WESTERN CAPE ACADEMIC HOSPITALS
ANTIMICROBIAL RECOMMENDATIONS

2013
Acknowledgements

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</tbody>
</table>
**ANTIMICROBIAL AGENTS AVAILABLE**

The doses stated are those generally prescribed for adults although exceptions may occur (where dose per kg is used, the calculation was performed for a 70 kg patient).

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DOSE</th>
<th>DOSING INTERVAL</th>
<th>HOSPITAL COST (per day, in rands)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANTIMICROBIALS – oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500mg</td>
<td>8 hourly</td>
<td>0.83</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500mg</td>
<td>daily</td>
<td>7.34</td>
</tr>
<tr>
<td>Cefixime</td>
<td>400mg</td>
<td>STAT</td>
<td>19.46</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>250mg</td>
<td>12 hourly</td>
<td>3.02</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>500mg</td>
<td>12 hourly</td>
<td>0.88</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500mg</td>
<td>12 hourly</td>
<td>4.63</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>450mg</td>
<td>8 hourly</td>
<td>7.90</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>1g</td>
<td>12 hourly</td>
<td>2.98</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>160/800mg (2 tabs)</td>
<td>12 hourly</td>
<td>0.51</td>
</tr>
<tr>
<td>Doxyxycline</td>
<td>100mg</td>
<td>12 hourly</td>
<td>0.39</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>500mg</td>
<td>6 hourly</td>
<td>4.62</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>1.2g</td>
<td>daily</td>
<td>1.36</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>750mg</td>
<td>daily</td>
<td>4.48</td>
</tr>
<tr>
<td>Flucloxacillin</td>
<td>500mg</td>
<td>6 hourly</td>
<td>3.57</td>
</tr>
<tr>
<td>Fusidic acid</td>
<td>500mg</td>
<td>8 hourly</td>
<td>106.20</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>300mg</td>
<td>daily</td>
<td>0.57</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600mg</td>
<td>12 hourly</td>
<td>564.49</td>
</tr>
<tr>
<td>Metronidazole suppository</td>
<td>1g</td>
<td>8 hourly</td>
<td>7.37</td>
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<td>Metronidazole</td>
<td>400mg</td>
<td>8 hourly</td>
<td>0.56</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400mg</td>
<td>daily</td>
<td>3.61</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>100mg</td>
<td>8 hourly</td>
<td>7.167</td>
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<tr>
<td>Para-amino Salicylic acid</td>
<td>4g</td>
<td>8 hourly</td>
<td>78.10</td>
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<tr>
<td>Penicillin V (strep pharyngitis)</td>
<td>500mg</td>
<td>12 hourly</td>
<td>0.67</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>1.5g</td>
<td>daily</td>
<td>0.87</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>600mg</td>
<td>daily</td>
<td>0.85</td>
</tr>
<tr>
<td>RHZE (4 drug combination for TB)</td>
<td>5 tablets</td>
<td>daily</td>
<td>3.28</td>
</tr>
<tr>
<td>Terizidone</td>
<td>250mg</td>
<td>8 hourly</td>
<td>19.63</td>
</tr>
<tr>
<td><strong>ANTIVIRALS – oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>300mg</td>
<td>12 hourly</td>
<td>6.47</td>
</tr>
<tr>
<td>Aciclovir H. simplex</td>
<td>400mg</td>
<td>8 hourly</td>
<td>1.95</td>
</tr>
<tr>
<td>Aciclovir H. zoster</td>
<td>800mg</td>
<td>5 times daily</td>
<td>6.50</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (Aluvia)</td>
<td>2 tablets</td>
<td>12 hourly</td>
<td>7.69</td>
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<tr>
<td>Lamivudine</td>
<td>150mg</td>
<td>12 hourly</td>
<td>0.74</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>300mg</td>
<td>12 hourly</td>
<td>2.26</td>
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<tr>
<td>Stavudine</td>
<td>30mg</td>
<td>12 hourly</td>
<td>0.44</td>
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<tr>
<td>Didanosine</td>
<td>400mg</td>
<td>daily</td>
<td>3.75</td>
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<tr>
<td>Tenofovir</td>
<td>300mg</td>
<td>daily</td>
<td>1.96</td>
</tr>
</tbody>
</table>

*4-drug combination tablets (Rifampicin, isoniazid(H), pyrazinamide, Ethambutol) are provided by different suppliers under various trade names e.g. RIFAFOUR E-200, RIMSTAR and MYRIN PLUS. We recommend the use of the abbreviation RHZE when prescribing.*
# ANTIFUNGALS – oral

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Frequency</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole</td>
<td>400mg</td>
<td>daily</td>
<td>2.86</td>
</tr>
<tr>
<td>Griseofulvin</td>
<td>500mg</td>
<td>daily</td>
<td>2.46</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>200mg</td>
<td>12 hourly</td>
<td>14.75</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>400mg</td>
<td>daily</td>
<td>5.79</td>
</tr>
<tr>
<td>Nystatin suspension</td>
<td>1ml</td>
<td>6 hourly</td>
<td>1.26</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>200mg</td>
<td>12 hourly</td>
<td>204.30</td>
</tr>
</tbody>
</table>

# ANTIHELMINTHICS – oral

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Frequency</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mebendazole</td>
<td>100mg</td>
<td>12 hourly</td>
<td>0.63</td>
</tr>
<tr>
<td>Albendazole</td>
<td>400mg</td>
<td>stat</td>
<td>2.50</td>
</tr>
<tr>
<td>Praziquantel</td>
<td>3.5g</td>
<td>daily</td>
<td>194.68</td>
</tr>
</tbody>
</table>

# ANTIMICROBIALS – parenteral

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Frequency</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>1g</td>
<td>daily</td>
<td>9.94</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>1g</td>
<td>6 hourly</td>
<td>12.96</td>
</tr>
<tr>
<td>Capreomycin*</td>
<td>1g</td>
<td>daily</td>
<td>89.80</td>
</tr>
<tr>
<td>Cefazolin (prophylactic use)</td>
<td>1g</td>
<td>stat</td>
<td>4.52</td>
</tr>
<tr>
<td>Cefepime</td>
<td>1g (2g for Pseudomonas) 12 hourly</td>
<td>45.144</td>
<td></td>
</tr>
<tr>
<td>Ceftazidine</td>
<td>1g (2g for Pseudomonas) 8 hourly</td>
<td>98.22</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>1g</td>
<td>daily</td>
<td>4.55</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2g (for meningitis) 12 hourly</td>
<td>9.10</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>1g</td>
<td>8 hourly</td>
<td>10.82</td>
</tr>
<tr>
<td>Cefuroxime)</td>
<td>750mg</td>
<td>8 hourly</td>
<td>26.58</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>500mg</td>
<td>6 hourly</td>
<td>48.92</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>400mg</td>
<td>8 hourly</td>
<td>167.58</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500mg</td>
<td>12 hourly</td>
<td>216.49</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>600mg</td>
<td>8 hourly</td>
<td>34.14</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>2g</td>
<td>6 hourly</td>
<td>116.91</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>1.2g</td>
<td>8 hourly</td>
<td>39.60</td>
</tr>
<tr>
<td>Colistin</td>
<td>3 MU</td>
<td>8 hourly</td>
<td>184.68</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>160/800mg (2 amps) 12 hourly</td>
<td>9.96</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1g</td>
<td>6 hourly</td>
<td>671.20</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>1g</td>
<td>daily</td>
<td>368.33</td>
</tr>
<tr>
<td>Fusidic acid</td>
<td>500mg</td>
<td>8 hourly</td>
<td>410.97</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>420mg</td>
<td>daily</td>
<td>11.61</td>
</tr>
<tr>
<td>Imipenem</td>
<td>500mg</td>
<td>6 hourly</td>
<td>217.24</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>300mg</td>
<td>daily</td>
<td>362.10</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>1g</td>
<td>daily</td>
<td>12.46</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600mg</td>
<td>12 hourly</td>
<td>573.10</td>
</tr>
<tr>
<td>Meropenem</td>
<td>1g</td>
<td>8 hourly</td>
<td>377.85</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>500mg</td>
<td>8 hourly</td>
<td>16.17</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400mg</td>
<td>daily</td>
<td>289.12</td>
</tr>
<tr>
<td>Ofloxacin*</td>
<td>400mg</td>
<td>12 hourly</td>
<td>1222.81</td>
</tr>
<tr>
<td>Penicillin benzathine</td>
<td>2.4MU</td>
<td>weekly</td>
<td>12.30</td>
</tr>
<tr>
<td>Penicillin G (benzyl)</td>
<td>2MU</td>
<td>6 hourly</td>
<td>(using a 1MU vial) 44.64</td>
</tr>
<tr>
<td>Penicillin procaine</td>
<td>600 000U</td>
<td>daily</td>
<td>15.11</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>4.5g</td>
<td>8 hourly</td>
<td>180.00</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>600mg</td>
<td>daily</td>
<td>314.41</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>1g</td>
<td>daily</td>
<td>5.54</td>
</tr>
</tbody>
</table>

* not available at TBH
Teicoplanin 400mg daily 144.78
Tobramycin 420mg daily (six 80mg vials) 59.34
Vancomycin 1.5g 12 hourly 215.18

ANTIVIRALS – parenteral
Aciclovir 500mg 8 hourly 311.40
Ganciclovir 350mg 12 hourly 767.48

ANTIFUNGALS – parenteral
Amphotericin B (1mg/kg) 70mg daily 69.66
Amphotericin B (bladder washouts) 50mg/l daily (incl 1lt water for injection) 84.22
Fluconazole 400mg daily 37.21
Voriconazole 200mg 12 hourly 694.62

GENERAL COMMENTS

This handbook is not intended to be an antibiotic textbook nor to replace the antibiotic section of the SAMF. Its function is to indicate the GSH and TBH antibiotic recommendations and to provide some additional therapeutic suggestions for a number of clinical situations. These guidelines pertain to local antibiotic sensitivity patterns and may not be appropriate in other areas.

Awareness of cost

Choices often exist between antibiotics of equal efficacy and safety but differing cost. Where such a choice exists the cheaper agent should be used whenever possible. If a more expensive agent is used empirically, a change to a cheaper, appropriate agent should be made as soon as the sensitivity report is available.

The cost of the same antibiotic can differ markedly depending on its route of administration e.g. IV versus oral or rectal metronidazole, IV versus oral cotrimoxazole, IV versus IM penicillin (see page 5)

Direct IV administration by slow injection into the drip tubing can be used for many agents e.g. aminoglycosides, penicillins and cephalosporins. This avoids the costs of minibags and additional lines.

Dose

There is an erroneous belief that maximal doses are always best. The dose most frequently used in adults is given in the listing on pages 5-8. However, doses should be tailored to individual patients and may differ according to the site of infection. Always consider a loading dose in critically ill patients requiring ICU admission and ensure that the antibiotic is administered as soon an infectious aetiology is considered. Delays result in poorer outcomes.

Duration of therapy

Duration of therapy should be determined by clinical factors such as site of infection, severity of illness and response to treatment. As a general guide, antibiotics can be discontinued within 48-72 hours of the temperature returning to normal. Infections at
certain sites (e.g. pyelonephritis, osteitis or endocarditis) or with particular organisms, may require more prolonged therapy. Guidelines are given in the text where this is relevant. In uncomplicated infections oral antibiotics or an early change from IV to oral therapy is frequently justified.

With all antibiotics, but particularly with toxic agents, an ongoing re-evaluation of the patient’s infection should occur with the aim of stopping the antibiotic as soon as it is no longer necessary.

**Antibiotic levels**

Measurement of serum antibiotic levels should be routinely performed when administering aminoglycosides or vancomycin.

For aminoglycosides trough levels should be monitored about twice weekly if the renal function is normal. If the appropriate dose has been calculated on a mg/kg basis, determination of peak levels for efficacy may not be indicated. However, in critically ill, overweight or underweight patients, peak levels should be performed to establish that the dose is adequate. Peak levels are taken one hour after a bolus IM or IV, or one hour after an IV infusion is commenced. Trough levels are taken just before the next dose. Requests for levels should be submitted to the pharmacology laboratory.

For vancomycin a peak level is usually not necessary. The first trough level should be measured just before the fourth dose. Thereafter trough levels should be measured twice a week (provided they are in the therapeutic range). In patients with sensitive organisms, trough vancomycin levels should be maintained between 10 and 15 mg/l, but higher concentrations are recommended for organisms with higher MICs (consult with microbiology or infectious diseases and see “Vancomycin” below).

When vancomycin is administered to patients in renal failure a stat dose should be followed by a “random” measurement of the vancomycin level one to five days later, depending on the degree of renal dysfunction. Once the therapeutic range is reached (see above) the next dose of vancomycin should be given. Vancomycin levels should not be allowed to fall below the therapeutic range.

**Antibiotic prescribing in renal impairment**

Drug adjustments are based on the patient’s estimated endogenous creatinine clearance using the modified Cockroft and Gault formula:

\[
\text{Creatinine clearance (ml/min)} = \frac{(140 - \text{age}) \times \text{Wt (kg)}}{\text{serum creatinine (μmol/l)}}
\]

(For women multiply calculated creatinine clearance by 0.85 to adjust for lower contribution of muscle mass to total body weight.) Alternatively use the eGFR provided by NHLS (note that this differs somewhat from the creatinine clearance, but either can be used to guide dosing)

Most antibiotic dosages need to be adjusted in the setting of renal failure. Patients receiving dialysis may require dose adjustments especially if the dialysis leads to increased clearance of the drug.
The following agents listed need **not** be adjusted in renal failure. All other antibiotics, antifungals and HIV drugs require dose adjustments in renal insufficiency.

**Antibiotics:** azithromycin, ceftriaxone, ciprofloxacin, clindamycin, doxycycline, linezolid, moxifloxacin, rifabutin, rifampicin, isoniazid  
**Antifungals:** amphotericin B, itraconazole and voriconazole  
**Antivirals:** abacavir, efavirenz, nevirapine, lopinavir

Consult the following references for further information:
- South African Medical Formulary
- The Sanford Guide to Antimicrobial Therapy

### Nosocomial Infection

**Definition**

Nosocomial infection can be defined as an infection occurring at least 48 hours after hospital admission. Infections that arise within 30 days of an operation and other infections that follow discharge from hospital may also be classified as hospital acquired depending on the nature of the infection.

**Diagnosis**

- The diagnosis of nosocomial sepsis is firstly based on clinical features. Always attempt to make a clinical assessment of the likely source of infection.
- It is essential to obtain appropriate microbiology cultures, including properly collected blood cultures, before antimicrobial therapy is initiated in view of the high risk of multi-drug resistant organisms.

**Choice of antibiotics**

- Choice of empiric antibiotic therapy is influenced by knowledge of local pathogens and antibiotic sensitivities, as well as by the nature and severity of the patient’s condition, duration of hospitalization, location in the hospital (general ward vs ICU), previous infection or colonisation with particular pathogens and previous antibiotic therapy.

  - Common nosocomial pathogens in the Western Cape include extended spectrum beta lactamase (ESBL)-producing *Enterobacteriaceae*, (resistant to all penicillins and cephalosporins), cloxacillin-resistant staphylococci (MRSA) and carbapenem-resistant Acinetobacter species. More recently multi-drug resistant *Pseudomonas aeruginosa* and carbapenem resistant *Enterobacteriaceae* (CRE) have been emerging as nosocomial pathogens, although these are (for the moment) not as common.

- ICUs have the highest prevalence of nosocomial infections as well as the greatest proportion of antibiotic resistance.

- For severely ill patients initial intravenous broad-spectrum antibiotic therapy is recommended. De-escalation to more narrow- spectrum specific therapy, according to microbiological results, is important for patient safety (as it reduces the risk of e.g. antibiotic-associated diarrhoea) and reduces the selection of drug resistance. (Höffken & Niederman, Chest 2002; 122: 2183)

- Antimicrobial regimens should always be reassessed after 48 – 72 hours. A switch to oral therapy may be possible or a different regimen may be needed.
• The Study of the Efficacy of Nosocomial Infection Control (SENIC) demonstrated that a third of nosocomial infection might be prevented with appropriate infection control measures.

**Antibiotic Stewardship**

Due to the limited number of antibiotics currently available, the increasing problem of antibiotic resistance among bacterial pathogens, and the lack of antibiotics in development, appropriate use of antibiotics is becoming ever more important to preserve the antibiotics we have. The following measures (some of which have been mentioned already) are therefore strongly recommended:

• Always think carefully about whether an antibiotic is actually necessary.
• Always send appropriate cultures BEFORE starting antibiotic therapy
• Where possible, avoid antibiotics with overlapping activity
• If starting antibiotics empirically, always review after 3 days.
  o Are antibiotics still indicated?
  o If so, is the current choice appropriate?
• Consider de-escalation once culture results are available
• Consider switching from IV to oral once the patient is stable
• Stop antibiotics as soon as possible

**NOTES ON SPECIFIC AGENTS**

**PENICILLINS**

*Penicillin allergic patients*

Different alternatives are appropriate in different clinical situations. For soft tissue infections, clindamycin can be used. Erythromycin is not recommended for severe infections as many staphylococci and some strains of *Streptococcus pyogenes* (group A β haemolytic streptococcus) are resistant. For pneumonia, ceftriaxone (unless penicillin allergy was severe – see below) or moxifloxacin are suitable agents. Where a penicillin/aminoglycoside combination is being used, e.g. in abdominal infections, it may be appropriate to replace both agents with a second or third generation cephalosporin in penicillin allergic patients. Cross hypersensitivity reactions between penicillins and cephalosporins may occur in up to 5% of cases, but the risk is much lower with third generation cephalosporins (e.g. ceftriaxone). **With a history of severe penicillin allergy e.g. anaphylaxis, it would be inadvisable to use a cephalosporin if a suitable alternative were available. However in some situations (e.g. meningitis), if suitable alternatives are not readily available, antibiotics should not be delayed, and ceftriaxone should be used with careful observation**

**AMOXICILLIN**

• For most indications 500mg 8 hourly is the appropriate dose.
• Amoxicillin should not be used for pharyngitis as severe skin reactions can occur when this is due to Epstein-Barr virus. Oral penicillin V 500mg 12 hourly, given for ten days is equally effective.
• In respiratory tract infections, amoxicillin remains the oral drug of choice for pneumococci.
**PENICILLIN**

There are numerous preparations of injectable penicillins available in the pharmacy. As the trade names may change from time to time it is suggested that to avoid confusion the following terminology be adopted when prescribing:

**NOTE:** the term "bicillin" is particularly confusing and should no longer be used.

<table>
<thead>
<tr>
<th>RECOMMENDED TERMINOLOGY</th>
<th>ROUTE</th>
<th>COMPONENTS</th>
<th>AMPOULE CONTENT</th>
<th>INDICATIONS</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzathine penicillin</td>
<td>IM</td>
<td>benzathine penicillin</td>
<td>1,2MU</td>
<td>prophylaxis for: rheumatic fever, recurrent cellulitis, recurrent meningococcal meningitis streptococcal sore throat</td>
<td>1,2MU every third week</td>
</tr>
<tr>
<td>(provides sustained low levels of penicillin)</td>
<td></td>
<td></td>
<td>2,4MU</td>
<td>syphilis</td>
<td>1,2MU stat</td>
</tr>
<tr>
<td>procaine penicillin</td>
<td>IM</td>
<td>procaine penicillin</td>
<td>300 000U</td>
<td>replaces benzyl penicillin when a daily or twice daily IM injection preferred to IV therapy syphilis</td>
<td>600 000U daily</td>
</tr>
<tr>
<td>penicillin G</td>
<td>IV</td>
<td>sodium benzyl penicillin</td>
<td>1MU</td>
<td>infections for which oral or IM preparations are not suitable endocarditis and meningitis</td>
<td>2MU 6 hourly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5MU</td>
<td></td>
<td>5MU 6 hourly or 4MU 4 hourly¹</td>
</tr>
</tbody>
</table>

¹ For the IV administration of penicillin G a 4 hourly or constant infusion regimen is preferable. Six hourly dosing can be used when dictated by staff shortages.
CLOXACILLIN

This agent is primarily used to treat staphylococcal infections and, if the isolate is sensitive to cloxacillin, cloxacillin is the best agent. It is worth remembering that cloxacillin-susceptible staphylococci are susceptible to most other beta-lactams except penicillin, amoxicillin, ampicillin and piperacillin. Thus in cases of a mixed infection, co-amoxiclav or a cephalosporin can be used to successfully treat a cloxacillin-susceptible staphylococcus. However, the converse is also true - staphylococci that are resistant to cloxacillin are resistant to ALL (currently available) beta-lactam agents.

CO-AMOXICLAV

- The IV formulation must be administered immediately after reconstitution as the clavulanic acid begins to degrade after 20 minutes.
- The bacteriological spectrum includes streptococci, enterococci, staphylococci (cloxacillin-sensitive), community-acquired gram-negative bacilli, haemophili, (including those producing β-lactamase) and anaerobes – in view of the latter, it is unnecessary to add metronidazole to co-amoxiclav
- The most convenient and cost-effective oral dose is 1g 12 hourly – can be used for infection at any site amenable to oral therapy. NOTE: The common causative organisms for upper and lower respiratory tract infections remain sensitive to amoxicillin in the majority of instances and co-amoxiclav should therefore not be routinely prescribed for uncomplicated infections at these sites.

CEPHALOSPORINS

- Cephalosporins are broad spectrum agents with some individual differences.
- First generation cephalosporins cover mainly gram-positive organisms (streptococci and cloxacillin-sensitive staphylococci) but do have some gram-negative cover as well.
- Second, third and fourth generation cephalosporins may be used as an alternative to aminoglycosides in the treatment of gram-negative infections
- All have streptococcal cover that makes the addition of penicillin unnecessary (cefazidime is an exception).
- Currently available cephalosporins do not have any activity against enterococci.
- Cefazolin, cefuroxime, ceftriaxone, cefotaxime and cefepime have good activity against cloxacillin-sensitive staphylococci.
- Cefixime 400 mg STAT is the treatment of choice for gonorrhoea
- Cefotaxime and ceftriaxone have the same antimicrobial activity, but differ in pharmacology. Ceftriaxone has greater protein binding and hence a longer half-life which allows for once or twice daily dosing.

ADVISORY ISSUED BY ROCHE RE CEFTRIAXONE:
Ceftriaxone, which may be used as a once daily intravenous or intramuscular injection, is currently the most cost-effective third generation cephalosporin available. However, Roche has recently released the following safety advice: "Rocephin (a trade name for ceftriaxone) and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites. As a further theoretical consideration and
based on 5 half-lives of ceftriaxone, Rocephin and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient”. This recommendation was made following reports of intravascular or pulmonary precipitations in neonates, treated with ceftriaxone and calcium-containing IV solutions (including Ringer’s lactate).

- Ceftazidime and cefepime are active against many strains of *Pseudomonas aeruginosa*.
- Third and fourth generation cephalosporins are used in CNS infections (at higher doses) because therapeutic levels are readily achievable in the CSF.
- Increasing resistance in hospital gram-negatives has made cephalosporins an inappropriate choice for empiric therapy in nosocomial infections.
- The only oral cephalosporin available at GSH and TBH is cefuroxime. At GSH this is a restricted agent and is only used in cases where co-amoxiclav is inappropriate for some reason.

**CARBAPENEMS**

Carbapenems are very broad-spectrum beta-lactam antibiotics, with activity against many Gram-positive and Gram-negative aerobic and anaerobic bacteria. Carbapenems are not active against cloxacillin-resistant staphylococci. Their use is generally limited to severe nosocomial infections. If carbapenems are used empirically for nosocomial infections, it is very important to ‘step-down’ to a narrower-spectrum agent if the results of susceptibility tests become available. *Overuse of carbapenems promotes the emergence of resistance.*

- Imipenem and meropenem have a similar spectrum of activity. Meropenem is the preferred agent for CNS infections.
- Ertapenem is not active against *Pseudomonas* and *Acinetobacter*, but has good activity against ESBL-producing *Enterobacteriaceae*. It is therefore most suitable for empiric treatment of severe nosocomial infections where *Acinetobacter* and *Pseudomonas* are not frequently encountered, e.g. outside the ICU setting. There is no data on the CNS penetration of ertapenem and it is thus NOT recommended for CNS infections.

**QUINOLONES**

- Ciprofloxacin has excellent activity against Haemophilus, Legionella and gram-negative rods including Pseudomonas. It is the drug of choice for shigellosis, typhoid, and *uncomplicated* UTIs, as defined in the treatment section. It also has some activity against staphylococci, chlamydia and mycobacteria but is seldom used for these indications. It has no useful activity against streptococci or anaerobes.
- When treating *Pseudomonas aeruginosa* infections a higher dose (750mg bd oral or 400mg 8 hourly IV) should be used.
- Stat dose for UTI should be 500mg.
- Ofloxacin has a spectrum of activity almost identical to that of ciprofloxacin. It is currently used mainly in the treatment of patients with MDR TB, although it is being replaced by moxifloxacin for this indication.
- Moxifloxacin is a new quinolone with improved activity against streptococci and anaerobes. It retains all the activity of the earlier quinolones, including legionella but is not useful in the treatment of pseudomonas infections. Its spectrum makes it an extremely useful agent in the treatment of respiratory tract infections and it is
currently reserved for this indication for patients who are allergic to penicillin. It is also being used for treatment of MDR-TB (see above)

- The IV formulations of all quinolones should be used in severely ill patients as oral absorption is impaired.

COTRIMOXAZOLE

- Cotrimoxazole is seldom used nowadays outside of HIV infection due to high prevalence of resistance among community acquired isolates and the high frequency of severe hypersensitivity reactions.
- Its main use is in HIV-positive persons for prophylaxis and treatment of Pneumocystis and other infections.
- Although adverse reactions are not uncommon, the lack of alternative therapies means that it may be worthwhile to attempt desensitisation.

- The following protocol describes a simple approach for cotrimoxazole desensitization

Use cotrimoxazole suspension 240mg/5ml.
Desensitisation must be conducted in hospital and should be done WITHOUT antihistamine or steroid cover.

Take 1ml co-trimoxazole suspension (240mg/5ml) and dilute to 1litre with distilled water and shake very well (**mixture A**)

Now take 1ml of mixture A and dilute with distilled water to 10ml. (**mixture B**).

<table>
<thead>
<tr>
<th>Time</th>
<th>Dose</th>
<th>Dose in mls of undiluted cotrimoxazole suspension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time 0</td>
<td>Administer 5ml of mixture B. (Discard balance of mixture B)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Time 1hr</td>
<td>Administer 5ml of mixture A (after shaking well)</td>
<td>0.005</td>
</tr>
<tr>
<td>Time 2hr</td>
<td>Administer 50ml of mixture A (after shaking well) (Discard balance of mixture A)</td>
<td>0.05</td>
</tr>
<tr>
<td>Time 3hr</td>
<td>Administer 0.5ml of co-trimox suspension diluted to 5ml with water</td>
<td>0.5</td>
</tr>
<tr>
<td>Time 4hr</td>
<td>Administer 5ml of cotrimox suspension</td>
<td>5.0</td>
</tr>
<tr>
<td>Time 5hr</td>
<td>Administer 2 single strength cotrimox tablets</td>
<td></td>
</tr>
<tr>
<td>Time 6 hr</td>
<td>Start full-dose cotrimoxazole</td>
<td></td>
</tr>
</tbody>
</table>

AMINOGLYCOSIDES

- The total daily dose should be given as a single daily dose, except when used for synergy in infective endocarditis.

- The practice of using beta-lactams plus aminoglycosides for synergy is generally not indicated (recent meta-analyses show no benefit) – exceptions are infective endocarditis and certain resistant organisms (eg pseudomonas, enterococci).

- The recommended maximum duration of usage is 14 days. The need to continue empiric aminoglycoside treatment should be reviewed after 48 hours according to clinical response and microbiological data.

- Peak levels as indicated below need to be achieved for effective bacterial killing.
To avoid toxicity the antibiotic should be allowed to fall to the trough levels indicated below, before the next dose is given.

Aminoglycoside toxicity is more common in elderly patients and alternative agents such as beta-lactam antibiotics should generally be used in patients of sixty years or older.

Co-administration with other nephrotoxic and ototoxic drugs should be avoided if possible (eg vancomycin, amphotericin B, tenofovir).

Remember that aminoglycoside-induced nephrotoxicity is generally reversible, whilst ototoxicity is often irreversible. Essential to discontinue aminoglycosides if hearing loss or vertigo occur.

THE FOLLOWING DOSING SCHEDULES APPLY TO BOTH ADULTS AND CHILDREN

<table>
<thead>
<tr>
<th>AMINOGLYCOSIDE DOSING SCHEDULE1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>THE MOST IMPORTANT DOSE IS THE FIRST ONE - DO NOT UNDERDOSE</strong></td>
</tr>
<tr>
<td>ANTIBIOTIC</td>
</tr>
<tr>
<td>Gram-negative infection - normal renal function</td>
</tr>
<tr>
<td>gentamicin/tobramycin</td>
</tr>
<tr>
<td>amikacin</td>
</tr>
<tr>
<td>Gram-negative infection - poor renal function</td>
</tr>
<tr>
<td>gentamicin/tobramycin</td>
</tr>
<tr>
<td>amikacin</td>
</tr>
<tr>
<td>Streptococcal and enterococcal endocarditis3</td>
</tr>
<tr>
<td>gentamicin/tobramycin</td>
</tr>
</tbody>
</table>

1 Doses calculated according to total body mass in obese patients may result in toxicity. Because of the narrow margin between effective and toxic levels, doses should be individualised according to age, weight and renal function. Obese patients should be dosed according to ideal body weight with a correction factor:

\[
\text{Adjusted body weight} = \text{ideal body weight} + [0.4 \times (\text{actual body weight} - \text{ideal body weight})]
\]

2 Peak levels are taken one hour after a bolus IM or IV or one hour after an IV infusion is commenced. Trough levels are taken just before the next dose is given.

3 Aminoglycosides used in combination with penicillin for the treatment of streptococcal or enterococcal endocarditis are given for their synergistic action and need only be administered at half the dosage used for gram-negative infections.

4 A range is given to provide some flexibility when calculating doses. Remember that gentamicin is provided in vials of 80mg - round the calculated dose up to the next multiple of 80 for the initial dose and then adjust if necessary according to levels.
VANCOMYCIN

- Vancomycin is not an aminoglycoside, it is a glycopeptide, and only has activity against gram-positive organisms.
- Cloxacillin is a more effective anti-staphylococcal agent than vancomycin and should therefore be used as staphylococcal cover in empiric therapy for community-acquired infections or if the isolate is sensitive to cloxacillin.
- Vancomycin dosing is based on actual body weight and renal function so all patients should be weighed and GFR estimated. ALL patients should receive a loading dose of 25-30mg/kg and ALL subsequent doses should be 10-15 mg/kg (unless inadequate trough levels achieved). The dosing interval and measurement of trough concentrations are based on renal function as in table below

<table>
<thead>
<tr>
<th>eGFR (ml/min)</th>
<th>Dosing interval (hrs)</th>
<th>Measurement of trough concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;80</td>
<td>12</td>
<td>Before 3rd dose</td>
</tr>
<tr>
<td>40-79</td>
<td>24</td>
<td>Before 3rd dose</td>
</tr>
<tr>
<td>25-40</td>
<td>48</td>
<td>Before 2nd dose</td>
</tr>
<tr>
<td>&lt;25 or haemodialysis or CAPD</td>
<td>When trough level &lt;15</td>
<td>After 3 days</td>
</tr>
</tbody>
</table>

Vancomycin is not significantly removed by conventional intermittent haemodialysis. Dosing and monitoring as for those with GFR <25 ml/min

- For most staphylococci trough levels of 10-15 mg/L will be therapeutic. This is normally achieved with the doses suggested above; however trough levels should always be checked as detailed in the table in order to ascertain whether such levels are being achieved. If the trough is less than 10mg/L, increase the dose. If the trough is >15 mg/L increase the dosing interval. If in doubt, consult pharmacology / microbiology / infectious diseases for advice
- Patients with complicated infections or infections due to staphylococci with higher MICs (>1mg/L) will require higher doses (40mg/kg/day) in order to achieve trough levels of 15-20 mg/l. If patient is on continuous infusion, maintain levels between 15-20 mg
- Vancomycin must be given by slow intravenous infusion, rate not to exceed 1g per hour to avoid the “red man syndrome”, which is due to histamine release (this is not a hypersensitivity reaction)
- As the plasma level of vancomycin appropriate for each patient is dependent on the MIC of the organism being treated, it is essential that every attempt be made to identify the suspected pathogen. Before vancomycin therapy is considered, suitable specimens (including at least TWO blood cultures) must be submitted to the microbiology laboratory.

COLISTIN

- This is a polymyxin antibiotic, whose use was virtually discontinued due to side effects and the availability of safer and more effective agents. However, with the emergence of multi-resistant gram-negative bacilli (esp A. baumannii), the drug has made a comeback. It should ONLY be used if infection with highly-resistant gram-negative organisms has been proven or is strongly suspected, and its use should always be discussed with a microbiologist or infectious disease specialist
Colistin is not registered by the MCC in South Africa and is only available on section 21 release. Stocks are maintained by both GSH & TBH pharmacies.

It is both nephro- and neurotoxic, although the degree of toxicity has probably been overestimated, and recent research suggests that it may not be as toxic as previously thought. However, renal function should be monitored while the drug is being used, and the agent should be discontinued as soon as clinically appropriate.

Dosing of colistin is still unclear, as different formulations and dosing recommendations can be found worldwide. The dosing recommendation used locally is a loading dose of 9 - 12 million units, followed by 4.5 million units 12 hourly (if renal function normal). See Table below for dosing recommendations.

### IV Colistin dosing guideline for the treatment of MDR gram negative infections in the critically ill

<table>
<thead>
<tr>
<th>Dose</th>
<th>Patient category</th>
<th>Dosing suggestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading</td>
<td>All patient categories</td>
<td>9 - 12 MU*</td>
</tr>
<tr>
<td>Maintenance</td>
<td>eGFR &gt; 60</td>
<td>4.5 MU 12hourly</td>
</tr>
<tr>
<td></td>
<td>eGFR 30-60</td>
<td>3 MU 12hourly</td>
</tr>
<tr>
<td></td>
<td>eGFR 10-30</td>
<td>2 MU 12hourly</td>
</tr>
<tr>
<td></td>
<td>eGFR &lt; 10</td>
<td>1 MU 12hourly</td>
</tr>
<tr>
<td></td>
<td>Intermittent hemodialysis</td>
<td>1 MU 12hourly plus 0.5-1 MU after each episode of dialysis</td>
</tr>
<tr>
<td></td>
<td>Continuous renal replacement</td>
<td>8 MU 12hourly</td>
</tr>
</tbody>
</table>

Reworked adult dose in MU (million units) CMS adjusted to estimated Glomerular Filtration Rate (eGFR), based on dosing recommendations by Garonzick 2011, Li 2006, Markou 2008, Plachouras 2009 and Sanford 2012.

* Administration of loading dose is critical patients with severe sepsis.12 MU CMS for 70kg (ideal body weight) and 9MU for 55 kg patients.

When using colistin for treatment of multi-resistant Gram-negative bacilli, there is some evidence (from observational studies and pharmacological modelling studies) that combination therapy with a 2nd agent (such as a carbapenem, or rifampicin) may be of benefit – both for clinical outcomes as well as to reduce the risk of colistin resistance. It is not clear whether combination therapy should be used for all multi-drug resistant organisms, or only the potentially more virulent organisms (eg *Pseudomonas aeruginosa* and members of the *Enterobacteriaceae*). All such cases should be discussed with an infectious disease specialist, pharmacologist or microbiologist.

**METRONIDAZOLE**

- Oral metronidazole is freely available and is the preferred route of administration unless patients are severely ill or have an ileus, when intravenous metronidazole should be used.
- Metronidazole suppositories do not provide superior levels and are more expensive.
**ANTIFUNGAL AGENTS**

**AMPOTERICIN B**
- Given as a single dose by IV infusion over a 4 hour period.
- Febrile reactions are the most common and can be minimised by pretreatment with paracetamol or, in severe cases, hydrocortisone (50mg).
- A dose of 0.7mg/kg is used for suspected or confirmed Candida infection.
- The dose should be increased to 1mg/kg/day (maximum 1.5mg/kg/day) when treating cryptococcal meningitis and certain filamentous fungal infections.
- Pre-existing renal impairment does not require alteration of the calculated daily dose. However, if renal function deteriorates significantly while on therapy consider changing to an alternative agent. Nephrotoxicity is almost always reversible.
- Alternate day dosing does not decrease renal toxicity but can be used for patient convenience. A double dose is then given (max 1.5mg/kg/dose) on alternate days.
- The renal toxicity of amphotericin B is decreased if patients are well hydrated. Pre and post-infusion hydration with 500ml saline (if clinical condition allows).
- Renal function and potassium and magnesium levels should be monitored twice weekly. Aggressive replacement of potassium and magnesium should be undertaken. FBCs should be monitored with prolonged therapy due to the risk of anaemia developing.

**FLUCONAZOLE**
- Fluconazole is available as an alternative antifungal agent when it is not appropriate to use amphotericin B. Amphotericin B remains the drug of choice for systemic fungal infections in most cases.
- Fluconazole has no activity against filamentous fungi such as Aspergillus and should not be substituted for amphotericin when such infections are suspected.
- Fluconazole is available in both oral and IV forms.
- A restricted agent at GSH except for AIDS patients with cryptococcal meningitis or oesophageal candidiasis – free fluconazole is available for these patients.

**ITRACONAZOLE**
- An alternative therapy to amphotericin for invasive aspergillosis, disseminated histoplasmosis, difficult dermatophycoses and other mould infections.
- A restricted agent at GSH and TBH

**VORICONAZOLE**
- Extremely expensive agent, restricted for invasive aspergillosis, for which it is the agent of choice.

**Voriconazole for invasive aspergillosis**
Invasive aspergillosis is an uncommon opportunistic infection in patients with haematological malignancies or post transplant. It has a very high mortality rate. Definitive diagnosis is difficult to achieve. Voriconazole has been shown to be the drug of choice for invasive aspergillosis (N Engl J Med 2002;347:408-15), however it is extremely expensive. At TBH contact the infectious diseases department. At GSH voriconazole 200 mg PO 12 hourly (**give loading dose of 400mg 12hourly for first two doses**) for 12
weeks will be made available for invasive aspergillosis, using the diagnostic criteria below (please obtain release from a microbiologist):

**Definite invasive aspergillosis**
- culture from a normally sterile site
- hyphae consistent with aspergillus on biopsy or aspirate plus culture from the same organ
- CXR evidence (not attributable to other factors) and culture from bronchoalveolar-lavage fluid

**Probable invasive aspergillosis**
- hyphae consistent with aspergillus in a biopsy specimen or aspirate without culture
- halo or an air-crescent sign on CT scan of the lung
- CXR evidence (not attributable to other factors) **plus either** hyphae consistent with the aspergillus in bronchoalveolar-lavage fluid or sputum or a sputum culture
- opacification of a sinus on CT or MRI **plus either** hyphae consistent with aspergillus on biopsy or culture

**KETOCONAZOLE**
- For antifungal therapy this has been superseded by fluconazole and itraconazole. Its use at GSH and TBH is limited to exploiting its inhibition of the metabolism of ciclosporin.

**ANTIVIRAL AGENTS**

**ACICLOVIR** is active against herpes simplex virus (HSV) and varicella-zoster virus (VZV) infections. The drug is formulated as a tablet, syrup, IV and as a topical preparation. Topical aciclovir for eye use is restricted to the Ophthalmology Department. Topical aciclovir cream has no role in the clinical management of any other HSV or VZV infections.

The dose and treatment duration of aciclovir depends on the clinical indication:

Severe or complicated HSV/VZV diseases:
- HSV encephalitis: The diagnosis should be confirmed by HSV PCR on CSF, but treatment should commence immediately upon clinical suspicion. Aciclovir is given 10mg/kg 8 hourly IV for 14-21 days. For neonatal infections a higher dose and prolonged treatment is recommended – 20mg/kg 8 hourly IV for 3 weeks. [Ref: Kimberlin D, HSV meningitis and encephalitis in neonates. Herpes 2004;11(2):65A-76A.]
- Severe systemic HSV infection/HSV hepatitis: The diagnosis should be confirmed by HSV PCR on a blood sample, but if diagnosis is suspected, empiric treatment should commence immediately. Consult the virology consultant on call. Aciclovir 5mg/kg IV 8 hourly for 7-14 days is indicated if the diagnosis is confirmed.
- Complicated chickenpox - e.g. pneumonia or immunocompromised patient. Acyclovir 10mg/kg IV 8 hourly. Oral aciclovir 800 mg five times daily can be used to complete the treatment course of 7-14 days when the patient has improved.
HSV/VZV disease in the immunocompromised patient

- Severe shingles (disseminated zoster or zoster ophthalmicus): Aciclovir 10mg/kg IV 8 hourly. Oral aciclovir 800 mg five times daily can be used to complete the treatment course of 7-14 days when the patient has improved.
- Any active shingles: Aciclovir 800mg orally 5 times/day for 7 days
- Episodic oral or genital herpes: Oral aciclovir 400mg 8 hourly for 7-14 days.
- Chronic suppression for frequent recurrences: Aciclovir 400mg orally 12 hourly.

Localised HSV disease in the immunocompetent patient

- Severe oral herpes: oral aciclovir 400mg 8 hourly for 7 days.
- Primary genital herpes: oral aciclovir 400mg 8 hourly for 7 days.
- Episodic genital herpes: oral aciclovir 800mg 8 hourly for 2 days [Ref: Wald,A; Two-Day Regimen of Acyclovir for Treatment of Recurrent Genital Herpes Simplex Virus Type 2 Infection. CID 2002; 34:944-8]
- Chronic suppression: Aciclovir 400mg orally 12 hourly.

Aciclovir reduces short term morbidity but does not alter recurrence rates. In immunocompetent person it needs to be started within 72 hours of onset for primary HSV infections and within 24 hours of onset of a recurrent episode.

VZV disease in the immunocompetent patient

- Chickenpox in adult: oral aciclovir 800mg 5 times a day for 7 days
- Shingles: oral aciclovir 800mg 5 times a day for 7 days

Aciclovir given within the first 72 hours of the onset of shingles significantly shortens the healing process of acute zoster, alleviates pain and reduces the incidence of other acute/chronic complications. For the treatment of chickenpox, aciclovir needs to be given within 24 hours of the onset of rash for it to have a beneficial effect.

GANCICLOVIR is the drug of choice for treating cytomegalovirus (CMV) disease in immunocompromised patients. The drug is only available as an IV formulation (oral valganciclovir is available for transplant patients after induction therapy). CMV disease needs induction treatment with IV ganciclovir 5mg/kg 12 hourly for 14 - 21 days, followed in most cases by maintenance therapy (either ganciclovir weekly by intra-ocular injections for CMV retinitis or IV 5mg/kg daily). GIT CMV disease in HIV infection does not routinely require maintenance therapy.

CMV disease should be managed in conjunction with the Division of Infectious Diseases, Department of Medicine. For treatment of CMV retinitis, please consult the ophthalmology department.

ANTIRETROVIRAL THERAPY (ART)

For long-term treatment of disease

- CD4 count <350 cells/mm3 irrespective of WHO clinical stage

OR

- Irrespective of CD4 count
  - All types of TB
  - HIV positive women who are pregnant or breast feeding
  - Cryptococcal meningitis
  - WHO stage 3 or 4

- HIV positive patients who do not require ART can be managed at their nearest primary care centre, whereas those eligible for ART should be referred to their closest...
primary level HIV clinic that is accredited for ART roll-out. Tertiary level HIV care and other specialist clinics for HIV-related disorders are available at GSH or TBH.

Two ART regimens are available:
- In adults first line (regimen 1): A fixed dose combination tablet consisting of tenofovir, emtricitabine and efavirenz is taken once a day.
- Second line (regimen 2): Zidovudine, lamivudine and lopinavir/ritonavir. Switching from the first to second line is based on virological criteria (note that viral load measures are expensive and should only be requested by the adult or paediatric ID clinics, or in consultation with an ID specialist in the case of in-patients).

See the Antiviral prophylaxis section for recommendations regarding various post exposure prophylaxis regimens.

RESTRICTED AGENTS

Antibiotic Restrictions at Groote Schuur Hospital and Tygerberg Hospital.

Antibiotic stewardship ward rounds have been introduced in both medical and surgical wards, as a way of monitoring and reviewing antibiotic prescribing practices. Experience (both here and internationally) is that this is a more effective way of practicing antibiotic stewardship than the previous model involving the need to have antibiotics released by the on-call microbiologist or ID physician.

As part of the new approach to antibiotic stewardship, the practice of requiring antibiotic release by microbiology/ID has been changed. In future, certain antibiotics will be available in the wards on consultant authorization. The consultant looking after the case MUST either sign the prescription chart him/herself, or phone pharmacy (GSH ext 6145, TBH ext 4915) to authorize the antibiotic. Signatures or phone requests from junior staff will NOT be accepted after the first dose. Microbiology will still be available 24 hours /day for consultation where necessary and a limited list of agents will still require authorization from microbiology.

All antibiotic prescriptions should be reviewed regularly, both for the purposes of correlating the prescribed antibiotic with culture results and de-escalating if appropriate, as well as to consider stopping the antibiotic as soon as is clinically appropriate (often after 5 days).

<table>
<thead>
<tr>
<th>Agents restricted to consultant signature or consultant telephonic authorization</th>
<th>Agents still requiring microbiology / ID authorization:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICUs:</strong></td>
<td><strong>ICU</strong></td>
</tr>
<tr>
<td>Colistin</td>
<td>Tigecycline</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Aztreonam</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Linezolid</td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
</tr>
<tr>
<td><strong>General wards:</strong></td>
<td><strong>General wards - Above list plus:</strong></td>
</tr>
<tr>
<td>IV ciprofloxacin</td>
<td>Colistin</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Meropenem</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>Imipenem</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td></td>
</tr>
</tbody>
</table>
For **antibacterial** agents:

GSH: Contact microbiologist on call (speed dial 76652 / 082 907 5282), alternatively Infectious Diseases Consultant on call.

TBH: Contact microbiologist on call via exchange alternatively contact the Infectious Diseases Consultant on call.

For **antiviral** agents:

Contact exchange for virologist on call, alternatively contact the Infectious Diseases consultant on call (TBH).
THERAPY

Dosages are as listed on page 5 unless otherwise indicated.

APPROPRIATE CULTURES SHOULD ALWAYS BE SENT BEFORE ANTIBiotics ARE STARTED WHENEVER POSSIBLE

SEVERE SEPSIS

Empiric therapy

*If the source of infection known* treatment should be directed towards the most likely causative organism(s)

- suspected sepsis of gut origin penicillin, gentamicin and metronidazole
- suspected sepsis of urinary tract origin gentamicin alone

*Febrile neutropaenic patients* piperacillin/tazobactam and amikacin or imipenem (consult your local laboratory or microbiologist for susceptibility data)

- If no response after 5-7 days add amphotericin B.
- Vancomycin if there is evidence of IV line infection

*Suspected staphylococcal septicaemia* Cloxacillin 2g 6 hourly

- community acquired
- hospital acquired Vancomycin

*Suspected gram-negative septicaemia* gentamicin or ceftriaxone

- community acquired amikacin or ertapenem
- hospital acquired (non-ICU related) Ceftriaxone initially.

- HIV positive patients often have non-typhoid salmonella bacteraemia and the empiric choice of antibiotic should cover these organisms

6 weeks of therapy can be completed with oral ciprofloxacin or cotrimoxazole depending on organism susceptibility.

Patients who relapse after the initial episode should have an extra-gastrointestinal source sought and be placed on long-term suppressive therapy

**Directed therapy:**

Change to the most appropriate and cost effective antimicrobial once organism sensitivities are known.
ENDOCARDITIS

It is preferable to wait for a diagnosis based on culture or serology before starting therapy. However, patients who present with severe disease of rapid onset require empiric therapy directed against staphylococci immediately following cultures. Consultation with infectious diseases/microbiology is advised.

Empiric therapy

Native valve

penicillin 6MU 6 hourly) for four weeks plus gentamicin (3mg/kg/day given 12 hourly) for 2 weeks

If staphylococcal infection suspected (acute onset) add cloxacillin (3g 6 hourly)

Prosthetic valve

vancomycin (30mg/kg/day given 12 hourly) and rifampicin (15mg/kg/day given 12 hourly - oral) for 6 weeks plus gentamicin (3mg/kg/day given 12 hourly) for 2 weeks

Directed therapy (All doses as for empiric therapy)

Streptococcal (native valve) – all MICs refer to penicillin

- Viridans streptococci fully susceptible to penicillin (MIC ≤0,12mg/l)

penicillin alone for 4 weeks

The addition of gentamicin as above may be required where the disease is judged to have been present for more than three months at diagnosis.

SHORT COURSE THERAPY: (ONLY IN CONSULTATION WITH INFECTIOUS DISEASES OR CARDIOLOGY SPECIALIST)

Two weeks of therapy using either penicillin or ceftriaxone 2g daily with gentamicin, in doses as given above, has been shown to be effective (Clin Micro & Infection Oct 1998;4 -supp3:S17-S26).

This regimen should not be considered for patients with extracardiac foci of infection or intracardiac abscess. (Transoesophageal echocardiogram is strongly recommended to exclude such complications.) Patients should also not have any degree of haemodynamic compromise, conduction disorder or embolic complication.

OUTPATIENT THERAPY(ONLY IN CONSULTATION WITH INFECTIOUS DISEASES OR CARDIOLOGY SPECIALIST)

Suitable cases may be treated as outpatients using a once daily dose of ceftriaxone 2g for 4 weeks (JAMA Jan 8 1992;267(2):264-267.

Patients should have no haemodynamic compromise, conduction disorder or embolic complication. Outpatient clinical review by a competent health care worker should occur every few days.
- Moderately susceptible viridans streptococci (MIC >0,12 and <0,5mg/l) penicillin and gentamicin for 2 weeks followed by penicillin alone for a further 2 weeks

- Moderately resistant viridans streptococci (MIC ≥0,5 and <4mg/l), penicillin and gentamicin both for 4 weeks 6 weeks of therapy may be required in cases with a history of > 3 months, or mitral valve involvement See note (a) below

- Penicillin susceptible enterococci See note (a) below

- Abiotrophia/Granulicatella spp. (nutritionally variant streptococci) penicillin and gentamicin for 6 weeks

- Fully resistant viridans streptococci (MIC ≥4mg/l) vancomycin plus gentamicin for six weeks.

- Penicillin resistant enterococci See note (a) below

**Streptococcal (prosthetic valves)**

- Viridans streptococci fully susceptible to penicillin (MIC ≤0,12mg/l) penicillin alone for 6 weeks Gentamicin can be added for the first 2 weeks, however, the addition of gentamicin has not demonstrated superior cure rates compared with penicillin alone for highly susceptible strains. Gentamicin should not be used if the creatinine clearance is <30ml/min (Circulation 2005; 111: 3167)

- Moderately susceptible (MIC >0,12 and <0,5mg/l) penicillin and gentamicin for 6 weeks

- Moderately resistant viridans streptococci (MIC ≥0,5 and <4mg/l), penicillin and gentamicin for 6 weeks See note (a) below

- Penicillin susceptible enterococci See note (a) below

- Abiotrophia/Granulicatella spp. vancomycin and gentamicin for 6 weeks

- Fully resistant viridans streptococci (MIC ≥4mg/l) See note (a) below

- Penicillin resistant enterococci See note (a) below

Notes:

a. If an enterococcus shows high-level gentamicin resistance, streptomycin can be substituted for gentamicin. However, the laboratory should be consulted to determine whether the organism is susceptible to streptomycin.

b. In patients unable to tolerate penicillin, vancomycin or ceftriaxone can be used as an alternative (ceftiraxone not suitable for enterococcal infection). However, it is crucial to establish the nature of the penicillin allergy, and microbiology / infectious disease consultation is advised in all cases.

c. In the exceedingly rare instance of a vancomycin-resistant enterococcal endocarditis, please consult with microbiology / infectious diseases unit.
**Staphylococcal**  
*(cloxacillin/methicillin sensitive)*

- **native valve**: cloxacillin for 4-6 weeks  
  two weeks of cloxacillin with one week of gentamicin has been shown to be effective in [uncomplicated right-sided endocarditis](https://www.ncbi.nlm.nih.gov/pubmed/9017055) with vegetations of <2cm. ([Ann Intern Med 1996;125:969-74](https://www.annals.org/article.aspx?doi=10.7326/0003-4819-125-7-199609150-00010))

- **prosthetic valve**: cloxacillin plus rifampicin for 6-8 weeks plus gentamicin for 2 weeks. If the isolate is resistant to rifampicin, fucidic acid can be used.

In the rare occurrence of a penicillin sensitive staphylococcus, penicillin should be used in preference to cloxacillin.

**Staphylococcal**  
*(cloxacillin/methicillin resistant)*

- **native valve**: vancomycin for 4-6 weeks – as vancomycin is a less active agent than cloxacillin it is recommended to add a second agent according to sensitivities: rifampicin, fusidic acid or gentamicin can be used

- **prosthetic valve**: vancomycin and rifampicin for 6-8 weeks plus gentamicin for 2 weeks

**Infections of vascular grafts:**

These should in general be treated as for prosthetic valve infections. Gram negative infections are however more likely in grafts in the abdomino-femoral area and a suitable agent should be added to the above regimens. High dose oral ciprofloxacin can be requested in these cases.

**RESPIRATORY TRACT INFECTIONS**

In respiratory tract infections moxifloxacin is a suitable alternative in penicillin allergic patients.

**Upper respiratory tract infections:**

- **pharyngitis (S. pyogenes)**: Benzathine penicillin 1.2 MU IMI stat or oral penicillin V 500 mg 12 hourly for 10 days

- **otitis media and sinusitis**
  - **acute**: amoxicillin (5 days for otitis & 10 days for sinusitis)
  - **chronic**: co-amoxiclav
Lower respiratory tract infections:

*acute bronchitis*  
*antibiotics are not indicated*

*acute exacerbations of chronic bronchitis*  
amoxicillin or doxycyline (co-amoxiclav or quinolones may be requested in special circumstances)

Penicillin (IV) or amoxicillin remain the drugs of choice for *Streptococcus pneumoniae*

Pneumococci isolated from blood cultures have their penicillin susceptibility reported according to meningitis criteria. Those reported as “R”, but where the penicillin MIC is ≤2mg/l may still be treated with penicillin if the site of infection is not the central nervous system.

**Pneumonia**

**Empiric therapy**

*Community acquired*

**mild to moderate**

- <65 years, no co-morbidity
  
  OUTPATIENT: - a single dose of IV (or IM) penicillin followed by oral amoxicillin 1g 8 hourly 5 days
  
  IN-PATIENT: IV penicillin or ampicillin 5 days- add oral doxycycline or erythromycin if no response at 48 hours

- >65 years or co-morbidity (i.e. cardio-respiratory illness, diabetes, alcoholism, HIV etc.)
  
  ceftriaxone 1g/day- add oral doxycycline or erythromycin if no response at 48 hours

**severe**

HIV-positive patients of any age with bilateral diffuse interstitial infiltrates on CXR plus evidence of hypoxia or desaturation of >5% on effort - submit induced sputum specimen to the microbiology laboratory for PCP immunofluorescence

- ceftriaxone 1g/day *plus* IV clarithromycin

Add cotrimoxazole to the above regimens to treat presumed pneumocystis pneumonia - one tablet (80/400mg) for each 4kg body weight per day. This dose should be divided into 3 or 4 doses a day giving no more than 4 tablets per dose

Adjunctive prednisone 40mg 12 hourly should be given to hypoxic patients. This is given for 5 days followed by 40mg daily for 5 days and then 20mg daily for 11 days
Hospital acquired general wards  
ertapenem 5 days
In patients where there is clinical (e.g. associated line sepsis) or laboratory evidence to suggest a staphylococcal aetiology the addition of vancomycin should be considered pending culture and sensitivity results

ventilator associated  
In certain units within a hospital, the use of agents such as piperacillin/tazobactam, carbapenems or quinolones may be dictated by the prevalence of highly resistant organisms (consult microbiologist).

Aspiration pneumonia, lung abscess  
penicillin and metronidazole (if penicillin allergic use clindamycin alone). Switch to oral co-amoxiclav as soon as appropriate. Add appropriate gram-negative cover if the aspiration occurred while in hospital or a nursing home or in alcoholics, or if patient has had recent antibiotic exposure. Depending on your local hospital gram-negative resistance profile, a suitable agent could be ceftriaxone, piperacillin/tazobactam, ertapenem or imipenem/meropenem.

NOTE: A Gram stain of a well-collected sputum may provide valuable information as to the causative agent.

Hospital acquired organisms are more likely to be resistant to ceftriaxone

Routine use of serology to diagnose “atypical” pneumonia is not recommended as this seldom influences management because convalescent serum is required to show a rise in antibody titres.

A urinary legionella antigen test is available for diagnosis of legionella infection.

Tuberculosis
all sites (new and retreatment cases >8 years)  
2 months initial phase:  
given 7 times/week  
30-37 kg - 2 tabs RHZE  
38-54 kg - 3 tabs RHZE  
55-70 kg - 4 tabs RHZE  
>70 kg - 5 tabs RHZE

4 months continuation phase*  
given 7 times/week  
30-37 kg - 2 tabs RH (150/75)  
38-54 kg - 3 tabs RH (150/75)  
55-70 kg - 2 tabs RH (300/150)  
>70 kg - 2 tabs RH (300/150)
CNS or bone & joint involvement
in patients unable to swallow tablets

Treatment duration for 9 months

Pyrazinamide tablets can be crushed and given by nasogastric tube.
Isoniazid and rifampicin are available in syrup.

in patients unable to absorb orally

Isoniazid and rifampicin IV (IV INH not available at TBH)
Streptomycin can be given IM.
IV amikacin is an alternative for streptomycin.
IV moxifloxacin can be obtained in selected cases

Drug resistant tuberculosis

TB culture and sensitivity should be requested in patients presenting with symptoms and signs suggestive of TB in the following settings:
- Past history of TB
- Health care worker/prisoner
- Contact with known drug resistant TB patient
- Failure of sputum conversion after 3 months of intensive phase TB chemotherapy

MDR-TB is a laboratory diagnosis defined as resistance to isoniazid and rifampicin with or without resistance to additional drugs.
Multiple resistances to other drugs not including rifampicin is defined as poly resistance and does not have the same connotation as MDR-TB.
XDR-TB is defined as an MDR strain plus resistance to any fluoroquinolone and any one of kanamycin, amikacin or capreomycin
Newly diagnosed patients with MDR/XDR TB need to be referred to the nearest MDR outpatient unit

Standard therapy:
i. Intensive 6 month treatment

- followed by:
ii. Maintenance treatment 18 months

a. Intensive treatment:
kanamycin 15mg/kg/day
ethionamide 500 – 750mg/day (< 50kg 500mg, >50kg 750mg/day)
moxifloxain 400mg daily
pyrazinamide 1000mg – 2000mg/day
terizidone <50kg 500mg/day, >50kg 750mg/day.

b. Maintenance treatment:
ethionamide 500 – 750mg/day
moxifloxacin 400mg daily
PZA 1000mg - 2000mg/day
terizidone <50kg 500mg/day, >50kg 750mg/day
Although it’s becoming increasingly difficult to apply an individualised treatment, in certain circumstances this may be necessary. In such circumstances please consult Professors Willcox, Dheda, Mendelson or Drs Dlamini and Boyles (GSH) or Drs. Taljaard, Prozesky, Botha (Tygerberg Adult Infectious Diseases Unit) or Professor Schaaf (Tygerberg Paediatrics)

Total duration of treatment should be at least 24 months.
All treatment must be fully supervised.

Progress should be monitored by monthly sputum smears and cultures for the duration of therapy.
Surgery should be considered in patients with localised disease which remains culture positive after 6 months treatment or possibly prophylactically to prevent relapse especially if relapse has previously occurred.

**hepatotoxicity**

TB drug-induced hepatitis is over-diagnosed: the case definition is transaminases more than 5-fold elevated or more than 3-fold elevated with symptoms/jaundice. Antituberculosis therapy should be discontinued. The basis for the TB diagnosis should be reviewed. If the grounds for diagnosing TB were reasonable then commence three antituberculosis drugs with low/no hepatotoxic potential (see background therapy below). Selected patients may then be rechallenged once symptoms of hepatitis have resolved, bilirubin levels return to normal and transaminases have decreased to <100. Rechallenge is **NOT** recommended for those who have had fulminant hepatitis (defined as hepatic encephalopathy with coagulopathy).

The rechallenge regimen of the American Thoracic Society (Am J Respir Crit Care Med 2006;174:935–52) have been followed as these are simple and quick. Rechallenge with PZA was previously not recommended, but a recent trial has shown that most patients tolerate it. PZA rechallenge should be considered in patients with severe TB (e.g. miliary, meningitis) or with drug resistance. Transaminase levels, especially ALT, should be monitored frequently (e.g. three times weekly) during rechallenge and every two weeks for a month following rechallenge.

If possible all patients with a drug induced liver injury should have their TB isolates sent for drug susceptibility testing. Do not rechallenge with an agent to which the isolate is resistant.

**rechallenge regimen:**

<table>
<thead>
<tr>
<th>Background therapy</th>
<th>Ethambutol, streptomycin and moxifloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>day 1</td>
<td>Rifampicin 450 or 600 mg daily depending on weight</td>
</tr>
<tr>
<td>day 3</td>
<td>Check ALT</td>
</tr>
<tr>
<td>day 4-6</td>
<td>Add INH 300mg daily</td>
</tr>
<tr>
<td>day 7</td>
<td>Check ALT</td>
</tr>
<tr>
<td>day 8</td>
<td>Consider PZA rechallenge (see text)</td>
</tr>
</tbody>
</table>
NB: Duration of therapy should be individualised after rechallenge – consult ID for advice. The following are guidelines:

- Pyrazinamide not rechallenged/not tolerated: stop moxifloxacin and streptomycin, continue isoniazid, rifampicin and ethambutol for total duration 9 months
- Rifampicin not tolerated: continue streptomycin (for 2 months) and moxifloxacin, isoniazid, and ethambutol for total duration of 18 months
- Isoniazid not tolerated: stop moxifloxacin and streptomycin, add ethionamide (if tolerated – otherwise use ofloxacin) to rifampicin and ethambutol for total duration 12 months

**Pneumocystis**
cotrimoxazole - one tablet (80/400mg) for each 4kg body weight per day This dose should be divided into 3 or 4 doses a day giving no more than 4 tablets per dose. IV therapy is seldom indicated Therapy should be continued for 3 weeks. Adjunctive prednisone 40mg 12 hourly should be given to hypoxic patients and tapered over 3 weeks. See page 42 for alternative and maintenance therapy.

**Nocardia**
cotrimoxazole - two tablets 12 hourly for at least six months. In CNS or disseminated disease, one tablet (80/400mg) for each 4kg body weight per day. This dose should be divided into 3 or 4 doses a day giving no more than 4 tablets per dose. Reduction in dose should be considered after a clinical response has been established.

alternative therapies are available - discuss with microbiologist

**Legionella**
a macrolide or a quinolone

**CNS INFECTIONS**

**Meningitis**

**Empiric therapy (presumed bacterial meningitis)**

- ceftriaxone 2g 12 hourly
  - if older than 50 yrs, alcoholic, immunocompromised or severely debilitated add ampicillin to above regimen to cover *Listeria* empirically

Adjunctive steroid therapy, given before antibiotic administration, has been shown to reduce the risk of deafness (0.15 mg/kg/dose dexamethasone or betamethasone given 6 hourly for 2-4 days). Steroids should only be given if the diagnosis of bacterial meningitis is certain and if the patient is HIV negative.

**Directed therapy**

**Penicillin sensitive organism**
penicillin 6MU 6 hourly

**Staphylococcus (cloxacillin sensitive)**
cloxacillin 3g 6 hourly

**Gram negative bacilli**
ceftriaxone as above for 21 days

**Listeria monocytogenes**
penicillin given as above or ampicillin (2g 4 hourly) for at least 21 days

**M. tuberculosis**
see under tuberculosis page 28

**Cryptococcus**
See under fungal infections page 40
If only penicillin has been used to treat meningococcal meningitis, ciprofloxacin 500 mg STAT must be given to the patient to eradicate nasopharyngeal carriage. This should be given at the end of penicillin therapy as adverse reactions to ciprofloxacin may be falsely attributed to the penicillin. As ceftriaxone will also eradicate nasal carriage, ciprofloxacin is not required if initial therapy was this agent.

**Brain abscess**

ceftriaxone (2g 12 hourly) plus metronidazole

In patients who present with no signs of inflammation and in those whose CRP rapidly returns to normal, two to three weeks of IV therapy is usually sufficient along with surgical drainage. Longer therapy may be required in patients who do not settle. IV therapy should be followed by oral therapy once the CRP has begun to fall if a suitable oral agent is available. This should be continued for two – three months with careful follow-up.

**URINARY TRACT INFECTIONS**

**Acute uncomplicated lower UTI**

Short course oral ciprofloxacin – 500mg 12 hourly for 3 days

This short course regimen should only be considered in otherwise healthy, non-pregnant women of childbearing age with symptoms of less than one week duration. Its use in other categories of patients is associated with an unacceptable failure rate.

**Complicated UTIs** (includes all men, catheterised patients, pregnant women and patients with abnormal urinary tracts)

- **lower tract infections**
  - Oral: ciprofloxacin (500mg 12 hourly), cefuroxime (250mg 12 hourly) or co-amoxiclav.
  - Parenteral: gentamicin or ceftriaxone if aminoglycosides not appropriate
  - therapy for 7 days (if quinolones used, 5 days may be sufficient)
  - if associated with a urinary catheter – remove or replace catheter

- **upper tract infections**
  - (patients with signs such as significant fever ≥38°C, rigors, vomiting or loin pain)
  - therapy as above, but for 10 - 14 days (7 days for a quinolone)

Empiric therapy should be modified once organism sensitivity is known. Amoxicillin is still useful in patients with sensitive organisms, but is inappropriate for empiric therapy due to high levels of resistance.
Candiduria

See recommendation pg 40 (Fungal Infections).

Prostatitis

- acute: quinolone for 14 days
- chronic: quinolone 6 weeks therapy required

OBSTETRIC AND GYNAECOLOGICAL INFECTIONS

Candida vaginitis

Clotrimazole vaginal pessary 500mg single dose. If vulval irritation, add clotrimazole cream to vulva twice daily continued for three days after symptoms resolve. For difficult cases fluconazole 150mg stat dose may be used if motivated for (Brit J Obs Gyn 1989;96:226).

Trichomoniasis

metronidazole 2g as a single dose

Pelvic infection

- stage 1: ceftriaxone 250mg IM STAT plus doxycycline for 14 days and metronidazole 400mg 12 hourly for 14 days
- Azithromycin for 7-10 days is an alternative to doxycycline
- stage 2 or 3: Penicillin, gentamicin plus metronidazole OR ceftriaxone plus metronidazole
(If using penicillin/gentamicin/metronidazole, add stat dose of ceftriaxone 250mg IM for gonorrhoea).
Change to oral doxycycline and co-amoxiclav. **There is no need to continue metronidazole once co-amoxiclav has been commenced.**

Intrauterine infection following rupture of membranes

ceftriaxone IV and metronidazole

Puerperal sepsis

penicillin and gentamicin (or ceftriaxone if breast feeding) plus metronidazole, followed by co-amoxiclav or cefuroxime plus metronidazole

Acute pyelonephritis in pregnancy

ceftriaxone followed by cefuroxime or co-amoxiclav orally for a total of 14 days
SEXUALLY TRANSMITTED INFECTIONS

Syndromic management:

**genital ulcer**

benzathine penicillin 2.4MU IM STAT plus
erythromycin 500mg 6 hourly for 7 days plus
aciclovir 400mg 8 hourly for 7 days

**vaginal discharge (if not due to candida)**

cefixime 400mg orally or ceftriaxone 250mg IM STAT plus
doxycycline 100mg 12 hourly for 7 days plus
metronidazole 2g STAT

**urethral discharge**

cefixime 400mg orally or ceftriaxone 250mg IM STAT plus
doxycycline 100mg 12 hourly for 7 days
If symptoms persist, and above therapy was adhered to, give metronidazole 2g stat.

**Syphilis**
If there are no clinical signs for staging, regard as latent

**primary and secondary**

benzathine penicillin (2.4MU IM as a single dose)
  or
erythromycin (500mg 6 hourly) for 14 days (only for pregnant women, who must be given a course of doxycycline after delivery as erythromycin does not reliably treat syphilis)
  or
ceftriaxone 1g daily for 14 days
  or
doxycycline (100mg 12 hourly) for 14 days

**latent and syphilis in HIV positive patients**

benzathine penicillin (2.4MU IM) at weekly intervals for 3 weeks
  or
erythromycin (500mg 6 hourly) for 28 days (only for pregnant women, who must be given a course of doxycycline after delivery as erythromycin does not reliably treat syphilis)
  or
ceftriaxone 1g daily for 14 days
  or
doxycycline (100mg 12 hourly) for 28 days

**neurosyphilis**

penicillin G (4MU 4 hourly) for 14 days or by continuous infusion. Consider adding two doses of benzathine penicillin (2,4 MU IM; one week apart) after completion of IV therapy
  or
procaine penicillin (2.4MU IM daily) plus probenecid (500mg 6 hourly) for 14 days

**pregnancy**

as above, but only penicillin reliably treats the baby - consider desensitisation in penicillin-allergic patients

**Gonorrhoea**

ceftriaxone 250mg STAT OR cefixime 400 mg PO STAT

**disseminated/arthritis**

ceftriaxone 1g daily for 2 weeks (ciprofloxacin can be used if sensitivity established)
<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydial infection</em></td>
<td>doxycycline (100mg 12 hourly) for 7 days</td>
</tr>
<tr>
<td><em>Chancroid</em></td>
<td>erythromycin 500mg 6 hourly for 7 days</td>
</tr>
<tr>
<td><em>Trichomonas</em></td>
<td>metronidazole 2g STAT</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>Can use metronidazole 2g STAT as in syndromic management but 400mg 12hourly for 7 days has been shown to be more effective</td>
</tr>
</tbody>
</table>

**PERITONITIS**

*Surgical*

*Spontaneous (in patients with pre-existing liver disease)*

*Peritonitis in dialysis patients*

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td>penicillin, gentamicin and metronidazole</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>ceftriaxone</td>
</tr>
<tr>
<td>Peritonitis in dialysis patients</td>
<td>Vancomycin: 2 gm IP. Repeat after 5-7 days if appropriate or 15 mg/ml in every exchange. Cefotaxime: 2 gm IP loading, 125 mg/l maintenance in every exchange or 1 gram daily in a single bag. Rationalise once sensitivity of the organism is known.</td>
</tr>
</tbody>
</table>

**GASTROINTESTINAL INFECTIONS**

*Shigellosis*

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid</td>
<td>ciprofloxacin for 7 days is the drug of choice (ceftriaxone for 7-14 days is an alternative)</td>
</tr>
<tr>
<td>Salmonellosis (non-typhoid salmonellas)</td>
<td>Fluid replacement only for most immunocompetent patients HIV positive patients should receive ciprofloxacin for 4 weeks due to the high risk of relapse.</td>
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*Amoebiasis (including liver abscess)*

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<td>Giardiasis</td>
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**GASTROINTESTINAL INFECTIONS**

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</tbody>
</table>
**Pseudomembranous colitis**

stop causative antimicrobial agent if possible
oral metronidazole 400mg 8 hourly for 10 days
or oral vancomycin 125mg 6 hourly for 10 days
if poor response or severe disease.

Consult with GIT unit in severe cases –
combination therapy (metronidazole plus
vancomycin) may be indicated.

**Isospora belli**

co-trimoxazole 2 tabs (2X80/400mg) 6 hourly for
10 days . Alternative ciprofloxacin 500mg 12hrly
if allergic
followed by maintenance therapy - see page 43
Discuss with ID specialist if recurrent infection

**Cryptosporidium**

no effective treatment available at present but
patients respond well to ART.

**Microsporidium**

albendazole 400mg 12 hourly for one month
(only some species respond)

**Helicobacter pylori**

metronidazole 400mg 12 hourly plus amoxicillin
1g 12 hourly plus a proton pump inhibitor for 14
days
clarithromycin can be substituted for either of
the above drugs for allergy or treatment failure

---

**HELMINTHIC INFESTATIONS**

**Ascaris, Trichuris, Enterobius, Taenia, hookworm**

albendazole 400mg stat or mebendazole
suspension 100mg 12 hourly for 3 days. In
heavy mixed infestations involving Trichuris, a
single daily dose of albendazole may be
inadequate and the dose may be given for 3
consecutive days.

**Hydatid disease**

albendazole 15mg/kg/day up to 800mg/day
given 12 hourly for at least three months
In difficult cases (e.g. bone) extended therapy
may be required.
If surgery or PAIR (Percutaneous Aspiration
Injection of scolicidal & Re-aspiration) is
considered, treat for at least four days before
and one month after the procedure.

**Cysticercosis**

The decision to treat will depend on
the anatomical situation of the
lesions. Patients with
intraventricular cysts will benefit from
chemotherapy whereas patients with
extensive intracranial disease may
not, due to the effects of treatment-
induced inflammation
albendazole 800mg/day given 12 hourly
(15mg/kg/day in children) for 8 days
praziquantel 50-100mg/kg/day given 8 hourly for
15-30 days.
Given together with corticosteroids to minimise
inflammatory reaction, eg. dexamethasone
8mg/day po in divided doses for 8 days
**Schistosomiasis**
praziquantel 40mg/kg as a single dose

**Fascioliasis**
Triclabendazole 10mg/kg single dose

**SOFT TISSUE INFECTIONS**

**Erysipelas**
penicillin IV or IM followed by oral penicillin or amoxicillin

**Cellulitis**
IV cloxacillin - convert to oral flucloxacillin 500mg 6 hourly (note that it is unnecessary to add penicillin as cloxacillin will also cover streptococci)

Clindamycin is available for penicillin allergic patients or cases where clinical response to cloxacillin is poor. Where infection with gram-negative bacilli and/or anaerobes is suspected (e.g. in diabetics or patients with peripheral vascular disease) add gentamicin and metronidazole or use co-amoxiclav.

**Wound infection**
cloxacillin IV or oral flucloxacillin
Many infected wounds do not require antibiotic therapy and resolve with drainage and dressing.
If a mixed infection is suspected (e.g. post gynaecological or abdominal surgery) - consider penicillin, aminoglycoside and metronidazole or co-amoxiclav.

**Clostridial myonecrosis**
metronidazole (or penicillin)

**Necrotising fasciitis**
penicillin, aminoglycoside and metronidazole
Substitution of penicillin and metronidazole with clindamycin may be considered, co-amoxiclav can be used if aminoglycoside contraindicated.

**Tetanus**
metronidazole 500mg 6 hourly for 7-10 days debride any wounds that are present

**BURNS**

**Streptococcus pyogenes**
co-amoxiclav or clindamycin for 10 days (used because penicillin often fails due to the presence of staphylococcal beta-lactamase in this situation)

**Septicaemia**
Therapy would depend on sensitivity patterns of organisms prevalent in the local burns unit
Rationalise once sensitivity of the organism known.
ORTHOPAEDIC INFECTIONS

**Septic arthritis, osteomyelitis empiric therapy**
cloxacillin IV, change to oral flucloxacillin 1g 6 hourly when appropriate - for a total of 4 - 6 weeks therapy
Fusidic acid may be added for non-response or relapse.

Therapy should be adjusted in response to blood or pus culture results.

- *gonococcal* ceftriaxone for 2 weeks or ciprofloxacin if sensitivity has been established in the laboratory

*Open fractures* see prophylaxis page 46

EYE INFECTIONS

**Conjunctivitis**
chloramphenicol eye drops or ointment
if no response or if culture indicates resistance, use ciprofloxacin eye drops (restricted)

- *gonococcal* ceftriaxone 1g as a stat dose

**Blepharitis**
tetracycline eye ointment or fusidic acid eye drops (available only to the Ophthalmology Dept. or on request)
doxycline 100mg daily for 3 months has been successful in difficult cases

**Corneal ulcers**
quinolone eye drops - if no response or if indicated by culture results, change to topical and subconjunctival gentamicin and cefazolin

**Herpetic ulcers**
topical acyclovir

**Endophthalmitis**
intravitreal vancomycin 1mg and ceftazidime 2.25mg with dexamethasone 0.2mg unless fungal infection suspected
oral ciprofloxacin 750mg 12 hourly may be added in difficult cases

**Post intraocular surgery** no standard recommendation at present

**Fungal infections**
these infections are rare and no standard recommendation exists - consult the Ophthalmology Dept.

IV amphotericin B may be considered in severe cases.

**Penetrating eye injuries** see prophylaxis page 46
FUNGAL INFECTIONS

Aspergillosis

invasive

voriconazole 200 mg 12 hourly (400mg 12 hourly loading dose on first day) is the agent of choice

amphotericin B 1mg/kg/day The duration of therapy is yet to be defined but total doses of 2 - 2.5g are usually recommended.

Candidiasis

oral

nystatin suspension 1ml 6 hourly swirled and swallowed

oesophageal

fluconazole 200 mg daily for two weeks

specify if patient is HIV positive so that pharmacy can issue donated stock – this does not require microbiology release

vaginal

Local preparations are available and are recommended in pregnancy. For difficult cases fluconazole 150mg stat dose may be used if motivated for (Brit J Obs Gyn 1989;96:226).

urinary tract

Asymptomatic candiduria in a catheterised patient does not need to be treated (Pappas, CID 2009;48:503), except in high risk patients (neonates, neutropenic patients, or those undergoing urological procedures. Removing or changing the catheter is the most appropriate action and should be the first response (if possible) in any patient with candiduria.

In symptomatic patients (or asymptomatic neonates or neutropenic patients), where candiduria is thought to be associated with disseminated candidiasis, then either fluconazole 400mg daily, or amphotericin B 0.7mg/kg/day should be used.

For candida cystitis, fluconazole 200mg daily for 2 weeks is recommended.

In refractory cases, or in cases with azole-resistant cystitis, amphotericin B bladder washouts may be useful. Give amphotericin B bladder washouts for 3 days using one litre per day of 50mg amphotericin B per litre. Instill an aliquot of 200-300ml, then cross-clamp the catheter for 60-90 minutes. Allow bladder to drain and then repeat the procedure.

positive blood cultures (in immunocompetent patients)

amphotericin B 0.7mg/kg/day If IV catheter related, the catheter should be removed Therapy should be continued for two weeks after the last positive blood culture. Blood cultures must to be repeated while the patient is on therapy. Fluconazole 400mg orally daily is an effective alternative. (NEJM 1994;331:1325-
positive blood cultures (in immunocompromised patients) or suspected metastatic infection (including endocarditis)

amphotericin B 0.7mg/kg/day The end point of therapy is ill defined. An approach is to continue therapy for one month after the patient becomes afebrile. In endocarditis surgery is almost always required and therapy should be continued for 6 - 10 weeks thereafter.

Intra-abdominal

Isolation of candida from the initial surgical specimens does not always require therapy. However repeated isolation or symptomatic infection should be treated with amphotericin B 0.7mg/kg/day for two weeks, or fluconazole 400mg daily

Cryptococcosis

HIV positive

amphotericin B 1 mg/kg/day + fluconazole 800mg daily for 14 days. In the acute phase daily therapeutic lumbar puncture, removing sufficient CSF to lower pressure to 18cm H₂O is important in patients with raised intracranial pressure. Thereafter fluconazole 400mg daily orally for 8 weeks followed by maintenance therapy. In recurrent infection, 800mg daily for 8 weeks followed by 400mg daily maintenance therapy

HIV negative

amphotericin B 1 mg/kg/day for 6 weeks or until antigen titre is negative or stable at 8 or less and cultures are negative. Note that the antigen may remain detectable for months after successful therapy. Infectious diseases should be consulted in all cases.

MALARIA

Uncomplicated Plasmodium falciparum

Disease severity is frequently underestimated, so careful monitoring is mandatory. Patients with uncomplicated malaria have mild symptoms, are ambulant, with normal mental function, and have no organ dysfunction.

If in any doubt of the severity of the malaria, discuss immediately with an ID specialist.

Oral artemether-lumefantrine (Coartem®) is indicated for non-severe cases of malaria.

Dose: 4 tablets (80mg artemether and 480mg lumefantrine per tablet) repeated after 8 hours on day one and then 12 hourly for a further 2 days.

Give each dose with fat containing food / drink to ensure adequate absorption.
**Severe P. falciparum**
e.g. impaired consciousness, convulsions, severe weakness, severe vomiting, dehydration, respiratory distress, macroscopic haematuria, abnormal bleeding (retinal haemorrhages, DIC), shock, visible jaundice, severe anaemia (Hb<5g/dl); hypoglycaemia (Hgt<2.2mmol/l); acidosis (pH<7.25 / bicarb < 15mmol/l); renal impairment (creatinine >250µmol/l); hyperlactataemia (venous lactate>4mmol/l); parasite density >4%.

**NB:** **ALL** severe falciparum malaria cases MUST be discussed with an ID specialist on admission

**IVI artesunate** is the preferred treatment. Dose: 2.4mg/kg IVI at 0, 12 and 24hr and then daily until able to tolerate oral treatment.

Only available at hospitals registered in the Parenteral Artesunate Access Programme, including Groote Schuur, Tygerberg, Jooste and Victoria Hospitals. Contact ID specialist on Call to assist with dosing and completion of forms for Section 21 MCC approval. To enrol in access programme, contact Prof Karen Barnes on 082 440 2542.

**ALTERNATIVE REGIMEN**
Commence therapy with **IV quinine** 20mg/kg stat given over 4 hours followed by 10mg/kg 8 hourly over 4 hours.

Once the patient improves, follow with artemether-lumefantrine, dosed as above.

Chloroquine 600 mg stat followed by 300 mg 8 hours later, then 300 mg daily for two days. This must be followed by primaquine base 15mg daily for 14 days to eradicate the hypnozoite stage in the liver and prevent relapse. Primaquine is currently available from GSH with MCC authorisation. Exclude G6PD deficiency before treating with primaquine.

**If unsure of species – treat for P. falciparum**

**TOXOPLASMOSIS**

- immunocompetent patients
  - no treatment usually required
  - pregnant women
    - spiramycin 3g/daily is the treatment of choice, but both this and the alternative, sulphadiazine are unavailable in S.A. Consider cotrimoxazole as below (risk to the foetus if used late in pregnancy)

- immunosuppressed patients both HIV positive and HIV negative patients
  - cotrimoxazole one tablet (80/400mg) for each 8kg body weight per day, given 12hourly. The usual dose is therefore 4 tabs 12hourly – given for 1 month – followed by half the dose (2 tabs) 12hrly for 3 months (AAC 1998;42:1346-9)
  - See page 42 for alternative and maintenance therapy.
BRUCELLOSIS
doxycycline 100mg 12 hourly for 6 weeks PLUS streptomycin daily for 3 weeks has been shown to be the most efficacious combination therapy, especially with bone involvement. Rifampicin 15mg/kg/day given 12 hourly for 6 weeks can replace the streptomycin if necessary.

TICK BITE FEVER
doxycycline 100mg 12 hourly for 7 days - if IV required use IV ciprofloxacin or chloramphenicol. clarithromycin is an alternative for milder disease when tetracyclines are contraindicated (eg in pregnancy, children <8 years old)

TREATMENT OF OPPORTUNISTIC INFECTIONS IN AIDS PATIENTS
(Alternative agents are given as these patients are very often intolerant of drugs) For details on cotrimoxazole desensitisation see cotrimoxazole page 14)

Maintenance therapy is sometimes referred to as secondary prophylaxis in other texts.
Patients on HAART who have CD4 counts of >200 for more than 6 months may discontinue maintenance therapy

*Pneumocystis*
cotrimoxazole - one tablet (80/400mg) for each 4kg body weight per day. This dose should be divided into 3 or 4 doses a day giving no more than 4 tablets per dose.

IV therapy is seldom indicated

or clindamycin plus primaquine 15mg daily

primaquine is currently only available with MCC release (consult Infectious Diseases if this therapy is contemplated).

Therapy should be continued for 3 weeks.

Adjunctive prednisone 40mg 12 hourly should be given to hypoxic patients. This is given for 5 days followed by 40mg daily for 5 days and then 20mg daily for 11 days.

maintenance therapy
cotrimoxazole 2 tabs (2X80/400mg) daily

or dapsone 100mg daily

*Toxoplasma*
cotrimoxazole one tablet (80/400mg) for each 8kg body weight per day, given 12hourly. The usual dose is therefore 4 tabs 12hourly – given for 1 month – followed by half the dose (2 tabs) 12hrly for 3 months

AAC 1998;42:1346-9

or clindamycin 600mg 8 hourly, pyrimethamine
50mg daily plus folinic acid 15 mg daily (to prevent bone marrow suppression from pyrimethamine – folic acid is ineffective) for 6 weeks.

**maintenance therapy**
cotrimoxazole 2 tabs (2X80/400mg) daily

**or**
clindamycin 300-450 8 hourly, pyrimethamine 25-50 mg daily plus folinic acid

**Cryptococcus neoformans**
amphotericin B 1 mg/kg/day + fluconazole 800mg daily for 14 days. In the acute phase daily therapeutic lumbar puncture, removing sufficient CSF to lower pressure to 18cm H₂O is important in patients with raised intracranial pressure.

Thereafter fluconazole 400mg daily orally for 8 weeks.

**maintenance therapy**
fluconazole 200mg daily for life, or until CD4 count >200 (provided minimum 12 months therapy has been given).

**relapse**
amphotericin B 1 mg/kg/day for 14 days

Thereafter fluconazole 800mg daily orally for 8 weeks followed by maintenance therapy using 400mg daily

**Candida (oesophageal)**
fluconazole 200 mg daily for two weeks

**maintenance therapy**
not usually recommended

**Mycobacterium avium complex**
clarithromycin 500mg 12 hourly plus ethambutol 15mg/kg/day (treatment is continued until CD4 count rises >100 on antiretroviral therapy). Azithromycin may be preferable to clarithromycin depending on ART regimen

**Herpes simplex**
aciclovir 400mg 8 hourly for 7 - 14 days

**maintenance therapy**
not usually recommended - acyclovir 400mg 12 hourly if frequent recurrences

**Isospora belli**
co-trimoxazole 2 tabs (2X80/400mg) 6 hourly for 10 days

**or**
ciprofloxacin 500mg 12 hourly for 10 days

**maintenance therapy**
cotrimoxazole 2 tabs (2X80/400mg) daily

**recurrence**
cotrimoxazole plus ciprofloxacin for 10 days followed by maintenance therapy as above
Cryptosporidium  no effective treatment available

Microsporidium  albendazole 400mg 12 hourly for one month

PROPHYLAXIS

SURGICAL PROPHYLAXIS

GENERAL PRINCIPLES

- The need for prophylactic antibiotic therapy is based on the risk of wound contamination
- Antibiotic prophylaxis is not required for clean operations/procedures in patients who have minimal risk of contamination. In all other situations, prophylaxis should be considered
- Prophylaxis must be given within 60 minutes before the first incision, usually at induction
- The prophylactic dose is a single dose equal to the standard therapeutic dose.
- A second dose is given only if there is massive blood loss or surgery is prolonged, i.e. 2-3 hours for cefazolin OR > 8 hours for metronidazole IV.
- Post-operative doses of prophylactic drugs are generally unnecessary.
- Prophylactic antibiotics do not replace the need for good surgical technique and adherence to infection control measures.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Antibiotic used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiothoracic surgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td>• further doses of 1g may be given 8 hourly for up to 24 hours. With bypass surgery or with excessive blood loss give a second 1g dose at 2-3 hours.</td>
</tr>
<tr>
<td>Lower limb amputation</td>
<td>• cefazolin, IV, 1 g *  PLUS</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Orthopaedic surgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td>• for trauma related procedures see pg 47</td>
</tr>
<tr>
<td>Head and neck surgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td>For procedures involving the oropharyngeal mucosa</td>
</tr>
<tr>
<td></td>
<td>ADD</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Abdominal surgery Upper</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td>GIT</td>
<td></td>
</tr>
</tbody>
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* If patient >80 kg use 2g dose
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<tr>
<td>Colorectal and appendix</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td><strong>PLUS</strong></td>
</tr>
<tr>
<td></td>
<td>• metronidazole IV, 500 mg</td>
</tr>
<tr>
<td></td>
<td>If perforation has occurred, treat patient for infection with a course of</td>
</tr>
<tr>
<td></td>
<td>appropriate antibiotics (refer to page 35 for treatment of peritonitis)</td>
</tr>
<tr>
<td>Biliary</td>
<td>Only for high risk patients: bile obstruction, jaundice, biliary stones or</td>
</tr>
<tr>
<td></td>
<td>cholecystitis, or re-operation, ERCP:</td>
</tr>
<tr>
<td></td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td><strong>PLUS</strong></td>
</tr>
<tr>
<td></td>
<td>• metronidazole IV, 500 mg</td>
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<tr>
<td>Pelvic surgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td><strong>PLUS</strong></td>
</tr>
<tr>
<td></td>
<td>• metronidazole IV, 500 mg</td>
</tr>
<tr>
<td>ENT surgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td>For procedures involving the oropharyngeal mucosa:</td>
</tr>
<tr>
<td></td>
<td>ADD</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Nephro-urological surgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
<tr>
<td></td>
<td>• Treat patients with preoperative bacteriuria according to urine MC+S.</td>
</tr>
<tr>
<td></td>
<td>• Trans-rectal prostate biopsy: oral ciprofloxacin 500mg 12hrs before and after</td>
</tr>
<tr>
<td></td>
<td>surgery</td>
</tr>
<tr>
<td></td>
<td>• Cystoscopy: 500mg ciprofloxacin before procedure</td>
</tr>
<tr>
<td>Ophthalmic surgery</td>
<td>• chloramphenicol 0.5% ophthalmic drops, instil 1 drop 2–4 hourly for 24 hours</td>
</tr>
<tr>
<td></td>
<td>prior to surgery, preferably use separate vial for each patient.</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>• cefazolin, IV, 1 g *</td>
</tr>
</tbody>
</table>

**SEVERE β-LACTAM ALLERGY**
In most situations use clindamycin, IV, 600 mg. Due to increasing clindamycin resistance in anaerobic bacteria, metronidazole may be added if anaerobic cover is needed.

Where Gram-negative cover is required, e.g., colo-rectal, biliary or pelvic surgery, add gentamicin 6 mg/kg as a single dose.

* If patient >80 kg use 2g dose
ANTIBIOTIC PROPHYLAXIS IN TRAUMA

Bites

- There is no clear evidence of benefit for antibiotic prophylaxis in minor animal bites.
- High dose oral co-amoxiclav should be used in severe animal bites and all human bites.
- In penicillin allergic patients tetracycline or clindamycin would be appropriate choices.
- Remember to check whether prophylaxis is needed for rabies, tetanus or HIV.

Open fractures

Distinguish between

- open fractures with minimal contamination which require cefazolin IV x 48 hrs
- open fractures with significant contamination (high risk of environmental contamination, delay in treatment or significant tissue destruction). These require early treatment with cloxacillin, gentamicin and metronidazole.

Head injuries

Compound depressed skull fractures and penetrating spinal cord injuries: Ceftriaxone 2g/day plus metronidazole for 5 days
CSF leaks: No prophylactic antibiotics

Penetrating eye injuries

Cefazolin 1g IV 8 hrly plus ciprofloxacin 750mg 12 hrly, both for 3 days

MEDICAL PROPHYLAXIS

RHEUMATIC FEVER
– prevention of recurrences (secondary prophylaxis)

- benzathine penicillin 1.2MU IM every 4 weeks (every 3 weeks if possible in motivated patients with severe cardiac lesions)
- Patients unable to have IM injections – penicillin V 250mg 12 hourly
- Penicillin-allergic patients, erythromycin 250mg 12 hourly

Duration:
- without proven carditis - 5 years after last attack or until 18 (whichever is longer)
- with mild carditis (mild regurgitation or healed carditis) - 10 years after last attack or until 25 (whichever is longer)
- with severe valvular disease - lifelong

ENDOCARDITIS PROPHYLAXIS

These recommendations are based on those of the American Heart Association as published in AHA Scientific Statement. 1998

Table 1 lists the cardiac conditions for which endocarditis prophylaxis is and is not recommended.
Table 2 lists the clinical situations in which endocarditis prophylaxis should be given.
TABLE 1 : CARDIAC CONDITIONS

ENDOCARDITIS PROPHYLAXIS RECOMMENDED
Prosthetic cardiac valves, including bioprosthetic and homograft valves
Previous bacterial endocarditis even in the absence of heart disease
Surgically constructed systemic-pulmonary shunts or conduits
Congenital cardiac malformations other than isolated secundum atrial septal defect*
Rheumatic and other acquired valvular dysfunction, even after valvular surgery*
Hypertrophic cardiomyopathy*
Mitrval valve prolapse with valvular regurgitation*

(*The need for prophylaxis in these conditions has been questioned and recent guidelines of both the AHA and British Society for Antimicrobial Chemotherapy have removed them from the list. This is currently under consideration by South African cardiologists.)

ENDOCARDITIS PROPHYLAXIS NOT RECOMMENDED
Isolated secundum atrial septal defect
Surgical repair without residua beyond 6 months of secundum atrial septal defect, ventricular septal defect, or patent ductus arteriosus
Previous coronary artery bypass graft surgery
Mitrval valve prolapse without valvular regurgitation#
Physiological, functional, or innocent heart murmurs
Previous Kawasaki disease without valvular dysfunction
Previous rheumatic fever without valvular dysfunction
Cardiac pacemaker and implanted defibrillators

TABLE 2: DENTAL OR SURGICAL PROCEDURES

ENDOCARDITIS PROPHYLAXIS RECOMMENDED
All dental procedures involving dento-gingival manipulation
Tonsillectomy and/or adenoidectomy
Surgical operations that involve intestinal or respiratory mucosa
Bronchoscopy with a rigid bronchoscope
Nasal packing and nasal intubation
Sclerotherapy for oesophageal varices
Oesophageal dilation
Oesophageal laser therapy
Biliary tract surgery
Gall stones – lithotripsy
ERCP
Cystoscopy
Urethral dilatation
Urethral catheterization if urinary tract infection is present#
Prostatic surgery
Incision and drainage of infected tissue#
Vaginal hysterectomy
Caesarean section
Vaginal delivery in the presence of infection# (includes prolonged labour with prolonged rupture of membranes and difficult manipulative vaginal deliveries)
Cosmetic piercing of tongue or involving oral mucosa (such procedures should be discouraged in patients who are at risk for endocarditis)

**ENDOCARDITIS PROPHYLAXIS NOT RECOMMENDED**
- Dental procedures not likely to induce gingival bleeding, such as simple adjustment of orthodontic appliances or fillings above the gum line
- Injection of local intraoral anaesthetic (except intraligamentary injections)
- Shedding of primary teeth
- Tympanostomy tube insertion
- Endotracheal intubation
- Bronchoscopy with a flexible bronchoscope, with or without biopsy
- Cardiac catheterization
- Transoesophageal ECG
- Oesophageal varices - banding
- Endoscopy with or without gastrointestinal biopsy
- Barium enema
- Proctoscopy
- Renal stones – lithotripsy
- Circumcision
- Cosmetic piercing involving urethral mucosa

In the absence of infection; urethral catheterization, dilatation and curettage, uncomplicated vaginal delivery, therapeutic abortion, sterilization procedures, or insertion or removal of intrauterine devices

*Antibiotic therapy should be directed against the known or most likely bacterial pathogen.

**TABLE 3: RECOMMENDED REGIMENS FOR DENTAL, ORAL OR UPPER RESPIRATORY TRACT PROCEDURES**

<table>
<thead>
<tr>
<th>Standard regimen</th>
<th>amoxicillin 3g orally 1 hour before procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal packing and nasal intubation</td>
<td>cloxacillin 2g IV at induction or just prior to procedure</td>
</tr>
<tr>
<td>Penicillin allergic patients and patients who are on long-term penicillin prophylaxis for rheumatic fever</td>
<td>clindamycin 600mg orally 1 hour before procedure</td>
</tr>
<tr>
<td>Patients unable to take oral medications</td>
<td>ampicillin 2g IV at induction or IM 30 minutes before procedure</td>
</tr>
<tr>
<td>Patients unable to take oral medications who are penicillin allergic or on long-term penicillin prophylaxis</td>
<td>clindamycin 600mg IV given in 50ml over 10 minutes at induction or up to 30 minutes before procedure</td>
</tr>
</tbody>
</table>
TABLE 4: RECOMMENDED REGIMENS FOR GENITOURINARY OR GASTROINTESTINAL PROCEDURES

For genitourinary or gastrointestinal procedures in which prophylaxis is recommended (see Table 2 above) the choice of agent is dictated by the common occurrence of enterococcal infections and the possibility of aerobic gram-negative organisms.

**Standard regimen**

ampicillin 2g IV plus gentamicin 1,5mg/kg at induction or up to 30 minutes before procedure. If surgery lasts more than 6 hours the parenteral regimen may be repeated once 6 hours after the initial dose. (Gentamicin would not normally be given at a dosage interval of 6 hours but this is done here for practical purposes - so that both drugs can be given together.)

**Penicillin allergic patients and patients who are on long-term penicillin prophylaxis for rheumatic disease**

vancomycin 1g given over 1 hour followed by gentamicin 1,5mg/kg at induction or up to 30 minutes before procedure. If surgery lasts more than 6 hours the gentamicin may be repeated 8 hours after the initial dose. No additional vancomycin is necessary.

**NOTE:** Patients with prosthetic heart valves were previously considered high-risk cases and parenteral prophylaxis was considered essential. The use of regimens as outlined above is now recommended for these patients.

**MALARIA PROPHYLAXIS**

Prophylaxis for malarious areas in sub-Saharan Africa:

- mefloquine 250mg weekly
- doxycycline 100mg daily
- atovaquone 250mg plus proguanil 100mg daily

Prophylaxis should be continued for 4 weeks after returning (except for atovaquone/proguanil which can be discontinued after 1 week).

**NOTE:** Avoidance of mosquito bites and application of insect repellents are vital adjuncts to chemoprophylaxis. Refer to Pharmacology Department, Medicines Information Centre – 406-6783/6780 or Dr Jantjie Taljaard at the Infectious Diseases Unit at Tygerberg Academic Hospital – 083 419 1452 if further information required.
MENINGOCOCCAL MENINGITIS PROPHYLAXIS

Prophylaxis is only given to household contacts and medical staff who have performed mouth to mouth resuscitation or endotracheal intubation on the patient. Ciprofloxacin 500mg STAT is the drug of choice. Alternatives include rifampicin or ceftriaxone.

Table 3: Antibiotics for chemoprophylaxis of meningococcal disease

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Dose</th>
<th>Route</th>
<th>Duration [Days]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>600mg bd.</td>
<td>10mg/kg bd.</td>
<td>PO</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>500mg</td>
<td>10mg/kg</td>
<td>PO</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>250mg</td>
<td>&lt;15 years 125mg</td>
<td>IM</td>
</tr>
</tbody>
</table>

ANTIVIRAL PROPHYLAXIS

HIV
PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV

- All pregnant women irrespective of CD4 count are eligible for ART and must be urgently referred to their nearest antiretroviral treatment centre to initiate HAART.
- For unbooked women nevirapine can be given in all stages of labour. It is only too late to give nevirapine if the baby is delivering imminently (the head is crowning).
- All babies on the PMTCT program should receive NVP daily after delivery for 6 weeks if they are formula fed or stop two weeks after weaning if breast-fed. Nevirapine dose for infants:
  - Birth weight 2.5 kg or more: 15 mg
  - Birth weight <2.5 kg:10 mg daily
  - If the baby delivers less than two hours after the mother takes nevirapine, the baby should receive a dose of nevirapine immediately after delivery.
  - Babies born more than two hours after the mother received nevirapine should receive a single dose at 6 - 72 hours.

HIV PROPHYLAXIS FOR RAPE SURVIVORS / POST-SEXUAL EXPOSURE

Rape survivors attending GSH and TBH within 72 hours of assault can obtain tenofovir PLUS emtricitabine (Truvada or Didivir) given once daily for 4 weeks, with monitoring as outlined for occupational exposures below. If the patient is able to tolerate a third drug, alluvia 2 tabs 12hrly should be administered. There is no evidence for starting ART after 72 hours.

References
MMWR January 21, 2005/Vol.54/RR-2
OCCUPATIONAL POST-EXPOSURE HIV PROPHYLAXIS

All exposures must be properly documented and followed up by the staff health clinic. Emergency post-exposure prophylaxis (PEP) is available in trauma unit (GSH) or Medical Emergencies F1 (TBH). The risk of a healthcare worker acquiring HIV following a percutaneous (needlestick or sharps) or mucosal splash injury with HIV-infected blood is very low at 0.3% and 0.09% respectively. The risk of acquiring HIV is increased when the sharps injury is deep, when the injury involves a hollow needle used in a vein or artery or when the source patient’s viral load is high. Zidovudine post-exposure has been shown to reduce the risk by 81%.

PEP should be started **immediately after the injury** even if the HIV status of the source patient is unknown. Delaying PEP will significantly reduce its efficacy and should be avoided. Animal data suggests that prophylaxis after 24 hours is ineffective and **every effort should be made to ensure that PEP is accessible to staff within this time period**. It is not unreasonable however to offer PEP up to 72 hours after the incident – these cases should be discussed with an ID specialist so that a clear risk-benefit assessment can be made. PEP should not be given to persons who are already HIV-infected.

Combination ART is advocated using 3 drugs (see table). Tenofovir and emtracitabine (Truvada or Didivir) od should be used as the backbone with addition lopinavir/ritonavir (Aluvia – 2 tablets 12 hourly (Southern African Journal of HIV Medicine 2008, Vol 9, No 3). Stavudine or zidovudine may be substituted for tenofovir, however zidovudine is strongly associated with gastrointestinal symptoms, especially within the first 2-3 days. If the source patient is on ART, the choice of PEP regimen should be discussed with an ID specialist. **All PEP must be continued for 28 days.**

PEP should **not** be offered for exposures to body fluids which carry no risk of infection (eg vomitus, urine, faeces or saliva) or when the source is known to be HIV seronegative. If there are features suggesting seroconversion illness, prophylaxis should be continued until the results of additional tests are available (discuss with an Infectious Diseases specialist).

Follow-up testing will be arranged through Staff Health. Other potentially transmissible pathogens such as hepatitis B, C and syphilis will be reviewed.

**Recommendations for post exposure prophylaxis (PEP) after exposure to infectious material (includes blood, CSF, semen, vaginal secretions & synovial/pleural/ pericardial/ peritoneal / amniotic fluid) from HIV seropositive patients.**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>HIV status of source patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive or Unknown*</td>
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<tr>
<td>Intact skin</td>
<td>No PEP</td>
</tr>
<tr>
<td>Mucosal splash/ Non-intact skin</td>
<td>3 Drugs</td>
</tr>
<tr>
<td>Percutaneous injury</td>
<td>3 Drugs</td>
</tr>
</tbody>
</table>

*If subsequent testing reveals the source to be HIV seronegative, PEP can be stopped. In the event of the source HIV status remaining unknown, the full 28 day course of PEP should be completed.
HEPATITIS A
- Household, community or health care workers in contact with a hepatitis A infected person can be given PEP if HepA IgG negative.
- Vaccine alone is favoured unless > 2 weeks since contact or if the contact is immunocompromised or has pre-existing liver disease where vaccine plus immune globulin should be given. The efficacy of the vaccine alone in persons over 40 years is not well established and HNIG should be given in addition.
- Infants < 1 year immunoglobulin should be given (vaccine not licensed for use in this age group)
  - Dose
    - Vaccine: 2 doses a month apart
    - Human normal immune globulin (HNIG): 0.02-0.04 ml/kg
    - Vaccine and immune globulin should be given at different sites

HEPATITIS B
- A previously vaccinated person with a surface antibody titre of > 10 IU/ml requires no PEP.
- Contacts are infectious if they are hepatitis B surface antigen-positive (HBsAg).
- Mucocutaneous exposure to blood and body fluids require PEP with hepatitis B immune globulin (HBIG) and vaccine.
- Institutional or household contacts (no defined exposure) require vaccine only.
- Newborns of HBsAg-positive mothers
  - If mother eAg positive: HBIG and vaccine (1st dose at birth)
  - If mother eAg negative: vaccine only (1st dose at birth)
- Dose (vaccine and immunoglobulin to be given at different sites)
  - HBIG (200 IU/2ml)
    - Newborn - <5 years: 200 IU
    - 5-9 years: 300 IU
    - >10 years: 500 IU
  - Vaccine: 3 doses at 0, 1 and 3 months

HEPATITIS C
- No effective PEP but early diagnosis and treatment is important.
- Baseline ALT and anti-HCV should be performed on the exposed healthcare worker.
- Follow-up testing at 6, 12 and 24 weeks advised. – do ALT and if increased do HCV RNA PCR

INFLUENZA
- Antiviral chemoprophylaxis for influenza is currently NOT recommended by the WHO. The WHO recommendations advise that post-exposure presumptive antiviral treatment may be of benefit in some higher risk situations, such as transplant patients, or patients with severe immunosuppression (e.g. those receiving chemotherapy). If such higher risk individuals have been exposed to a patient with influenza, strongly consider presumptive treatment with oseltamivir or zanamivir (Healthcare Workers’ Handbook on Influenza, April 2013: National Institute of Communicable Diseases/South African National Department of Health)
- Dose
  - Zanamivir: 10 mg twice daily (inhaled) for 10 days
  - Oseltamivir: 2 mg/kg/dose, maximum 75 mg/dose, twice a day for 5 days (extended treatment duration may be considered in selected cases)
MEASLES
- Household or community contacts.
- Vaccine (<72 hours post exposure) or HNIG can be given.
- Vaccine is not suitable for contacts <6 months old, pregnant women and immunocompromised contacts. These individuals should be given HNIG.
- Dose
  - Vaccine: 1 dose if >1 year old, if <1 year, repeat at 15 months
  - HNIG: 0.2-0.25 ml/kg (max 15 ml)

MUMPS
- No effective PEP.

RUBELLA
- No effective PEP.

RABIES
- Dog bites are the cause of most rabies cases in SA.
- PEP prophylaxis involves the use of vaccine ± rabies immune globulin (RIG).
- There is no cut-off time to start rabies PEP.
- Risk of acquiring rabies depends on the site and severity of the bite.
- Exposure
  - Low risk (superficial scratch – no bleeding, licking of broken skin): give vaccine only
  - High risk (bites and scratches that penetrate the skin and draw blood, licking of mucous membranes): RIG and vaccine
- Dose
  - Vaccine: 0.5-1 ml (depends on supplier) on day 0, 3, 7, 14 and 28 for immunocompromised persons and on day 0, 3, 7, and 14 for immunocompetent persons (MMWR Recomm Rep. 2010 Mar 19;59(RR-2):1-9). Vaccine is given into the deltoid (adults) or anterolateral thigh (infants). NOT into gluteus maximus.
  - RIG 20 IU/kg infiltrated into the wound, remainder into the buttock. Supplied in 2ml ampoules containing 300IU. Dose (ml) = body weight (kg) X 0.13.
- Clean the wound thoroughly with soap and water for 5 minutes then apply antiseptic solution e.g. 70% alcohol or iodine solution. Avoid suturing.
- Prophylactic antibiotics and tetanus toxoid should be given after high risk exposures.
- Late presentation (>48hrs) and immunocompromised people – as above but double dose of vaccine on day 0
- If previously immunised – only vaccine on day 0 & 3.

VARICELLA
- The recommended form of PEP following VZV exposure (chickenpox or shingles) depends on the context:
  - Healthy non-immune contacts: vaccine <72 hours post-exposure or acyclovir from day 7-21 post-exposure
  - Pregnant women who are not immune: Zoster immune globulin (ZIG) at any stage of pregnancy or acyclovir from day 7-21 post-exposure
  - Neonates born to mothers who develop chickenpox 7 days before, and up to 28 days after delivery: ZIG (acyclovir is a second option if ZIG is not available)
  - Infants under 6 months of age who are exposed to chickenpox (as maternal immunity is usually lost by 2-3 months): ZIG (acyclovir, a second option)
Immunocompromised patients: ZIG (vaccine is safe for most immunocompromised patients but the protective efficacy is less). Acyclovir is a second option.

- **Dose**
  - **Vaccine**
    - <13 years old: 1 dose
    - >13 years old: 2 doses 4 weeks apart
  - **Acyclovir**:
    - Adults: 800 mg 5 x daily
    - Children: 40 mg/kg/day in 4 divided doses
  - **ZIG (200 IU/2ml)**
    - 0-5 years: 2 ml
    - 6-10 years: 4 ml
    - 11-14 years: 5 ml
    - > 15 years: 6ml
ANTIMICROBIAL AGENTS IN PREGNANCY

GENERALLY CONTRAINDICATED
albendazole
erythromycin estolate
doxycycline
streptomycin
tetracyclines

TRY TO AVOID, USE ONLY IF ESSENTIAL
amikacin
nalidixic acid
aminoglycosides
ofloxacin (avoid during 1st trimester)
chloramphenicol*
pentamidine
ciprofloxacin (avoid during 1st trimester)
piperacillin/tazobactam
colistin
praziquantel (avoid during 1st trimester)
co-trimoxazole*
primaquine
fluconazole (dose-dependent toxicity)
pyrimethamine
ganciclovir
quinine
gentamicin
quinolones (avoid during 1st trimester)
griseofulvin
sulphonamides*
imipenem
trimethoprim/sulfamethoxazole*
itraconazole
vancomycin
ketocanazole
linezolid
mebendazole (avoid during 1st trimester)

PROBABLY SAFE, USE WHEN CLEARLY INDICATED
acyclovir
erythromycin (avoid estolate derivative)
amoxicillin
ethambutol
ampicillin
ethionamide
ampicillin
isoniazid
ampicillin
methenamine mandelate
amphotericin B
metronidazole (avoid during 1st trimester)
cefazolin
nitrofurantoin*
ceftaxime
nystatin
ceftriaxone
penicillins
cephalosporins
piperacillin
clin damycin
pyrazinamide
cloxacillin
rifampicin (Vit K needed at birth)
co-amoxiclav
tenoflovir (limited data, concern about bone and renal toxicity)
efavirenz (try to avoid in 1st trimester)
zidovudine
ertapenem

*contraindicated near term

Compiled by the Medicines Information Centre, Division of Clinical Pharmacology, UCT
Need help? Phone 021-406 6829 or 021-406 6780 or 021-406 6783
ANTIMICROBIAL AGENTS DURING LACTATION

GENERALLY CONTRAINDICATED
chloramphenicol
metronidazole (if essential give 2g STAT and then bottle feed for 24 hours)

COMPATIBLE
amikacin
amoxicillin
ampicillin
acyclovir
cephalosporins
cloxacin
erythromycin
ethambutol
fluconazole
gentamycin
isoniazid (monitor infant for peripheral neuritis, hepatitis & pyridoxine deficiency)
mebendazole
nalidixic acid*
nystatin
penicillins
piperacillin
praziquantel (bottle feed for 72 hours)
quinine*
rifampicin
streptomycin
sulphonamides* (in healthy, full-term neonate. Avoid in ill, stressed or premature infants)
tetracycline
trimethoprim*
vancocmycin
* avoid in infants with G6PD deficiency

NO HUMAN DATA – PROBABLY COMPATIBLE
albendazole (in normal doses)
ethionamide

LIMITED HUMAN DATA – PROBABLY COMPATIBLE
ciprofloxacin          mefloquine
clindamycin           methenamine
colistin              nitrofurantoin*
imipenem              ofloxacin
meropenem              ertapenem
kanamycin              pyrazinamide
ketoconazole           primaquine

NO HUMAN DATA – POTENTIAL TOXICITY
griseofulvin
linezolid

Compiled by the Medicines Information Centre, Division of Clinical Pharmacology, UCT
Need help? Phone 021-406 6829 or 021-406 6780 or 021-406 6783
## ANTIMICROBIAL AGENTS IN PORPHYRIA

These ratings have been assigned on the basis of published information, a comparison of drugs of similar structure, personal experience and intuition. Published experience is not necessarily available to support every rating and ratings should serve as a guide only.

### AVOID

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<thead>
<tr>
<th>Drug</th>
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<tbody>
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<td>clindamycin</td>
<td>griseofulvin</td>
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</tr>
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</tr>
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<td>dapsone</td>
<td>ketoconazole</td>
<td>sulfonamides</td>
</tr>
<tr>
<td>sulfonamides</td>
<td>miconazole</td>
<td>trimethoprim</td>
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### MAY PROVE TO BE UNSAFE: USE WITH EXTREME CAUTION

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<td>tetracyclines</td>
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<td>nefartinavir</td>
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<tr>
<td>isoniazid</td>
<td>rifabutin</td>
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### USE WITH CAUTION

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### THOUGHT TO BE SAFE

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<td>didanosine</td>
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### INSUFFICIENT DATA FOR A RECOMMENDATION (AVOID IF POSSIBLE)

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</tr>
<tr>
<td></td>
<td>praziquantel</td>
<td></td>
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</tbody>
</table>

Compiled by Prof R Hift, MRC/UCT Liver Research Centre
Queries may be addressed to the Porphyria Information Centre, tel:406 6332.
ANTIBIOTIC STEWARDSHIP – THE 10 COMMANDMENTS!

1. Do not use antibiotics for non-bacterial (or non-infectious) causes of fever, leukocytosis etc.

2. Send appropriate cultures before starting antibiotic therapy.

3. Prescribe the narrowest spectrum agent that is appropriate for the infection.

4. Prescribe the correct dose – based on the patient’s weight, renal and/or liver function, as well as the suspected site of infection. If necessary, use therapeutic drug monitoring to ensure the correct dose has been prescribed.

5. Prescribe for an appropriate duration – for many infections a 5 day course of antibiotics is adequate.

6. Review the need for antibiotics on a regular basis. If a non-infectious cause for the symptoms / signs is found, stop the antibiotic/s.

7. Review culture results regularly, and switch to a narrower spectrum agent if possible and appropriate.

8. Switch to oral agents (if available) as soon as the patient is able to take orally, and is stable.

9. Avoid combination therapy where possible; there are some settings (often when choosing agents empirically) where combination therapy is justified to expand the antimicrobial spectrum.

10. Don’t be too shy or too proud to ask for advice.