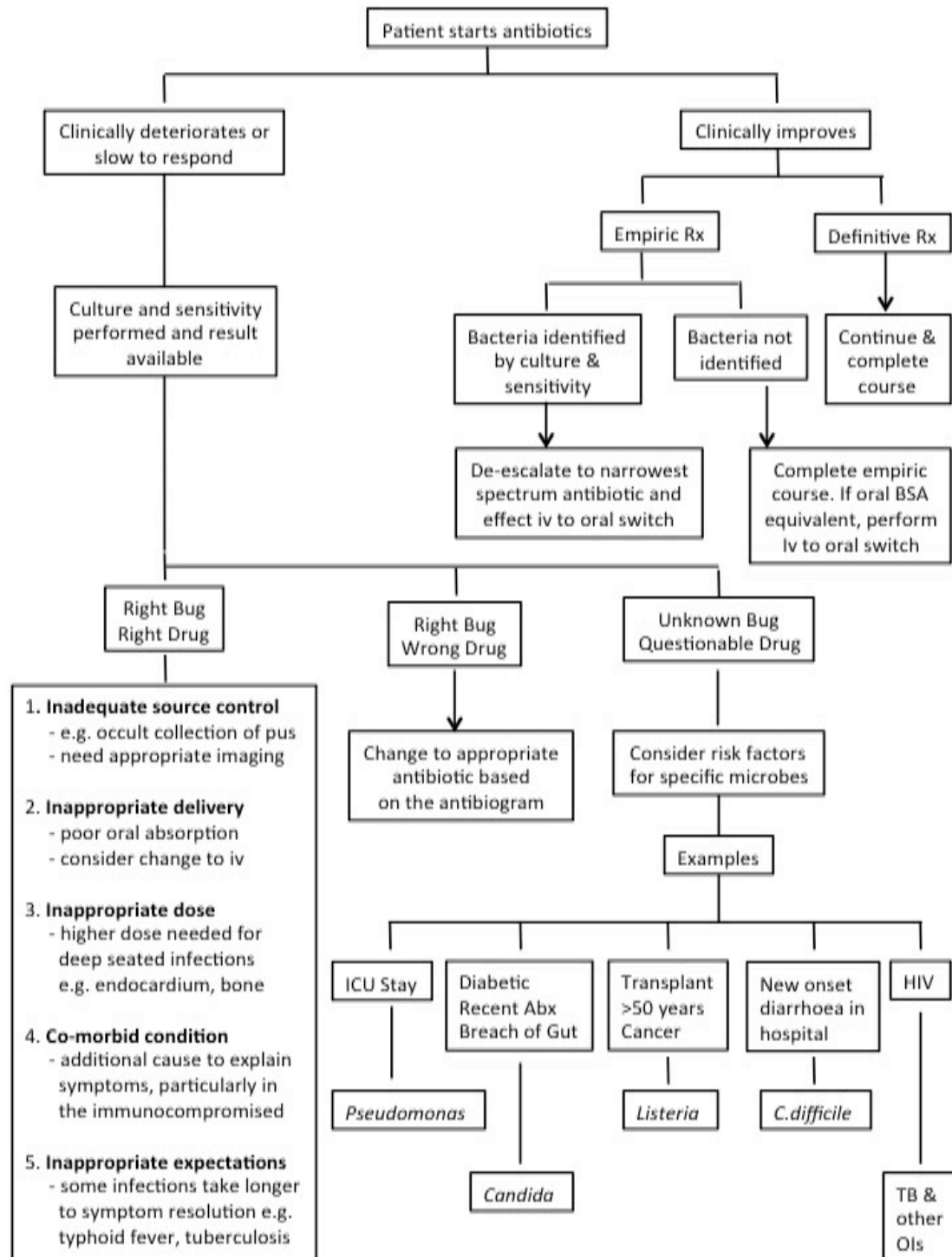
1. Verify the patient's identity and obtain verbal consent.
2. Assemble the correct materials required for blood culture:
  - blood culture bottle(s)
  - syringe (10 ml or more)
  - needle (22 gauge or more)
  - sterile gloves
  - tourniquet
  - adhesive strip
  - Cleaning solution\*
  - sterile pack containing cotton/gauze swabs, sterile paper x2 and waste bag
  - patient labels
  - sharps waste disposal bin
3. Apply tourniquet and select a suitable vein
4. Wash hands and apply sterile gloves
5. Clean the puncture site with cleaning solution using aseptic technique and allow 30 seconds for the disinfectant to dry
6. Place green sterile cover with opening over site for blood culture
7. Collect 10ml of blood per bottle from adults
8. Release tourniquet and remove needle
9. If not using the vacutainer system, disinfect the top of the blood culture bottle before inoculating blood
10. Do not change needles between blood sample collection and inoculation of blood culture bottle
11. Always fill blood culture bottle before filling vials for other tests
12. Label the blood culture bottle making sure not to cover the bar code label or the bottom of the bottle
13. Complete a laboratory request form in full
14. If there is a delay in getting the sample to the laboratory, do not refrigerate the bottle; rather leave it at room temperature
15. Document in the notes, the date and time that the blood culture was taken

\*Chlorhexidine-alcohol is recommended, but if using povidone iodine, it must be left to dry for at least 1 minute prior to performing culture

## Chapter 5

### Changing Antibiotics

Once antibiotics have been initiated the decision to change or stop therapy depends on the patient's clinical response and culture results (see algorithm).



Abx = Antibiotics, BSA = Broad spectrum antibiotics

## Chapter 6

### Infection prevention

The most important tools to prevent spread of infection are hand hygiene and contact precautions. Correct management of IV lines and urinary catheters are essential for reducing hospital-acquired infections.

#### Hand hygiene

##### WHEN:



##### HOW:

Use alcohol-based solutions for routine hand decontamination.

#### **Indications for soap and water:**

- Hands visibly dirty
- Hands contaminated with body fluids
- After using the restroom or eating
- Exposure *Clostridium difficile*

#### **Indications for gloves:**

- Patient interactions that involve exposure to blood, mucous membranes or non-intact skin
  - Suspected or proven *C. difficile*
- Always wash hands after glove use*



## Contact precautions

# **WARNING – STOP!**

# **CONTACT PRECAUTIONS**



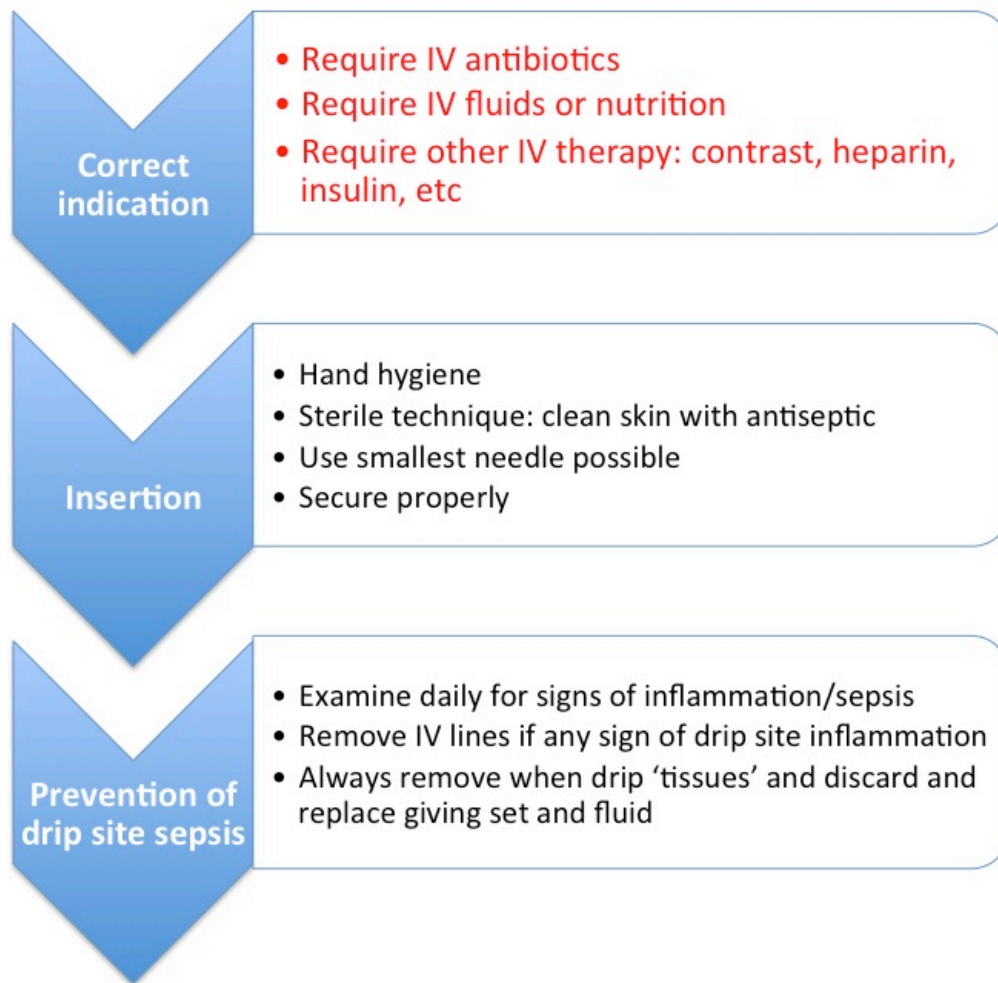
## **ALL STAFF AND VISITORS**

**GLOVES AND APRON FOR ALL PATIENT CONTACT**  
**DISINFECT/WASH YOUR HANDS BEFORE & AFTER**  
**PATIENT CONTACT**

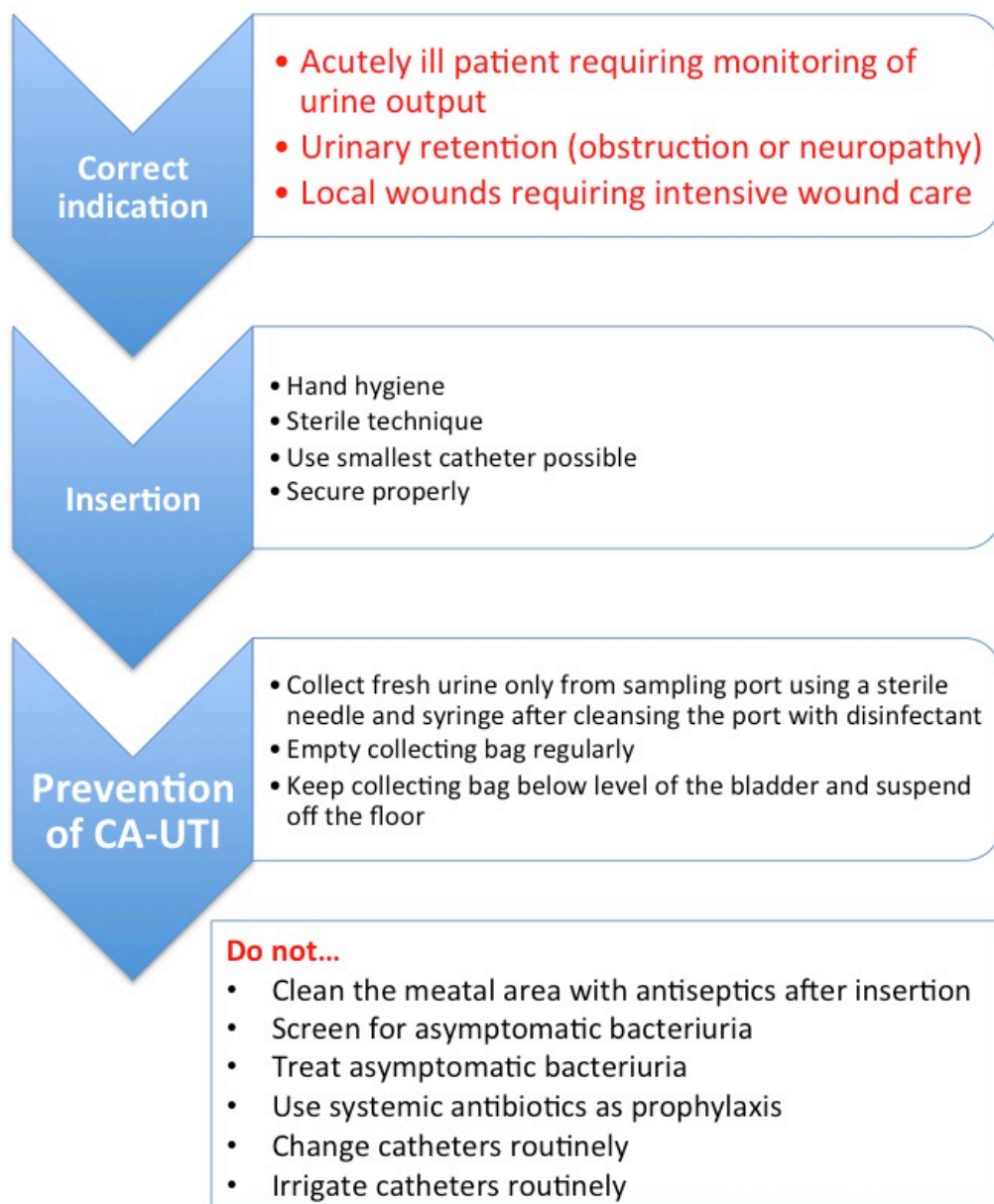
These should be implemented for any patient infected by or colonised with a drug-resistant bacterial pathogen other than tuberculosis (which requires airborne precautions to prevent small droplet spread). Contact precautions involve the following:

1. Clear signage indicating that contact precautions are in place
2. Patient preferably placed in isolation
3. Hand disinfection prior to patient contact
4. Mandatory use of apron and gloves when entering the patient's room, before any contact with the patient or their surroundings and during examination
5. Remove apron first, followed by gloves
6. Hand disinfection after disposal of apron and gloves (use soap and water for *C. difficile* exposure)
7. Contact precautions remain in place even after treatment with antibiotics and for every hospital or nursing care re-admission for a period of 6 months. For patients with *C. difficile* associated diarrhoea contact precautions can be withdrawn after completion of treatment and resolution of diarrhoea.

## Management of peripheral IV lines



## Management of urinary catheters



**Every time you see a patient you should be asking the questions:**

- 1. Can I stop or de-escalate antibiotics?**
- 2. Can I remove this urinary catheter?**
- 3. Can I remove this IV line?**

## Chapter 7

### Acute Upper Respiratory Tract Infection

Over-prescribing of antibiotics for upper respiratory tract infection (URTI) is a major driver of bacterial resistance in the community. URTI comprises three clinical syndromes depending on the site of infection; pharyngotonsillitis (sore throat), acute otitis media, and acute bacterial sinusitis.

#### Acute pharyngotonsillitis (sore throat)



Typical appearance of viral pharyngitis



Typical appearance of bacterial pharyngitis

#### Definition

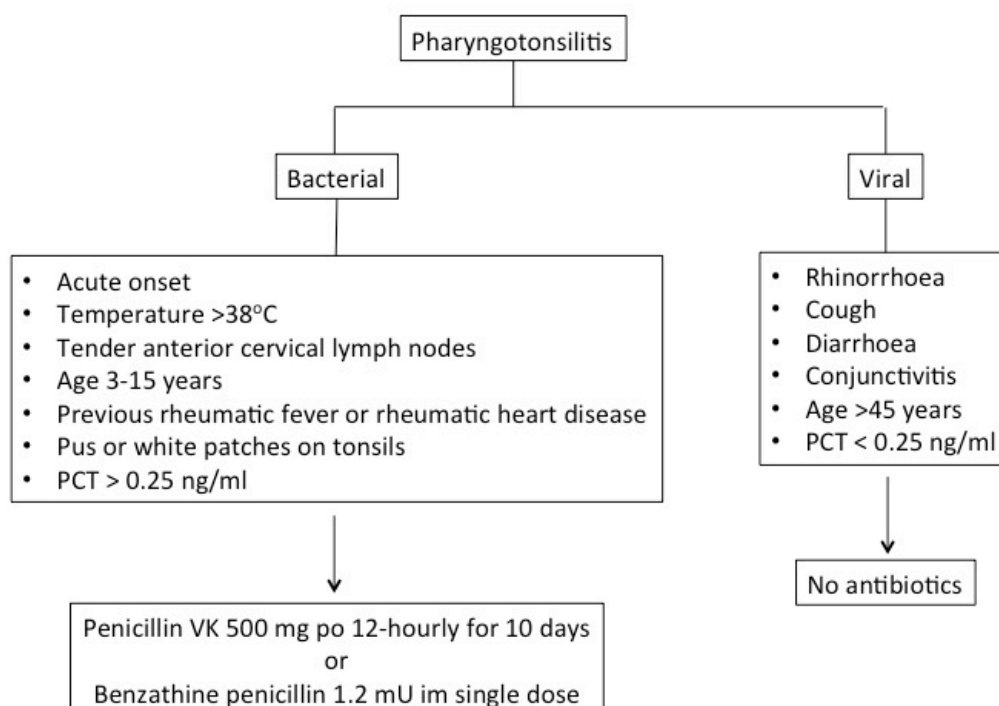
- Acute inflammation of the pharyngeal wall and tonsils.

### Likely pathogens

- Commonly respiratory viruses and Epstein-Barr virus. Around 5-30% caused by group A  $\beta$ -haemolytic streptococci (GABHS) (*S. pyogenes*).
- Viral and bacterial acute pharyngitis are self-limiting, including those caused by GABHS, hence, the primary reason for considering antibiotic therapy is to prevent Acute Rheumatic Fever (ARF)

### Clinical features

- Sore throat
- It is possible to differentiate bacterial from viral causes on clinical grounds.



### Penicillin allergy

Azithromycin 500 mg po daily for 3 days

## Acute otitis media

### Definition

Acute inflammation of the middle ear



Typical appearance of acute otitis media

#### **Likely pathogens**

- *Haemophilus influenza*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*

#### **Clinical features**

- Ear pain and decreased hearing
- Reddened and bulging tympanic membrane, which may be draining pus.

#### **Tests**

- None required

#### **Treatments**

- Initially analgesics and decongestants only
- Antibiotics if febrile or symptoms do not settle within 48 hrs

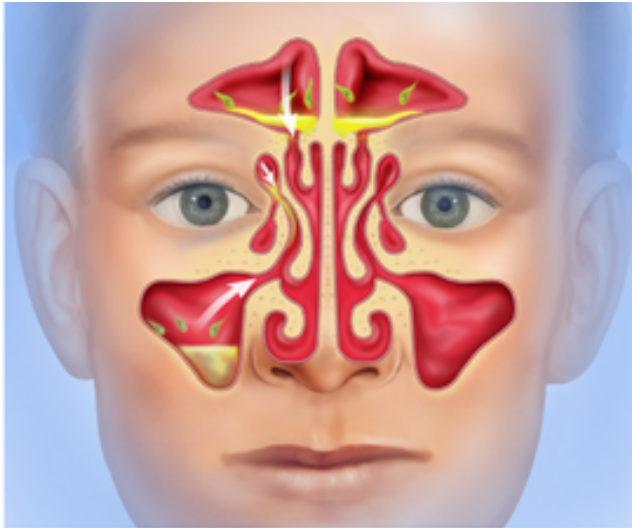
#### **First line**

Amoxicillin 1g po 8-hourly for 5 days

#### **Alternative in beta-lactam allergic patients**

Azithromycin 500 mg po daily for 3 days

#### **Acute bacterial sinusitis**



**Definition-** Acute bacterial infection of para-nasal sinuses

**Likely pathogens-** *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*

#### **Clinical features**

- Often preceded by a viral URTI
- Fever, facial tenderness, dental tenderness, nasal discharge, nasal congestion and anosmia.

#### **Tests**

- Usually none
- If failure of initial therapy a CT scan, fibre-optic endoscopy with aspiration and culture of pus may be necessary

#### **Treatments**

- Symptomatic treatment: paracetamol, decongestant, nasal steroids perform better than antibiotics
- Antibiotics should be prescribed if any of the following are present-
  - Symptoms lasting > 10 days
  - Fever >39°C
  - Purulent discharge
  - Facial pain
  - Biphasic illness with sinusitis following typical viral URTI

#### **First line**

Amoxicillin 1g 8 hourly for 5 days po

#### **Alternative for beta-lactam allergy**

Azithromycin 500 mg po daily for 3 days



## Chapter 8

# Lower Respiratory Tract Infection

### Acute bronchitis

#### Definition

Self-limited inflammatory process involving large and mid-sized airways

#### Common aetiologies

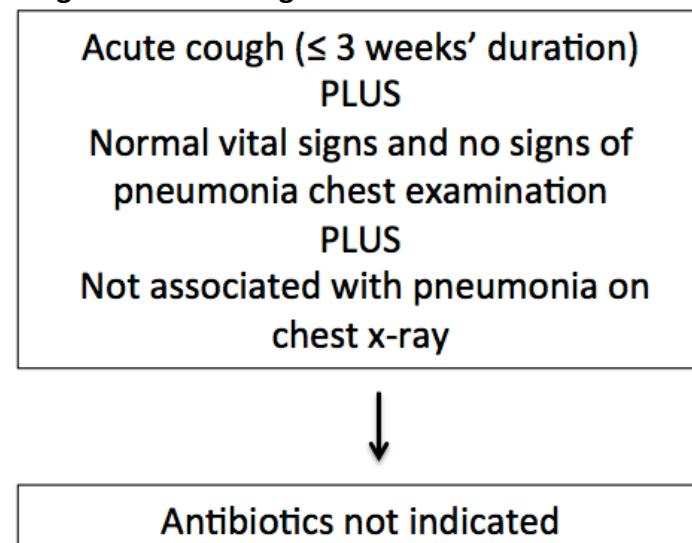
- Respiratory viruses (> 90%)
  - Influenza
  - Parainfluenza 3
  - Respiratory syncytial virus
  - Human metapneumovirus
- Non-viral (<10%)
  - Suspect if prolonged cough, longer incubation period, local outbreaks
    - *Mycoplasma pneumoniae*
    - *Chlamydia pneumoniae*
    - *Bordetella pertussis*
  - No association with *S. pneumoniae* or *H. influenzae* in patients without evidence of underlying lung disease

#### Tests

No investigations are required in the vast majority of cases:

- Gram stain not recommended
- Nasopharyngeal swab for influenza PCR not recommended for uncomplicated influenza-like illness

#### Diagnosis and management



\*Chest X-rays are not necessarily indicated for all patients with acute bronchitis and should be performed only if likely to influence management



## Acute Exacerbation of COPD (AECOPD)

### Definition

Acute increase in baseline dyspnoea, cough and/or sputum above the normal day-to-day variations, requiring a change in medication. Up to 80% of AECOPD have an infectious aetiology.

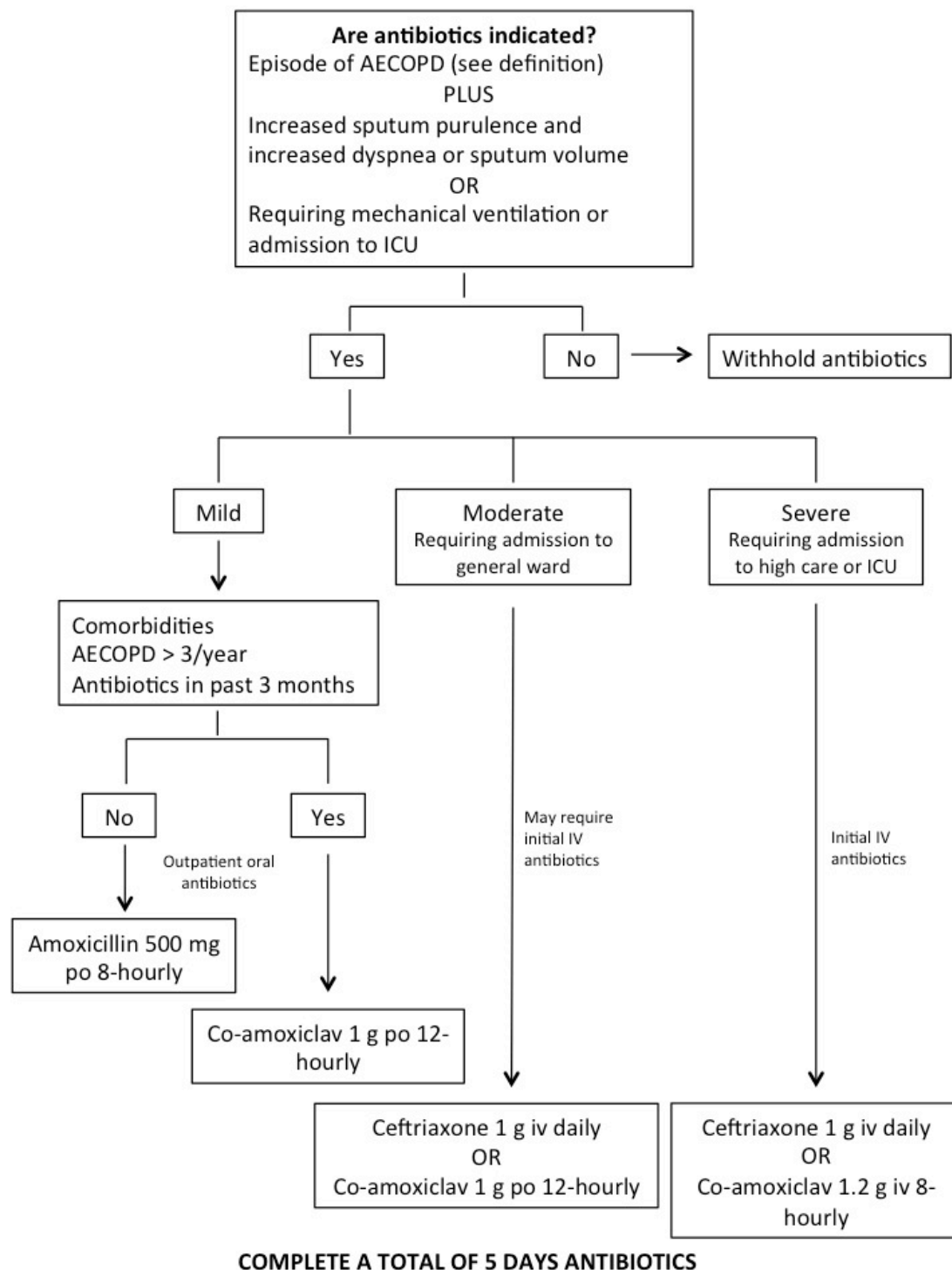
### Common aetiologies

- Viral (up to 50%) – more common in winter months
  - Rhinoviruses
  - Parainfluenza
  - Coronavirus
  - Influenza (in non-vaccinated)
  - RSV
- Bacterial
  - *H. influenzae*
  - *S. pneumoniae*
  - *M. catarrhalis*
  - Enterobacteriaceae (frequent hospitalisation and antibiotic use)
- Atypical bacteria are not implicated in AECOPD

### Tests

| Mild   | Moderate<br>(Requiring hospitalisation)   | Severe<br>(Requiring high care/ICU)   |
|--|---|---|
| <ul style="list-style-type: none"><li>– Sputum culture not routine</li><li>– CRP or PCT (if available)<ul style="list-style-type: none"><li>○ Withhold antibiotics if negative</li></ul></li></ul> | <ul style="list-style-type: none"><li>– Sputum culture if frequent admissions or poor response to antibiotics</li><li>– CRP or PCT (if available)<ul style="list-style-type: none"><li>○ Withhold antibiotics if negative</li></ul></li></ul> | <ul style="list-style-type: none"><li>– Sputum culture</li><li>– Blood culture if pyrexial</li><li>– Nasopharyngeal swab for influenza PCR if in flu season</li></ul> |

## Diagnosis and management



### Prevention

- Annual influenza vaccine recommended for all patients with COPD
- Pneumococcal polysaccharide (PPSV23) vaccine is recommended for all individuals over 65 years of age and anyone with COPD
- Antiviral chemoprophylaxis is not recommended

### Pneumonia

## Definition

Pneumonia is acute infection of lung parenchyma distal to the terminal bronchiole and causes consolidation.

## Common aetiologies of community acquired or health care associated pneumonia

| CAP                    |   | HCAP   |
|------------------------|---|--|
| Agent                  | Comments  | Increased risk for infection with MDR pathogens<br><br>– Similar organisms to CAP <ul style="list-style-type: none"> <li>○ Uncommonly legionella or viruses</li> </ul> – Gram negative bacilli <ul style="list-style-type: none"> <li>○ <i>P. aeruginosa</i></li> <li>○ <i>A. baumannii</i></li> <li>○ Enterobacteriaceae</li> </ul> – <i>S. aureus</i> (including MRSA) |
| <i>S. pneumoniae</i>   | Most common cause   |  |
| <i>H. influenzae</i>   | More common in COPD   |  |
| Tuberculosis           | More common in HIV  |  |
| ‘Atypical organisms’   | Not cultured  |  |
| – <i>M. pneumoniae</i> | No specific clinical/radiological features  |  |
| – Chlamydia spp.       | Suspect if risk factors or non-response to beta-lactams                                     |  |
| Oral anaerobes         | Risk factors: alcoholism, aspiration, lung abscess  |  |
| <i>P. jirovecii</i>    | HIV, bilateral infiltrates, desaturation on minimal exertion, poor response to beta-lactams |  |
| Respiratory viruses    | Seasonal<br>Risk factors: pregnancy, elderly, co-morbidities                                |  |

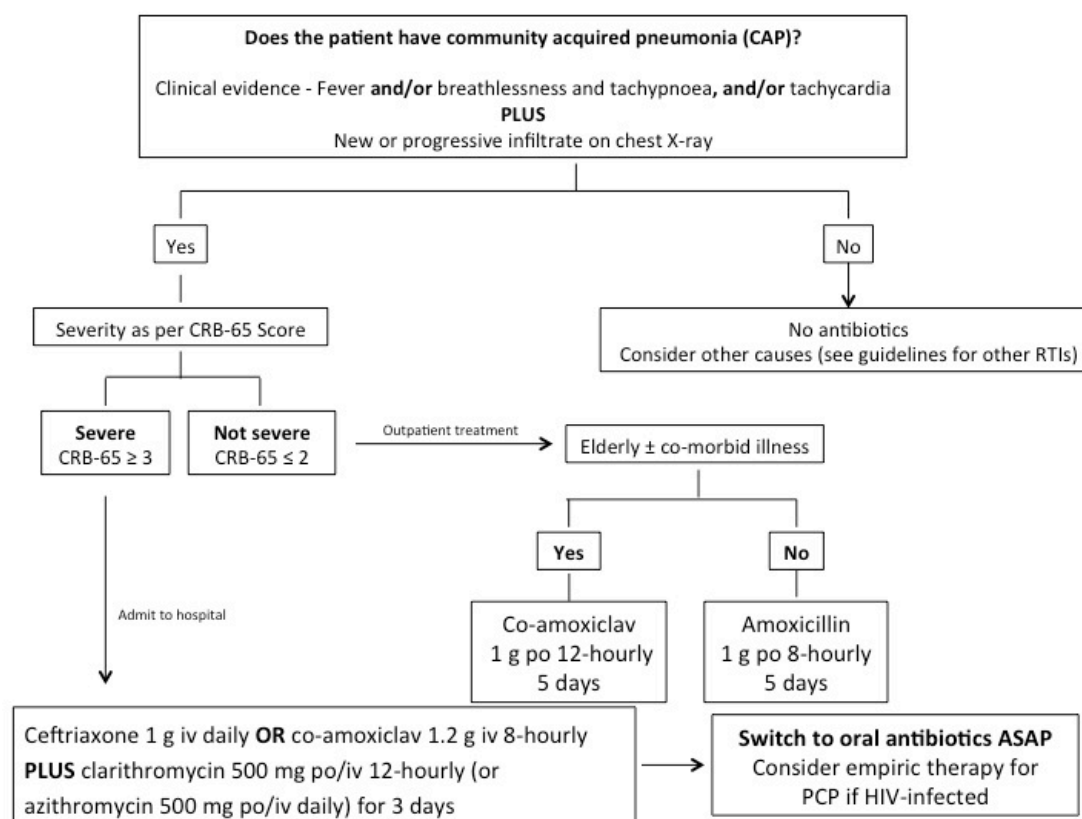
## Tests

| CAP   | HCAP   |
|---|--|
| <i>Only perform if likely to influence empiric management decisions</i><br><br>Mild (CRB-65 score $\leq 2$ ) <ul style="list-style-type: none"> <li>• Sputum culture and Xpert MTB/Rif if failed outpatient Abx therapy</li> </ul> Severe (CRB-65 $\geq 3$ ) or co-morbidities* <ul style="list-style-type: none"> <li>• Sputum Gram stain and culture</li> <li>• Blood culture</li> <li>• Sputum for <i>P. jirovecii</i> DFAT if HIV +ve</li> <li>• Urine Legionella antigen testing</li> <li>• NP swab for influenza PCR if flu season</li> </ul> | <i>Always send specimens prior to initiation of empiric antibiotics</i><br><br>In all cases <ul style="list-style-type: none"> <li>• Blood culture</li> <li>• Sputum Gram stain and culture</li> </ul> |

NP = Nasopharyngeal, DFAT = direct fluorescent antibody test

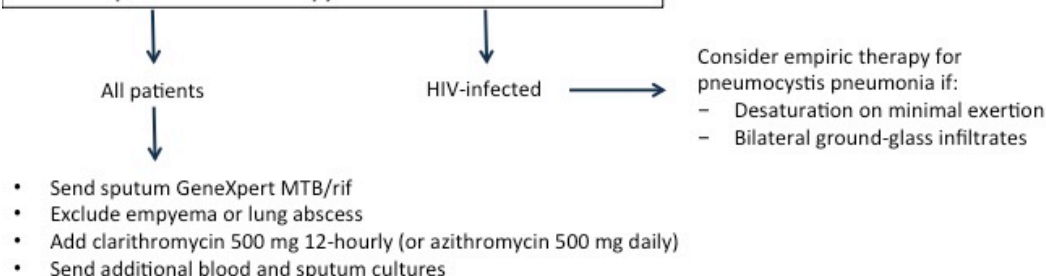
\* Chronic cardio-pulmonary disease, alcoholics, immune suppression (excluding HIV), CKD, cirrhosis

## Diagnosis and management



## Special circumstances

### 1. No response to initial therapy after 48 hours



### 2. Health care associated pneumonia

- Send blood and sputum cultures prior to initiating broad spectrum antibiotics
- Consult microbiologist or infectious diseases specialist about choice of appropriate empiric antibiotic

### 3. Penicillin allergy

- Moxifloxacin 400 mg po/iv daily or levofloxacin 500mg po 12-hourly (750mg iv 12-hourly in severe pneumonia)

## Chapter 9

# Intra-abdominal infection

### Definitions and causes

Infections in the abdomen can be divided into the following main groups:

1. Infections of the biliary system, including cholecystitis and cholangitis
2. Infections of the bowel, including appendicitis and diverticulitis
3. Intra-abdominal collections or abscesses
4. Peritonitis, including bowel perforations and spontaneous bacterial peritonitis (SBP) related to liver disease

### Common aetiologies

Empiric antibiotic therapy for community-acquired intra-abdominal infections should cover all of the following organisms:

- Enteric gram-negative bacilli: *E. coli*, *K. pneumoniae*
- Anaerobic organisms
- Enteric streptococci

Other possible causes in health care-associated infections or severely ill patients include:

- Enterococci
- Candida
- MRSA

### Tests

Most cases will require abdominal imaging (either ultrasound or CT), unless there is a clear indication for urgent laparotomy.

- Blood culture is recommended for patients with sepsis syndrome and suspected intra-abdominal infection.
- Culture of infected material is generally not helpful but is recommended in the following situations:
  - HCAI
  - SBP
  - Infections with incomplete source control (e.g. inability to clear liver abscess)
  - Re-do laparotomies

### Diagnosis and management

#### 1. Spontaneous bacterial peritonitis

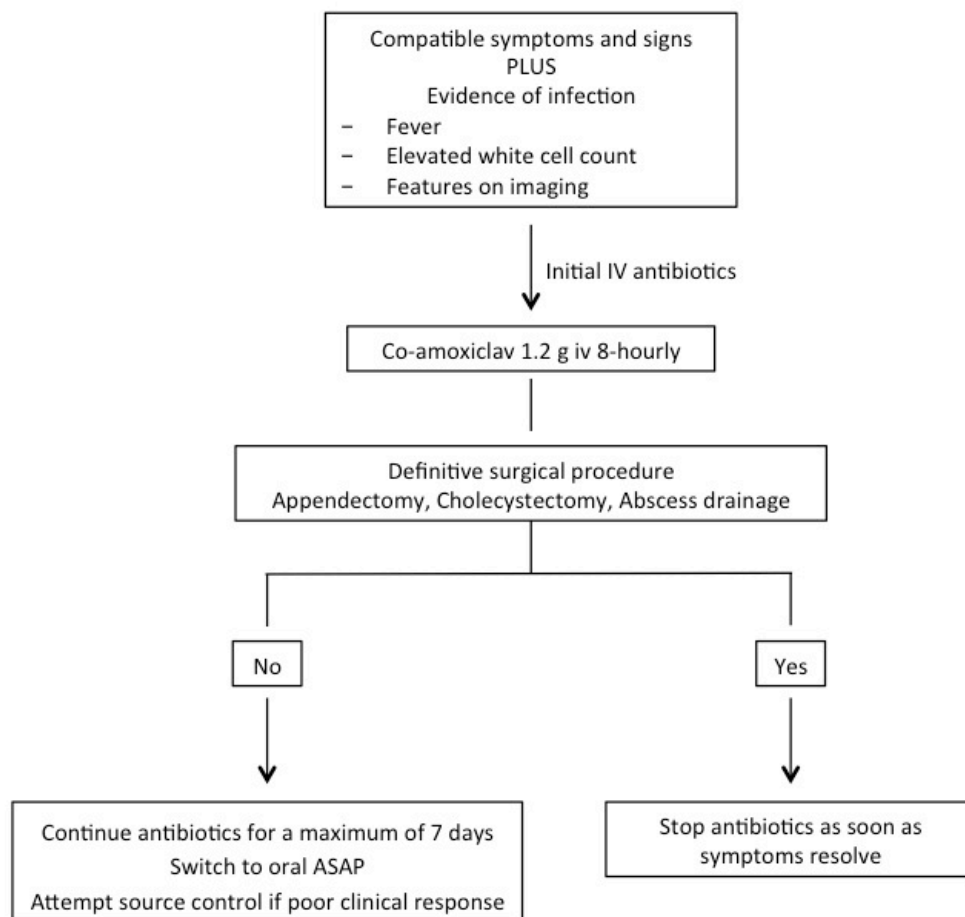
Diagnosis:

- Ascitic fluid aspirate with WCC > 250 cells/mm<sup>3</sup>
- Positive ascitic fluid culture (low sensitivity; high specificity if sample taken properly)

Management:

- Ceftriaxone 1 g IV daily for 5 days
- Add ampicillin 1 g QID in the following situations only:
  - Cholestatic liver disease
  - Fulminant liver failure (encephalopathy with coma)
  - Not responding to ceftriaxone after 48 hours

## 2. Most other intra-abdominal infections



### Alternative antibiotic regimens

- Co-amoxiclav unavailable:
  - Ampicillin 1 g iv 6 hourly PLUS gentamicin 6 mg/kg/day PLUS metronidazole 500 mg iv 8-HOURLY
  - OR
  - Ceftriaxone 1 g daily PLUS metronidazole 500 mg 8-hourly
- Severe Penicillin allergy:
  - Ciprofloxacin 400 mg iv 8-hourly PLUS metronidazole 500 mg iv 8-hourly

# Chapter 10

## Acute diarrhoea

### Definition

Diarrhoea for < 2 weeks duration

### Likely pathogens-

- Viruses (norovirus, rotavirus, adenoviruses, astrovirus),
- Bacteria (Salmonella, Campylobacter, Shigella, Enterotoxigenic *E. coli*, *C. difficile*) and bacterial toxins
- Protozoa (Cryptosporidium, Giardia, Cyclospora, Entamoeba)

### Clinical features

- Stool taking the shape of its container > 3 times per day
- Blood in stool
- Fever

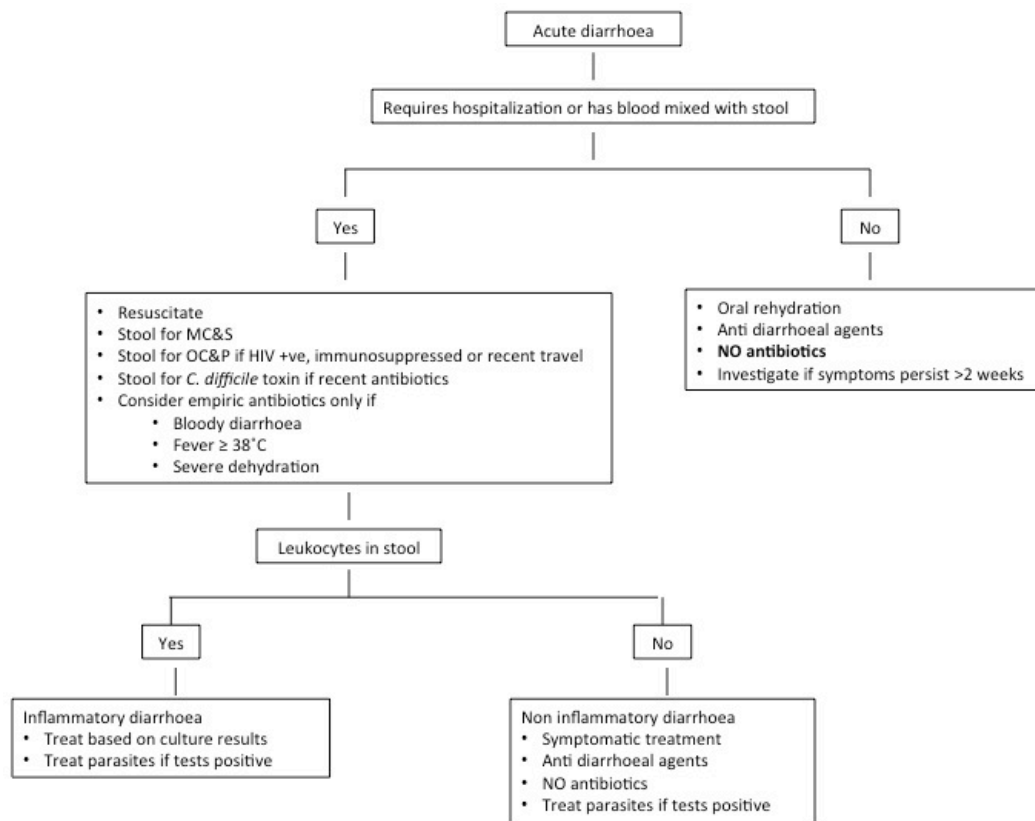
### History

- Food exposure
- Illness among close contacts
- Recent travel
- HIV status
- Recent antibiotics

### Tests (see algorithm)

The vast majority of episodes of diarrhoea DO NOT require antibiotics. Mild cases are usually self-limiting and require symptomatic treatment only. Moderate to severe cases require investigation +/- hospitalisation.

### Diagnosis and management

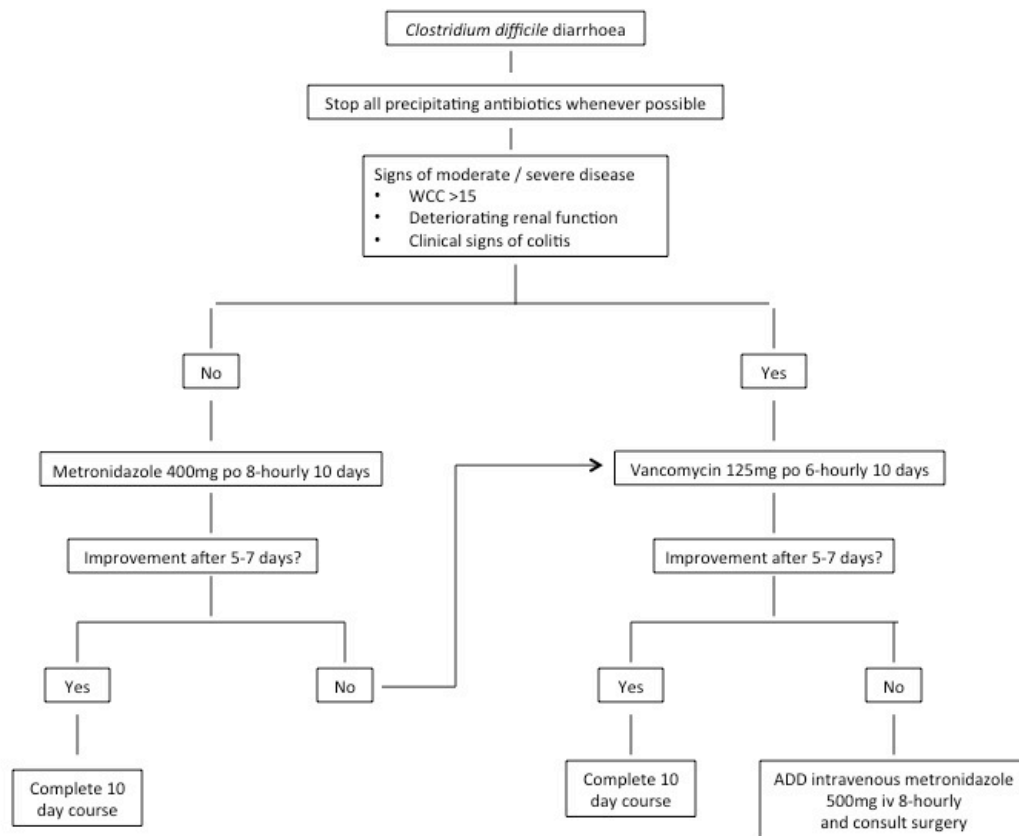


## Treatments

- Empiric:
  - Ciprofloxacin 500 mg po 12-hourly for 3 days pending results of culture and sensitivity
  - If bloody diarrhoea add empiric metronidazole 500 mg iv 8-hourly (or 400 mg po 8-hourly) for 5 days
- Definitive:
  - Based on culture results
- *Clostridium difficile* toxin or molecular test positive:
  - See algorithm
  - Resolution of symptoms generally occurs within 5-7 days, but it is not unusual for symptoms to persist for the first 3-5 days
  - 25% of patients with *C. difficile* will relapse



## Management of *C. difficile* diarrhoea



# Chapter 11

## Urinary tract infections

### Uncomplicated UTI

#### Definition

'Uncomplicated' refers to either a lower urinary tract infection or upper urinary tract infection (pyelonephritis) in non-pregnant women with structurally and neurologically normal genitourinary tracts. Acute uncomplicated cystitis is defined as:

- Symptomatic bladder infection characterised by a clinical syndrome of frequency, urgency, dysuria or suprapubic pain

#### Common aetiologies

| Pathogens   | Common contaminants of urine cultures  |
|---|--|
| <ul style="list-style-type: none"><li>• Enterobacteriaceae<ul style="list-style-type: none"><li>– <i>E. coli</i> (most common)</li><li>– <i>K. pneumoniae</i></li><li>– <i>Enterobacter</i> spp.</li><li>– <i>Proteus</i> spp.</li></ul></li><li>• Coagulase negative staphylococci<ul style="list-style-type: none"><li>– <i>S. saprophyticus</i></li></ul></li><li>• Group B streptococcus</li><li>• <i>Enterococcus</i> spp.</li></ul> | <ul style="list-style-type: none"><li>• <i>Candida</i> species</li><li>• <i>Enterococcus</i> spp.</li><li>• <i>Gardnerella vaginalis</i></li><li>• <i>Mycoplasma hominus</i></li><li>• <i>Ureaplasma urealyticum</i></li></ul> |

#### Tests

- Urine culture only for:
  - Reinfection, persistent or recurrent cystitis
  - Symptoms with negative dipstick
- Do not perform follow-up cultures if symptoms have resolved
- Do not perform screening cultures in asymptomatic diabetics, elderly or patients with indwelling urinary catheters

#### Diagnosis and management

The diagnosis of urinary tract infection requires the presence of compatible symptoms plus bacteriuria (bacteria in the urine) or indirect evidence of infection, such as:

- Urine dipstick leucocyte esterase or nitrite positive
- Urine microscopy showing > 1+ leucocytes

Asymptomatic bacteriuria (a positive urine culture from patients without symptoms referable to the urinary tract) should not be treated, except in pregnant women and prior to invasive urological procedures.



## Complicated UTI

### Definitions

A *symptomatic* urinary tract infection in:

- Individuals with functional or structural abnormalities of the genitourinary tract
- Men
- Pregnant women
- Patients with indwelling urinary catheters

### Common infectious aetiologies

Caused by the same pathogens as uncomplicated UTIs. Infections in patients with indwelling urinary catheters more likely to be caused by drug resistant organisms.

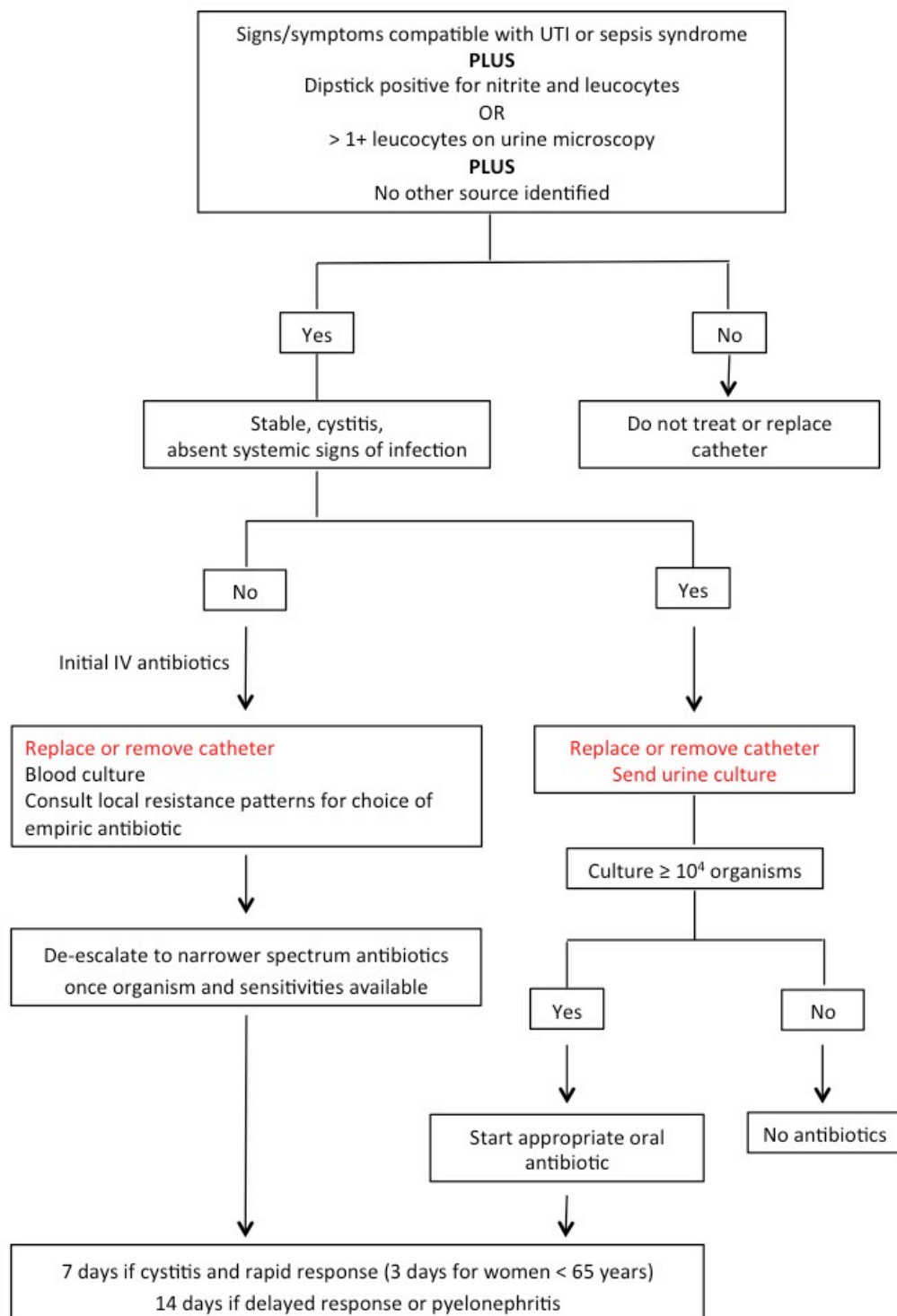
### Tests

Perform urine cultures in all of the above patient groups presenting with symptoms of UTI. In catheterised patients urine specimens should be obtained after catheter removal from a freshly placed catheter or voided midstream sample.

If fever/symptoms persist > 48 hours:

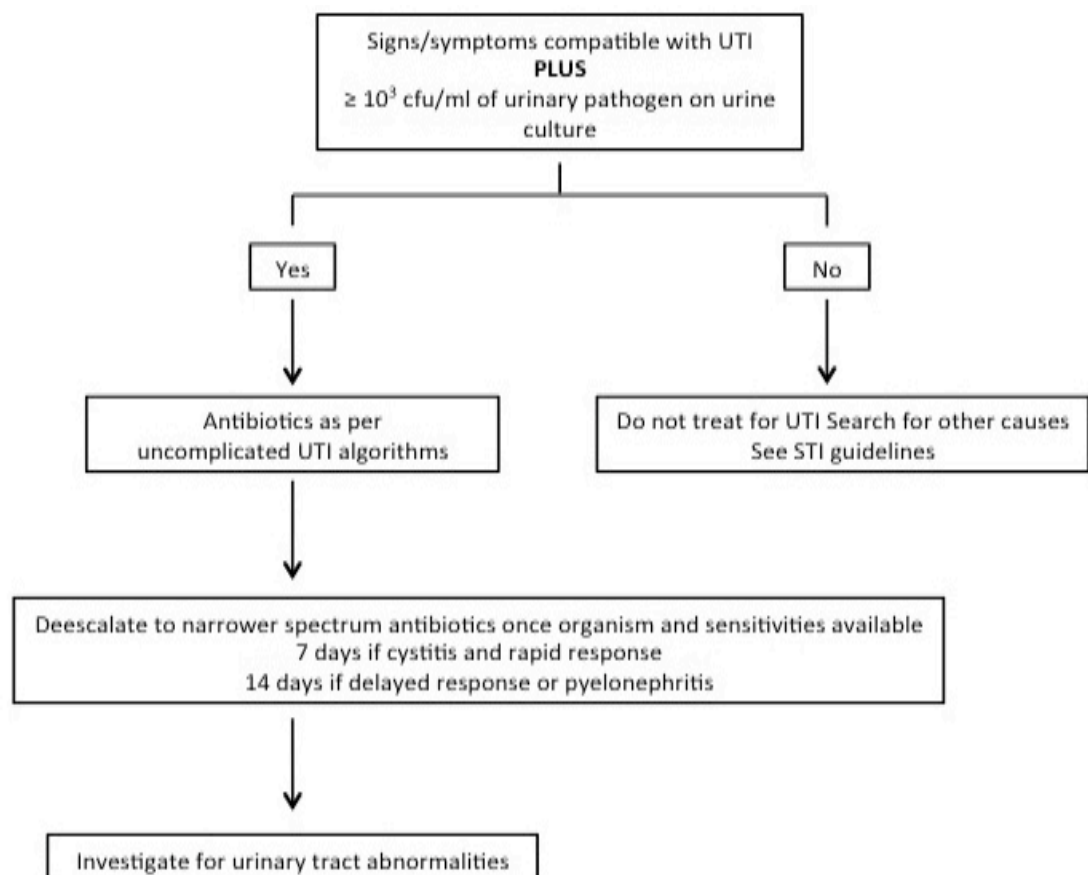
- Perform blood culture (in case of resistant bacteria)
- Image the urinary tract and abdomen to exclude collections

## Catheter-associated UTI



NB: non-specific signs of CA-UTI include fever or rigors, altered mental state and unexplained lethargy

## UTI in men



## UTI in pregnancy

### i. Asymptomatic bacteriuria

Pregnant women with asymptomatic bacteriuria are at increased risk of developing pyelonephritis. Therefore all pregnant women should be screened for bacteriuria.

#### Diagnosis:

- Any culture showing ≥ 10<sup>3</sup> cfu/ml of a single organism (or any *E. coli*) in an asymptomatic pregnant woman

#### Management:

- Appropriate oral antibiotic for 5 days (see below)
- Perform follow-up urine culture to confirm sterility

### ii. Cystitis and pyelonephritis

#### Diagnosis:

- As per uncomplicated UTI guidelines

- Always send urine culture

Management:

Ciprofloxacin is contraindicated in pregnancy. Therefore the following empiric antibiotics should be used, with de-escalation to narrower spectrum antibiotics once organism and sensitivities available:

- Cystitis or mild pyelonephritis:
  - Coamoxiclav 1 g po 12-hourly before the 3<sup>rd</sup> trimester. Cefuroxime 250 mg po 8-hourly is preferred in the 3<sup>rd</sup> trimester due to decreased risk of necrotizing enterocolitis
  - Duration 5 days for cystitis, 14 days for pyelonephritis
- Severe pyelonephritis
  - Treat as per uncomplicated UTI guidelines

## Chapter 12

# Sexually transmitted infections

### Vaginal discharge

#### Definitions

Vaginal and occasionally cervical infection characterised by discharge, itching or odour.

#### Common aetiologies

- Bacterial vaginosis (BV): replacement of normal flora by polymicrobial overgrowth
- Trichomoniasis: *T. vaginalis*
- Candidiasis: *Candida albicans*
- Cervicitis: *C. trachomatis* and *N. gonorrhoeae*

#### Tests

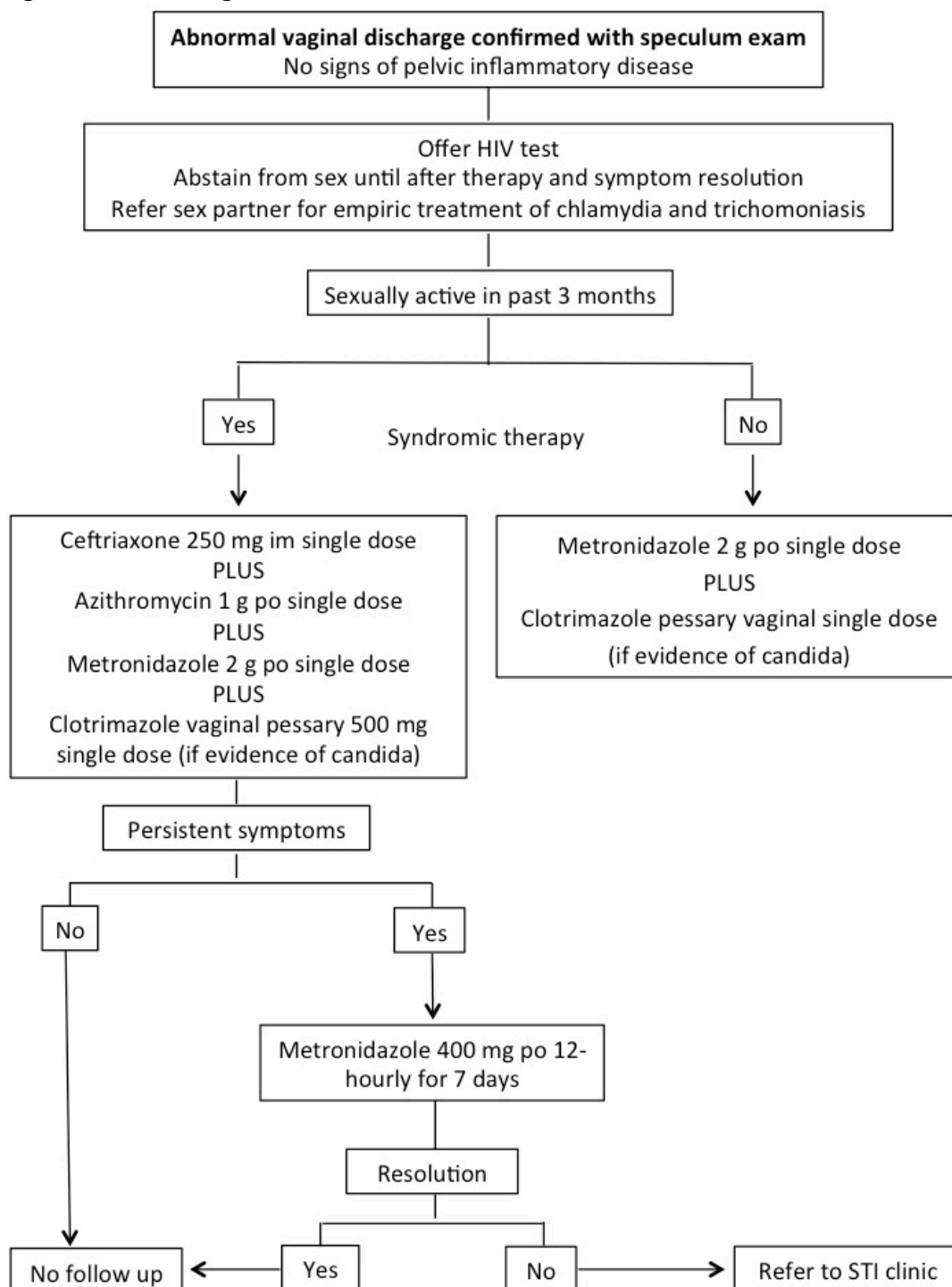
No tests are necessary to confirm specific causes at the initial presentation.

For recurrent or persistent symptoms, attempt to confirm diagnosis by office tests:

- Bacterial vaginosis
  - Clue cells on microscopy
  - pH of vaginal fluid > 4.5
  - Whiff test: fishy odour after addition of KOH to vaginal fluid
- Trichomoniasis
  - Wet prep slide to visualise motile organisms (sensitivity 70%)
- Candidiasis
  - Wet prep slide with KOH demonstrating yeasts and pseudohyphae



## Diagnosis and management



### Penicillin allergy (severe)

Omit ceftriaxone and increase azithromycin: 2 g po single dose

## Urethritis

### Definition

Urethral inflammation from infectious and non-infectious causes

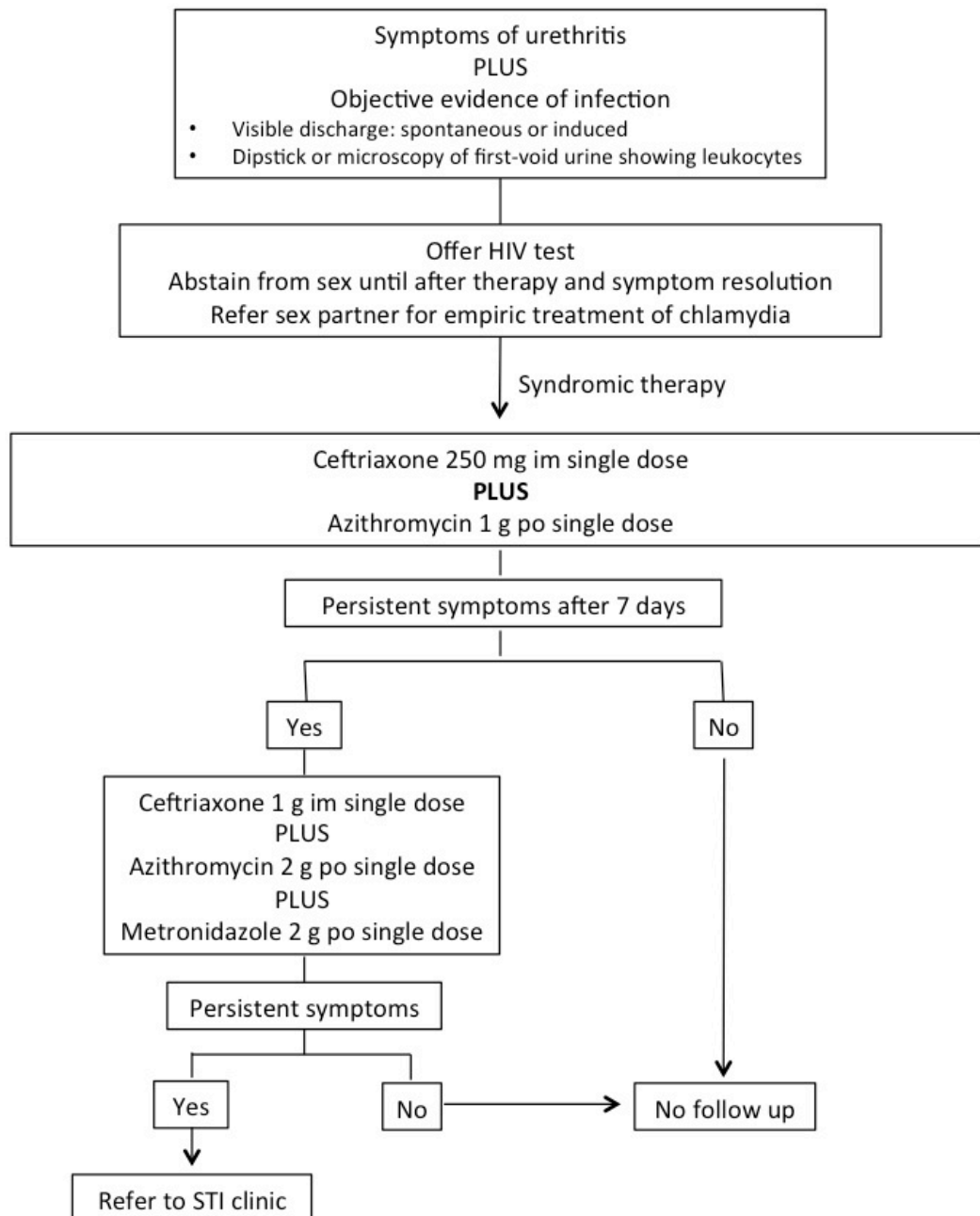
### Common aetiologies

- Gonococcal urethritis (*N. gonorrhoeae*)
- Non-gonococcal urethritis (NGU)
  - Chlamydia (*C. trachomatis*)
- Non-chlamydial NGU: usually no pathogen found

### Tests

Usually requires no special investigations.

### Diagnosis and management



## Genital ulcer syndrome (GUS)

### Definition

New genital, anal or perianal lesion after recent sexual activity.

### Common aetiologies

#### *Sexually transmitted*

- HSV and syphilis most common
- *H. ducreyi* (chancroid)
- *C. trachomatis* (LGV)

#### *Non-sexually transmitted*

- Infectious: folliculitis, candida, tuberculosis
- Non-infectious: trauma, malignancy, eczema, psoriasis, contact dermatitis (latex allergy), aphthous ulcers

## Diagnosis

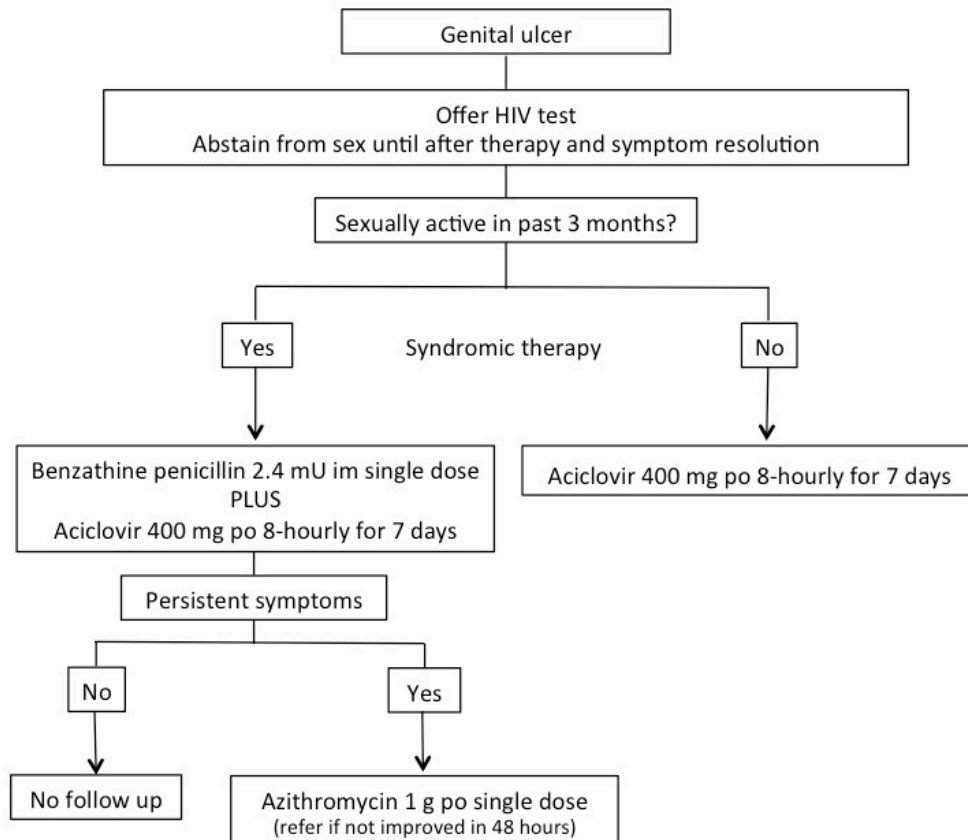
It is not possible to distinguish the causes on clinical grounds alone. Do not diagnose a venereal cause of GUS if no sexual activity in the past 3 months (except for reactivated HSV).

|                 |   |
|-----------------|---|
| Recurrent       | Herpes simplex reactivation                                     |
| Painless        | Primary syphilis<br>Lymphogranuloma venereum (LGV)              |
| Painful         | Herpes simplex (HSV)<br>Chancroid                               |
| Lymphadenopathy | Syphilis<br>HSV<br>LGV (massive, often unilateral)<br>Chancroid |

## Tests

Usually requires no investigations.

## Management



# Chapter 13

## Acute meningitis

### Definition

- Acute inflammation of the meninges of <7 days duration.

### Likely pathogens

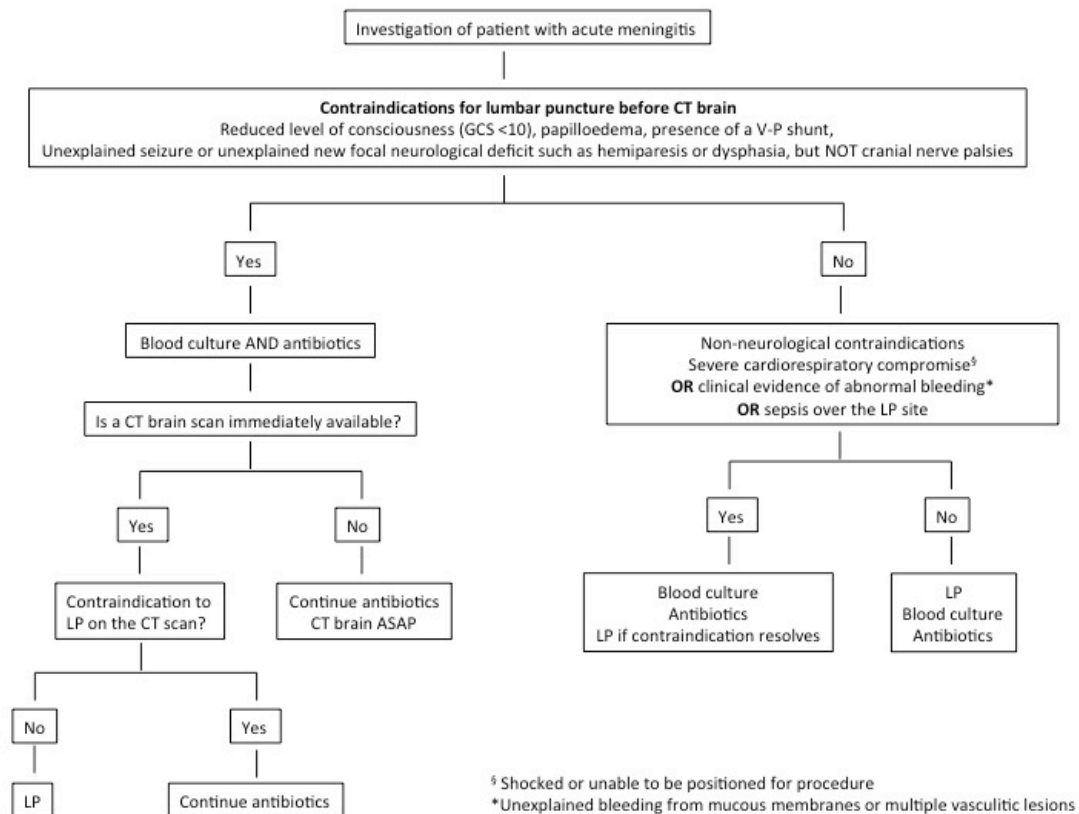
- Common – Various bacteria, viruses. TB meningitis can present acutely. Rare - fungi, protozoa and helminths
- Common bacterial pathogens are *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae* and *Listeria monocytogenes* (in immunocompromised and elderly patients).

### Clinical features

- Any 2 of the 4 cardinal features; headache, fever > 37.5°C, neck stiffness and altered mental status
- Supporting features are photophobia, blanching or purpuric rash and vomiting

### Tests

- See algorithm for lumbar puncture and CT brain



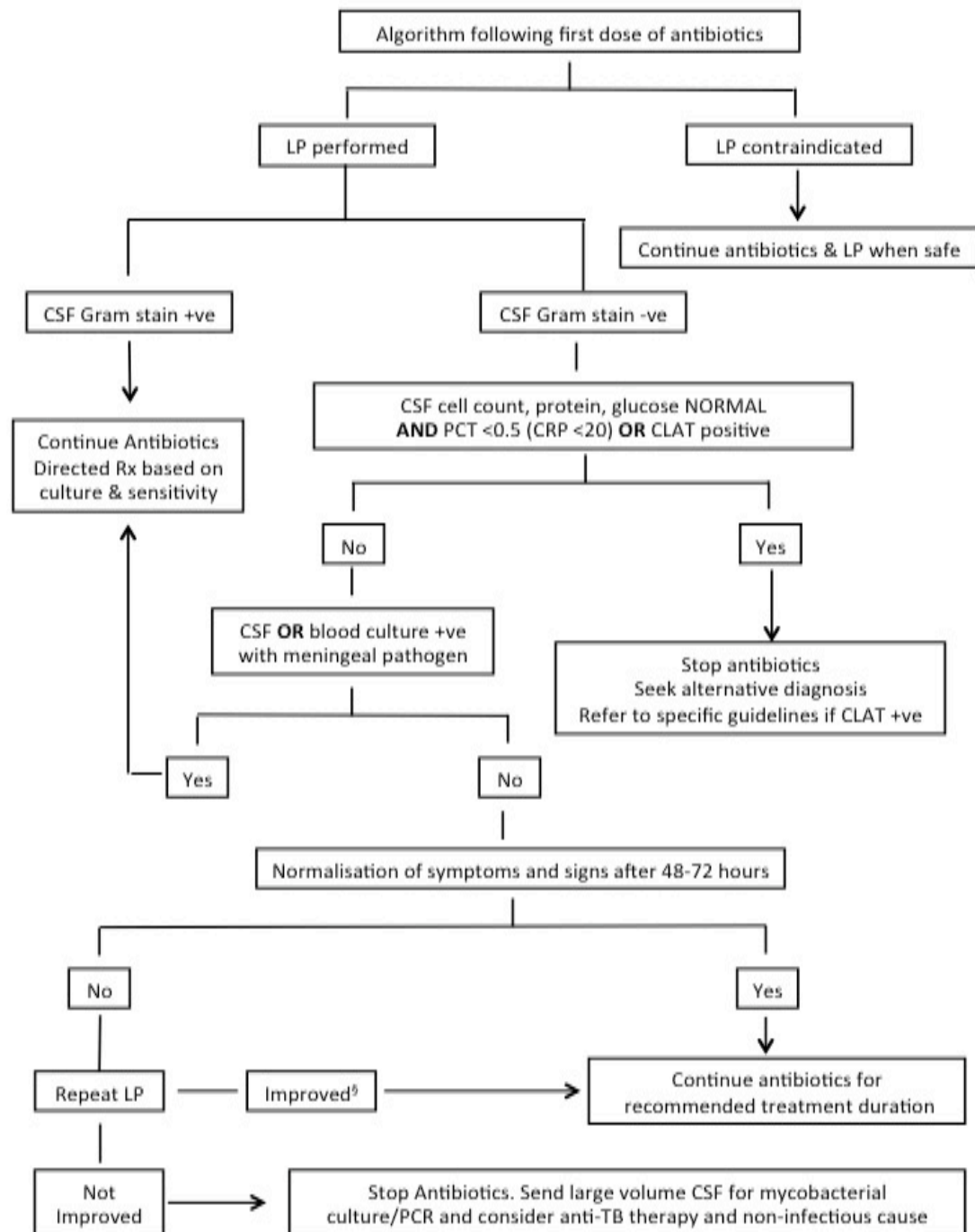
## Management

### General principles:

- Patients with suspected bacterial meningitis should receive ceftriaxone 2 g iv immediately. The dose for continued treatment is 2 g iv 12-hourly
- Penicillin allergy is not a contra-indication to use of ceftriaxone, unless the allergy was life threatening
- Blood culture and lumbar puncture should be performed before administration of antibiotics ONLY if this does not cause significant delay
- If bacterial meningitis is strongly suspected on the basis of clinical and CSF findings and all cultures are negative give ceftriaxone for 10 days
- Steroids are not recommended

### Specific therapy:

- *S pneumoniae*: duration 10 days
  - If MIC unknown or > 0.1 microg/ml: ceftriaxone 2 g iv 12-hourly
  - If MIC < 0.1 microg/ml: penicilin G 4 mU ivi 4-hourly or ampicillin 2 g iv 4-hourly
- *N meningitidis*: duration 7 days
  - Ceftriaxone 2 g iv 12-hourly
- *L monocytogenes*: duration 21 days
  - Ampicillin 2 g iv 4-hourly
- Gram-negative infection: duration 21 days
  - Community-acquired: cefepime 2 g iv 8-hourly or ceftazidime 2 g iv 8-hourly
  - Health care associated: meropenem 2 g iv 8-hourly



<sup>§</sup>Opening pressure, protein, total WCC and % neutrophils reduced. % lymphocytes & CSF/serum glucose increased

## Chapter 14

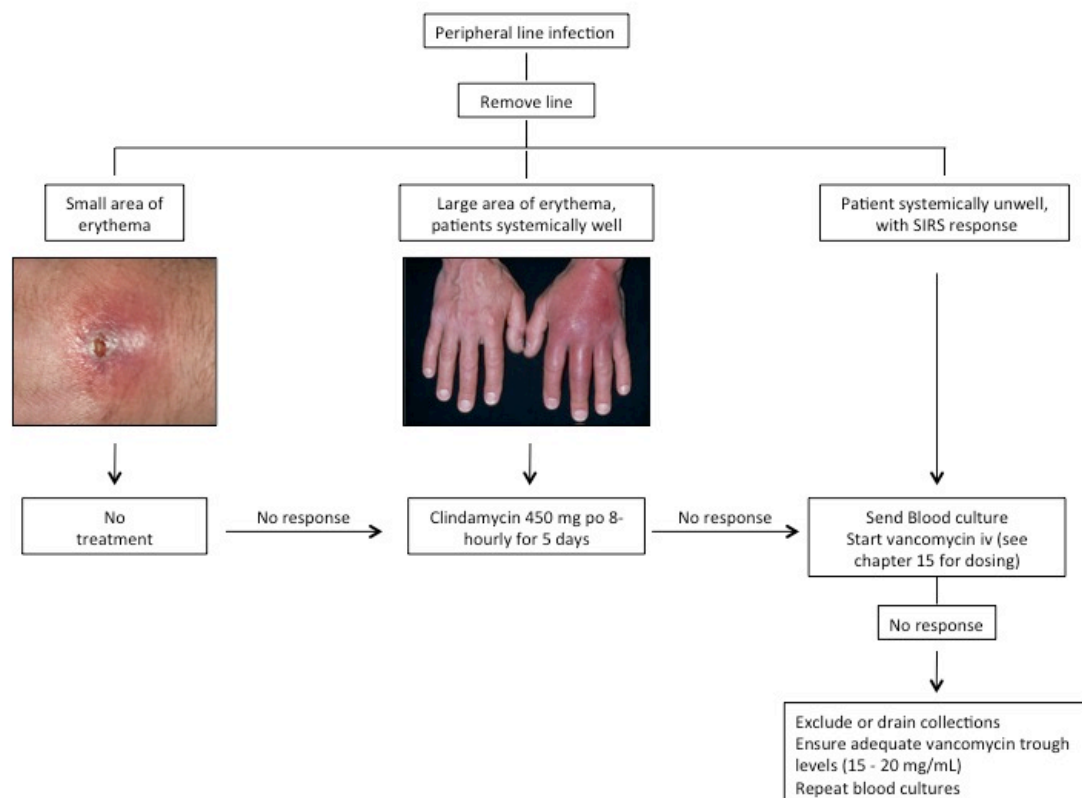
### Peripheral line sepsis

Peripheral line-related infections increase morbidity, mortality, antibiotic usage and length of stay. PREVENTION BY EARLY REMOVAL OF LINES IS THE KEY INTERVENTION. By definition these are healthcare associated infections (HCAI) with a high risk of resistant pathogens.

#### Likely pathogens

*Staphylococcus aureus* (MSSA/MRSA), Coagulase negative staphylococci, *Streptococcus* spp.

#### Diagnosis and management





## Chapter 15

### ***Staphylococcus aureus* bacteraemia**

*Staphylococcus aureus* (*S. aureus*) bloodstream infection carries a high mortality rate. It is commonly introduced by vascular line infections or other health-care associated interventions, but can result from invasive *S. aureus* at any site. *S. aureus* bacteraemia can disseminate to any organ including heart valves, bone and lungs, and therefore requires prolonged intravenous therapy with higher doses of appropriate antibiotics.

#### **Definitions and dosing**

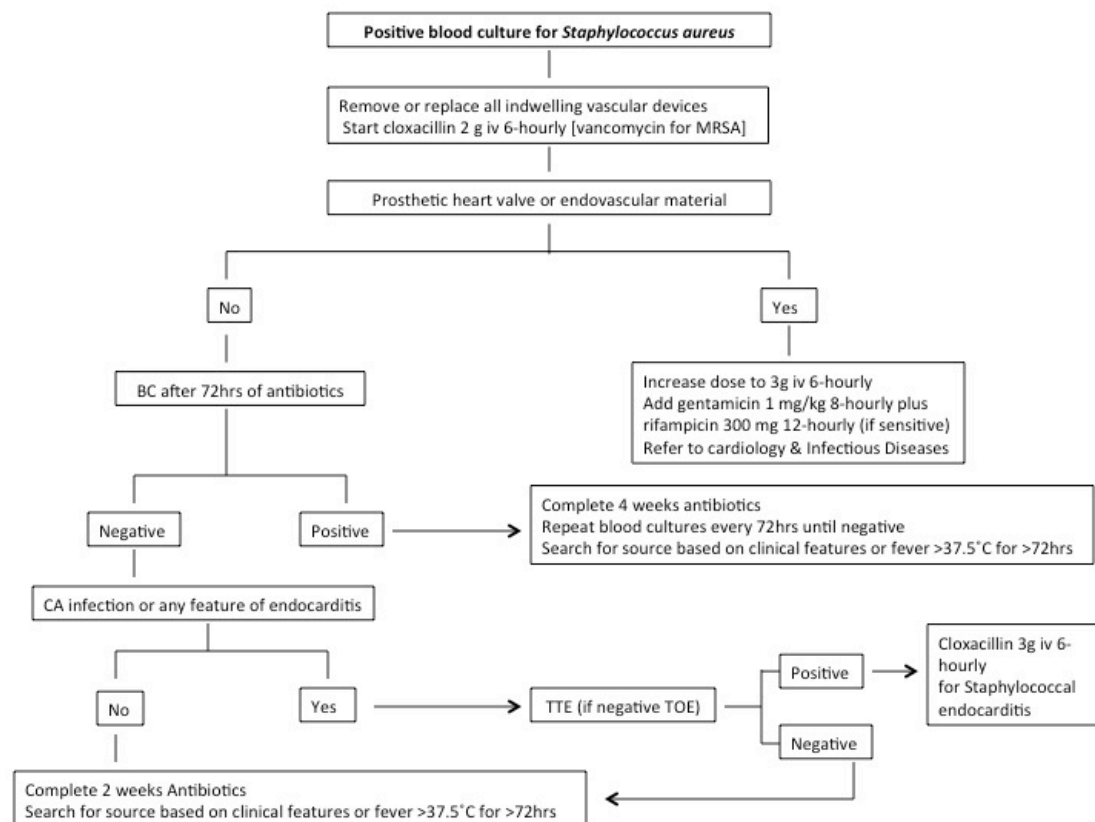
Methicillin sensitive *S. aureus* (MSSA)

- Sensitive to anti-staphylococcal beta-lactam antibiotics
- Cloxacillin is the treatment of choice:
  - Initial dose 2 g 6 hourly IV
  - Use 3 g 6 hourly for endocarditis, prosthetic heart valves or other endovascular material, meningitis and osteomyelitis

Methicillin resistant *S. aureus* (MRSA)

- Resistant to beta-lactam antibiotics
- Vancomycin is the treatment of choice:
  - Loading dose 25 – 30 mg/kg slow infusion
  - Thereafter 15-20 mg/kg BD (will require lower doses and/or less frequent intervals in renal impairment)
  - Measure trough levels before the 4<sup>th</sup> dose and aim for a target of 15 – 20 mg/L

## Management



Clinical features of complicated *S. aureus* bacteraemia include persistent fever, bone pain, new murmur or peripheral manifestations of endocarditis or focal neurological signs. Patients with these problems require directed investigations for source control and should be discussed with an infectious diseases specialist.

# Chapter 16

## Skin and soft tissue infections

### Cellulitis

#### Definition

Acute infection involving skin and subcutaneous tissue

- Commonly precipitated by minor trauma or underlying skin lesion

**Diagnosis** (Image: <http://treatmentofcellulitis.net>)

Clinical only:

- Redness, tenderness, local heat, non-raised edges

Differentiate from:

| Infections            | Non-infectious      |
|-----------------------|---------------------|
| Erysipelas            | DVT                 |
| Necrotising fasciitis | Insect bites        |
| Gas gangrene          | Fixed drug reaction |

#### Common aetiologies

- *Streptococci* (usually *S. pyogenes*)
- *S. aureus*

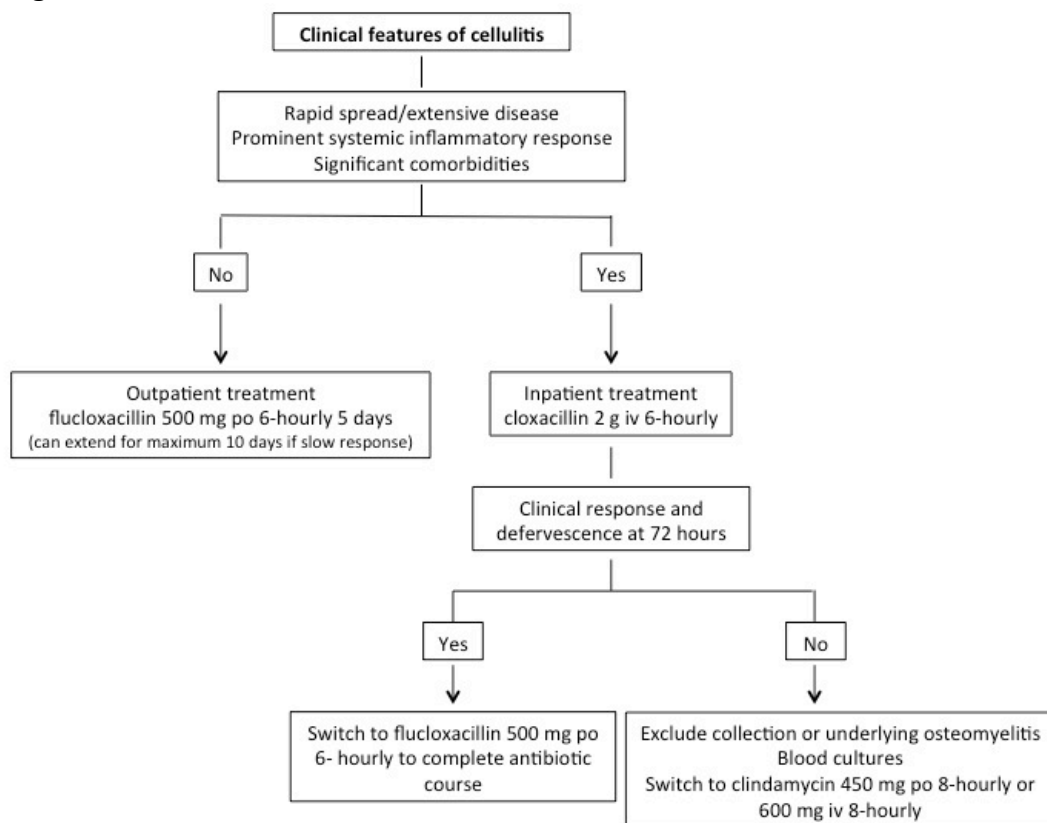
#### Tests

None recommended

- Blood cultures are rarely positive and not generally helpful unless extensive or severe infection.
- Superficial pus swabs are not helpful and should NOT be performed



## Management



## Cutaneous abscess

### Definition

Deep inflammatory nodule extending into subcutaneous tissue that develops from preceding folliculitis

### Common aetiologies

*S. aureus*

### Tests

None

### Management

All cases require surgical drainage.

#### *Uncomplicated cases*

- No antibiotics required

#### *Complicated cases* (surrounding cellulitis, located on face, systemic symptoms)

- Flucloxacillin 500 mg po 6-hourly for 5 days or co-amoxiclav 1g po 12-hourly
- In penicillin allergy use clindamycin 450 mg po 8 hourly

## Diabetic foot

### Definition

Chronic foot infections in diabetics

- Mild: limited to skin/superficial subcutaneous tissue < 2 cm beyond ulcer margin
- Moderate: cellulitis > 2 cm, deep fascial involvement, gangrene, abscess, osteomyelitis
- Severe: systemic complications

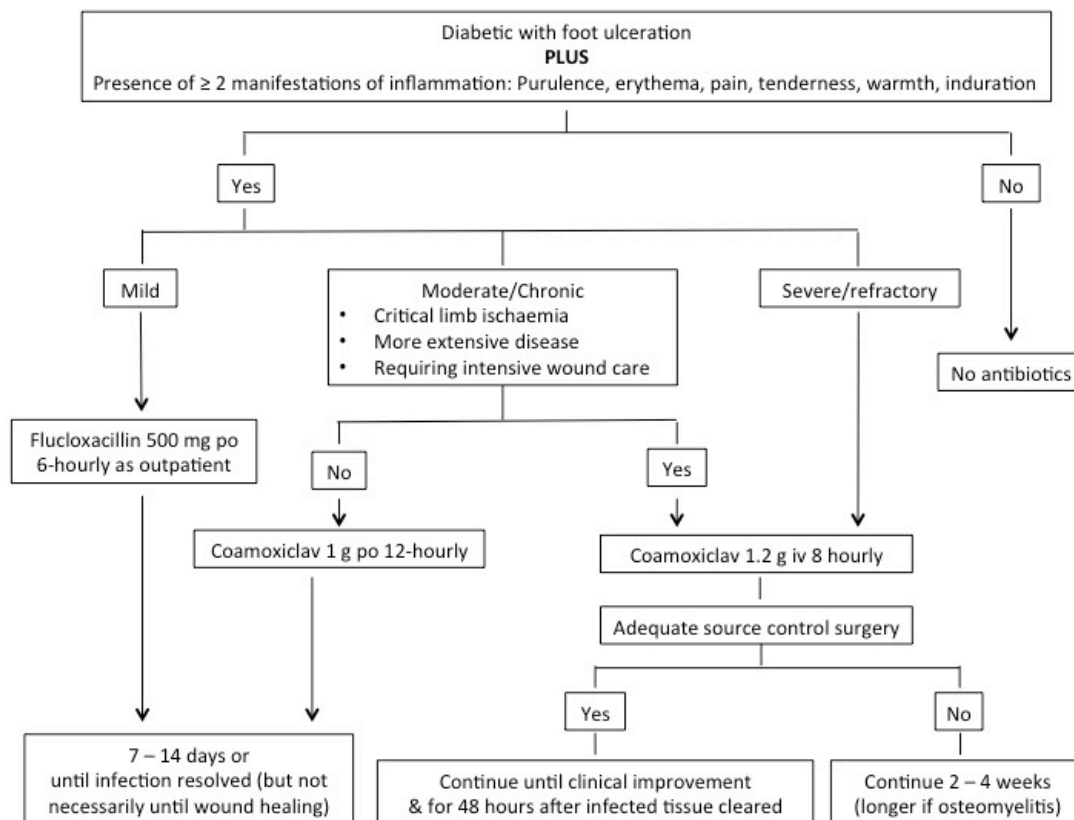
### Common aetiologies

- Mild infections or previously untreated
  - *S. aureus*
  - *Streptococci*
- Chronic lesions or previously treated
  - Above plus
  - Enterobacteriaceae
- Chronic, refractory or prolonged broad spectrum antibiotics
  - Above plus
  - Pseudomonas
  - Anaerobes
  - Enterococci

### Tests

None required in mild or previously untreated infections. Tissue cultures are recommended in all other scenarios. It is essential to clean and debride the lesion before obtaining specimens for culture. Blood cultures should be performed in severe infections.

## Diagnosis and management



### Penicillin allergy:

- *Mild/moderate infections:*  
Clindamycin 450 mg po 8-hourly (add ciprofloxacin 500mg po 12-hourly if requires admission)
- *Severe infections:*  
Clindamycin 600 mg iv 8-hourly PLUS ciprofloxacin 400 mg iv 8-hourly

### Wound management

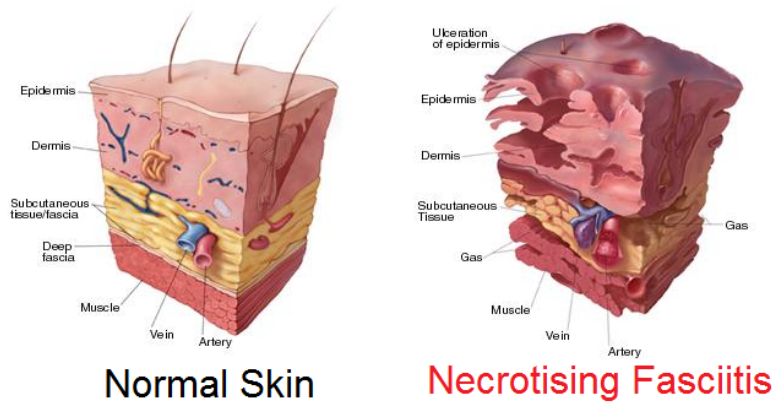
Optimal wound care is essential. Surgical consultation is recommended for the following problems:

- Deep abscess
- Bone or joint involvement
- Crepitus
- Gangrene
- Necrotising fasciitis
- Severe vascular insufficiency

## Necrotising fasciitis

**Definition** (image: <http://medicatoz.com/news/view?id=57>)

Acute severe infection involving subcutaneous soft tissues including the fascial layers. Usually precipitated by trauma, surgery, peri-rectal abscess, bedsores or bowel perforation.



### Common aetiologies

Usually polymicrobial infections:

- *Streptococci*
- Enterobacteriaceae
- Anaerobes

### Tests

Blood cultures and surgical tissue specimens.

### Diagnosis and management

Necrotising fasciitis is commonly associated with systemic toxicity manifested by fever, leukocytosis and possibly organ dysfunction. It rapidly progresses to cutaneous gangrene. Management involves the following:

1. Early and aggressive surgical debridement
2. Co-amoxiclav 1.2 g IV continued until clinical resolution

### Alternative antibiotic regimens

- If co-amoxiclav unavailable: ampicillin 1 g 6-hourly PLUS metronidazole 500 mg 8-hourly PLUS gentamicin 6 mg/kg/day, all iv
- For refractory infections and in penicillin allergy: clindamycin 600 mg 8-hourly PLUS ciprofloxacin 400 mg 8-hourly, both iv

# Chapter 17

## Bone and joint infections

### SEPTIC ARTHRITIS

#### Definition

Bacterial joint infection, usually due to haematogenous spread.

#### Common aetiologies

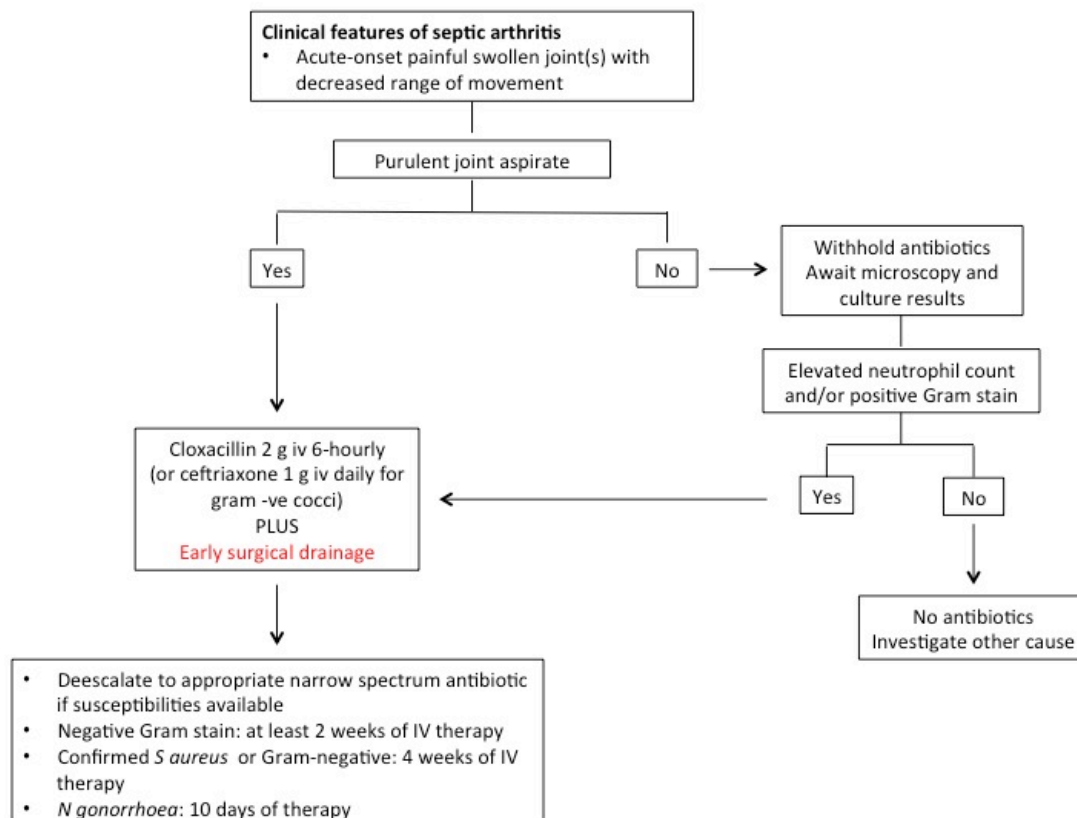
- Non-gonococcal
  - *S aureus* most common
  - *Streptococcus* spp. (*S pyogenes*, *S pneumoniae*, *S agalactiae*)
  - Gram-negative organisms (elderly, immunocompromised, comorbidities)
- *N gonorrhoeae*

#### Tests

In all cases:

- Joint aspirate BEFORE ANTIBIOTICS
  - Cell count plus differential: high neutrophil count in most cases
  - Gram stain and culture
  - Microscopy for crystals
- Plain X-ray

#### Diagnosis and management





## OSTEOMYELITIS

### Definition

Bacterial infection of bone due to contiguous spread from soft tissues, haematogenous seeding, or direct inoculation.

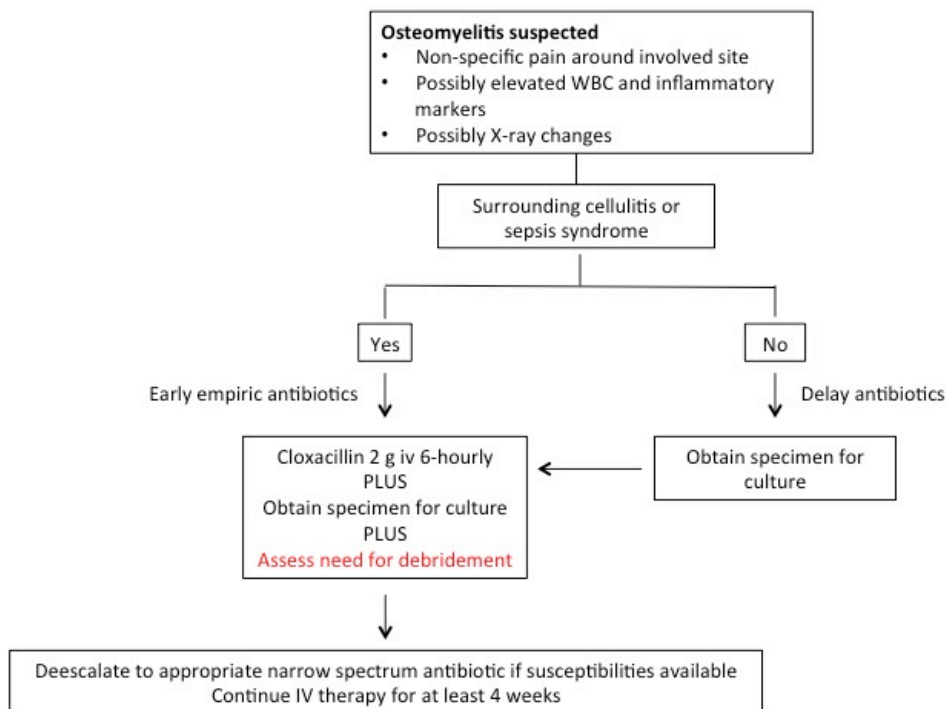
### Common aetiologies

- Common
  - *S aureus*
  - Coagulase-negative staphylococci
- Occasional
  - Streptococci
  - Enterococci
  - Gram-negative bacilli
- Other
  - *M tuberculosis*
  - Fungal infections

### Tests

- Always send specimens for culture
  - Deep tissue specimen: open surgical procedure or guided needle aspiration
  - Blood culture
- Imaging
  - Plain X-ray in all cases
  - May require other modalities such as bone scan, CT or MRI
- CRP may be useful to monitor response to therapy

### Diagnosis and management



#### Notes:

- May need to continue IV therapy for 6 weeks or longer
- Do not add rifampicin in cases without foreign material
- Consider tuberculosis if culture-negative or no clinical improvement
- Vancomycin is used for health care-associated osteomyelitis or confirmed MRSA (loading dose 23 – 30 mg/kg followed by 15 – 20 mg/kg 12-hourly; maintain trough levels 15 – 20 mg/mL)
- See Chapter 18 for management of open fractures
- Infections associated with prosthetic material should be discussed with an expert

## Chapter 18

### Prophylaxis

#### Surgery

Surgical prophylaxis aims to prevent infection following a predictable exposure to bacteria. Antibiotics are only required **during** exposure and a single dose taken pre-operatively is usually sufficient. A repeat dose should only be given if surgery is prolonged or there is massive blood loss. Choice of antibiotic depends on which bacteria are likely to be introduced by the operation, usually normal colonisers of skin or bowel. Examples are given below but refer to local policies for guidance.

| Type of surgery   | Prophylaxis  |
|---|--|
| Cardiothoracic<br>Upper GI<br>Neurosurgery<br>Orthopaedic (elective non-trauma) | Cefazolin 2g iv  |
| Lower limb amputation<br>Colorectal<br>Biliary<br>Pelvic<br>ENT                 | Cefazolin 2g iv<br>Plus<br>Metronidazole 500mg iv  |
| Ophthalmic  | Chloramphenicol 0.5% drops   |
| ERCP with obstruction   | Ciprofloxacin 500mg po 2h prior to the procedure or cefuroxime 1.5g iv or PIP/TZ 4.5g iv, both 1h prior to the procedure |
| Surgery for the implantation of any permanent prosthetic material               | Cefazolin 2g iv or cefuroxime 1.5g iv or vancomycin 1g iv as single dose   |
| Penetrating abdominal trauma or open fracture                                   | Cefazolin 2g iv + metronidazole 500mg IV and second dose if procedure > 3h   |

#### Head injuries

Closed head injuries with non-penetrating wounds **do not** require antibiotic prophylaxis even if there is a CSF leak. Compound depressed skull fractures and penetrating spinal cord injuries do require prophylaxis/pre-emptive treatment e.g. ceftriaxone plus metronidazole for 5 days.

#### Open long bone fractures

If early (< 5 hours) washout and debridement, provide prophylaxis with cefazolin 1g iv 12-hourly for 48 hours only. If long delay to washout or significant contamination, treat with coamoxiclav 1.2 g ivi 12-hourly for 5 days.

#### Infective endocarditis

The evidence base is weak and guidelines are largely based on expert opinion, which differs between countries and region. In general only those at the highest risk of

infective endocarditis should be offered prophylaxis and then only when the risk of bacteraemia from the procedure is high.

#### Conditions requiring prophylaxis

- Significant congenital or acquired cardiac abnormalities
- Prosthetic valves or valvular repair utilising prosthetic material
- Previous infective endocarditis

#### Procedures requiring prophylaxis

- Dental procedures involving manipulations of the gingival or periapical region of the teeth or perforating the oral mucosa.

Examples of regimens are given in the table.

| Procedure                                  | Regimen                                      | Alternative                                  |
|--|--|--|
| Dental, oral or upper respiratory tract    | Amoxicillin 3g po                            | Clindamycin 600mg iv                         |
| Genitourinary, gastrointestinal or biliary | Ampicillin 2g iv<br>Plus gentamicin 1.5mg/kg | Vancomycin 1g iv<br>Plus gentamicin 1.5mg/kg |

#### Rheumatic fever

- Secondary prophylaxis should be prescribed for all patients following rheumatic fever to prevent recurrences

##### Duration

- Without carditis 5 years after last attack or 21 years (whichever is longer)
- With mild carditis 10 years after last attack or 21 years (whichever is longer)
- With carditis and residual heart disease 10 years or until age 40 (whichever is longer). Sometimes life-long prophylaxis.

##### Regimen

- Benzathine penicillin 1.2MU IM every 3-4 weeks or penicillin V 250mg po 12-hourly. If penicillin allergic azithromycin 250mg daily.