WESTERN CAPE
ACADEMIC HOSPITALS
ANTIMICROBIAL RECOMMENDATIONS

NATIONAL HEALTH
LABORATORY SERVICE

2013

Acknowledgements

This booklet has been made possible by valuable input from many different people at both Groote Schuur and Tygerberg Hospitals. As far as possible members of different departments were consulted about issues that particularly affect their discipline. Suggestions for changes are always welcome and should be communicated to Prof Andrew Whitelaw at Tygerberg Hospital and Dr Colleen Bamford at Groote Schuur.

For further advice please contact the microbiology departments at Tygerberg Hospital (021-9384006) or Groote Schuur Hospital (0829075282 – GSH speed-dial 76652 or 021-4045137)

NATIONAL HEALTH
LABORATORY SERVICE

This booklet is an initiative of the National Health Laboratory Service (NHLS) at Groote Schuur and Tygerberg Hospitals

Originally compiled by Dr S Oliver for the Departments of Medical Microbiology and Infectious Diseases Groote Schuur and Tygerberg Hospitals

TABLE OF CONTENTS

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).

DRUG NAME	DOSE	DOSING INTERVAL	HOSPITAL COST (per day, in rands)
ANTIMICROBIALS – oral			
Amoxicillin	500mg	8 hourly	0.83
Azithromycin	500mg	daily	7.34
Cefixime	400mg	STAT	19.46
Cefuroxime	250mg	12 hourly	3.02
Ciprofloxacin	500mg	12 hourly	0.88
Clarithromycin	500mg	12 hourly	4.63
Clindamycin	450mg	8 hourly	7.90
Co-amoxiclav	1g	12 hourly	2,98
Cotrimoxazole	160/800mg (2 tabs)	12 hourly	0.51
Doxycycline	100mg	12 hourly	0.39
Erythromycin	500mg	6 hourly	4.62
Ethambutol	1.2g	daily	1.36
Ethionamide	750mg	daily	4.48
Flucloxacillin	500mg	6 hourly	3.57
Fusidic acid	500mg	8 hourly	106.20
Isoniazid	300mg	daily	0.57
Linezolid	600mg	12 hourly	564.49
Metronidazole suppository	1g	8 hourly	7.37
Metronidazole	400mg	8 hourly	0.56
Moxifloxacin	400mg	daily	3.61
Nitrofurantoin	100mg	8 hourly	7.167
Para-amino Salicylic acid[#]	4g	8 hourly	78.10
Penicillin V (strep pharyngitis)	500mg	12 hourly	0.67
Pyrazinamide	1.5g	daily	0.87
Rifampicin	600mg	daily	0.85
RHZE (4 drug combination for TB)[*]	5 tablets	daily	3.28
Terizidone	250mg	8 hourly	19.63
ANTIVIRALS – oral			
Abacavir	300mg	12 hourly	6.47
Aciclovir H. simplex	400mg	8 hourly	1.95
H. zoster	800mg	5 times daily	6.50
Lopinavir/ritonavir (Aluvia)	2 tablets	12 hourly	7.69
Lamivudine	150mg	12 hourly	0.74
Zidovudine	300mg	12 hourly	2.26
Stavudine	30mg	12 hourly	0.44
Didanosine	400mg	daily	3.75
Tenofovir	300mg	daily	1.96

[*] 4-drug combination tablets (**R**ifampicin, isoniazid(**H**), pyra**Z**inamide, **E**thambutol) 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

Fluconazole	400mg	daily	2.86
Griseofulvin	500mg	daily	2.46
Itraconazole	200mg	12 hourly	14.75
Ketoconazole	400mg	daily	5.79
Nystatin suspension	1ml	6 hourly	1.26
Voriconazole	200mg	12 hourly	204.30

ANTIHELMINTHICS – oral

Mebendazole	100mg	12 hourly	0.63
Albendazole	400mg	stat	2.50
Praziquantel	3.5g	daily	194.68

ANTIMICROBIALS – parenteral

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

[#] 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:

$$\text{Creatinine clearance (ml/min)} = \frac{(140 - \text{age}) \times \text{Wt (kg)}}{\text{serum creatinine } (\mu\text{mol/l})}$$

(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.
  - Are antibiotics still indicated?
  - 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.

RECOMMENDED TERMINOLOGY	ROUTE	COMPONENTS	AMPOULE CONTENT	INDICATIONS	DOSE
benzathine penicillin (provides sustained low levels of penicillin)	IM	benzathine penicillin	1,2MU 2,4MU	prophylaxis for: rheumatic fever, recurrent cellulitis, recurrent meningococcal meningitis streptococcal sore throat syphilis	1,2MU every third week 1,2MU stat see page 34
procaine penicillin	IM	procaine penicillin	300 000U	replaces benzyl penicillin when a daily or twice daily IM injection preferred to IV therapy syphilis	600 000U daily see page 34
penicillin G	IV	sodium benzyl penicillin	1MU 5MU	infections for which oral or IM preparations are not suitable endocarditis and meningitis	2MU 6 hourly 5MU 6 hourly or 4MU 4 hourly[1]

[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 cephalosprin 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 ß-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 (ceftazidime 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).**

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

Medicines Information Centre, Division of Pharmacology
University of Cape Town Faculty of Health Sciences

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

AMINOGLYCOSIDE DOSING SCHEDULE[1]

THE MOST IMPORTANT DOSE IS THE FIRST ONE - DO NOT UNDERDOSE

ANTIBIOTIC	DAILY DOSE[1]	INTERVAL	PEAK[2] LEVEL (mg/l)	TROUGH[2] LEVEL (mg/l)
Gram-negative infection - normal renal function				
gentamicin/tobramycin	**6mg/kg**	**daily**	**>8**	**<1**
amikacin	**15mg/kg**	**daily**	**>30**	**<1**
Gram-negative infection - poor renal function				
gentamicin/tobramycin	**3-4mg/kg[4]**	**A peak of above 8mg/l must be achieved. Repeat dose when level <1mg/l. If interval required to achieve this is >48 hours consider alternative therapy.**		
amikacin	**10mg/kg**	**A peak of above 30mg/l must be achieved. Repeat dose when level <1mg/l but if interval required to achieve this is >48 hours consider alternative therapy**		
Streptococcal and enterococcal endocarditis[3]				
gentamicin/tobramycin	**3mg/kg**	**12 hourly**	**3-8**	**<1**

[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:

Adjusted body weight = ideal body weight + [0.4 × (actual body weight - 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

eGFR (ml/min)	Dosing interval (hrs)	Measurement of trough concentrations
>80	12	Before 3rd dose
40-79	24	Before 3rd dose
25-40	48	Before 2nd dose
<25 or haemodialysis or CAPD	When trough level <15	After 3 days

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

Dose	Patient category	Dosing suggestion
Loading	All patient categories	9 -12 MU*
Maintenance	eGFR > 60	4.5 MU 12hourly
	eGFR 30-60	3 MU 12hourly
	eGFR 10-30	2 MU 12hourly
	eGFR < 10	1 MU 12hourly
	Intermittent hemodialysis	1 MU 12hourly plus 0.5-1 MU after each episode of dialysis
	Continuous renal replacement	8 MU 12hourly

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

AMPHOTERICIN 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 haematolgical 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

Current national guidelines for eligibility are:

- CD4 count $\leq$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, emtracitabine 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).

Agents restricted to consultant signature or consultant telephonic authorization	**Agents still requiring microbiology / ID authorization:**
ICUs: • Colistin • Imipenem • Meropenem	ICU • Tigecycline • Aztreonam • Linezolid • Voriconazole
General wards: • IV ciprofloxacin • Vancomycin • Ertapenem • Piperacillin-tazobactam	General wards - Above list plus: • Colistin • Meropenem • Imipenem

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	
community acquired	Cloxacillin 2g 6 hourly
hospital acquired	Vancomycin
Suspected gram-negative septicaemia	
community acquired	gentamicin or ceftriaxone
hospital acquired (non-ICU related)	amikacin or ertapenem
HIV positive patients often have non-typhoid salmonella bacteraemia and the empiric choice of antibiotic should cover these organisms	Ceftriaxone initially. 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 <u>not</u> 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 susceptible enterococci
- Abiotrophia/Granulicatella spp. (nutritionally variant streptococci)

  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

- Fully resistant viridans streptococci (MIC ≥4mg/l)
- Penicillin resistant enterococci

  vancomycin plus gentamicin for six weeks.
  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 susceptible enterococci
- *Abiotrophia/Granulicatella* spp.

  penicillin and gentamicin for 6 weeks
  See note (a) below

- Fully resistant viridans streptococci (MIC ≥4mg/l)
- Penicillin resistant enterococci

  vancomycin and gentamicin for 6 weeks
  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 (ceftriaxone 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 with vegetations of <2cm. (Ann Intern Med 1996;125:969-74)
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 doxcycline or erythromycin if no response at 48 hours
severe		ceftriaxone 1g/day p*lus* IV clarithromycin
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		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**Error! Bookmark not defined.** 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	30-37kg - 2 tabs RH (150/75) 38-54kg - 3 tabs RH (150/75) 55-70kg - 2 tabs RH (300/150) >70kg - 2 tabs RH (300/150)

CNS or bone & joint involvement	Treatment duration for 9 months
in patients unable to swallow tablets	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: a. Intensive 6 month treatment	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.
- followed by: b. Maintenance treatment 18 months	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:

Background therapy	Ethambutol, streptomycin and moxifloxacin
day 1	Rifampicin 450 or 600 mg daily depending on weight
day 3	Check ALT
day 4-6	Add INH 300mg daily
day 7	Check ALT
day 8	Consider PZA rechallenge (see text)

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 $\geq 38^{o}C$, 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 7days 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)
		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 probenicid (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)

Chlamydial infection	doxycycline (100mg 12 hourly) for 7 days
Chancroid	erythromycin 500mg 6 hourly for 7 days
Trichomonas	metronidazole 2g STAT
Bacterial vaginosis	Can use metronidazole 2g STAT as in syndromic management but 400mg 12hourly for 7 days has been shown to be more effective

PERITONITIS

Surgical	penicillin, gentamicin and metronidazole
Spontaneous (in patients with pre-existing liver disease)	ceftriaxone
Peritonitis in dialysis patients	Vancomycin: 2 gm IP. Repeat after 5-7 days if appropriate or 15 mgm/l 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.

GASTROINTESTINAL INFECTIONS

Shigellosis	ciprofloxacin for 3 days (7 days may be required in HIV positive patients) If associated with bacteraemia treat for 7 days
Typhoid	ciprofloxacin for 7 days is the drug of choice (ceftriaxone for 7 -14 days is an alternative)
Salmonellosis (non-typhoid samonellas)	Fluid replacement only for most immunocompetent patients HIV positive patients should receive ciprofloxacin for 4 weeks due to the high risk of relapse.
Amoebiasis (including liver abscess)	metronidazole (800mg 8 hourly) for 10 days
Giardiasis	metronidazole (2g daily as a single dose) for 3 days

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 vancomyin) 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) doxycycline 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-

	1330), and should be used if the isolate is susceptible to azoles
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 H_2O 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*	Oral artemether-lumefantrine (Coartem®) is indicated for non-severe cases of malaria.
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.	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.
If in any doubt of the severity of the malaria, discuss immediately with an ID specialist.	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.
P. vivax or *P. ovale* malaria including	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 H_2O 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.

Type of surgery	Antibiotic used
Cardiothoracic surgery	• cefazolin, IV, 1 g [*] • 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.
Lower limb amputation	• cefazolin, IV, 1 g * **PLUS** • metronidazole, IV, 500 mg
Orthopaedic surgery	• cefazolin, IV, 1 g * • for trauma related procedures see pg 47
Head and neck surgery	• cefazolin, IV, 1 g * For procedures involving the oropharyngeal mucosa ADD • metronidazole, IV, 500 mg
Abdominal surgery Upper GIT	• cefazolin, IV, 1 g *

[*] If patient >80 kg use 2g dose

Type of surgery	Antibiotic used
Colorectal and appendix	• cefazolin, IV, 1 g [*] **PLUS** • metronidazole IV, 500 mg If perforation has occurred, treat patient for infection with a course of appropriate antibiotics (refer to page 35 for treatment of peritonitis)
Biliary	Only for high risk patients: bile obstruction, jaundice, biliary stones or cholecystitis, or re-operation, ERCP: • cefazolin, IV, 1 g * **PLUS** • metronidazole IV, 500 mg
Pelvic surgery	• cefazolin, IV, 1 g * **PLUS** • metronidazole IV, 500 mg
ENT surgery	• cefazolin, IV, 1 g * For procedures involving the oropharyngeal mucosa: ADD • metronidazole, IV, 500 mg
Nephro-urological surgery	• cefazolin, IV, 1 g * • Treat patients with preoperative bacteriuria according to urine MC+S. • Trans-rectal prostate biopsy: oral ciprofloxacin 500mg 12hrs before and after surgery • Cyctoscopy: 500mg ciprofloxacin before procedure
Ophthalmic surgery	• chloramphenicol 0.5% ophthalmic drops, instil 1 drop 2–4 hourly for 24 hours prior to surgery, preferably use separate vial for each patient.
Neurosurgery	• cefazolin, IV, 1 g *

SEVERE ß-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

and

- 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 cardiomyophathy*****

Mitral 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

Mitral 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

Standard regimen	amoxicillin 3g orally 1 hour before procedure
Nasal packing and nasal intubation	cloxacillin 2g IV at induction or just prior to procedure
Penicillin allergic patients and patients who are on long-term penicillin prophylaxis for rheumatic fever	clindamycin 600mg orally 1 hour before procedure
Patients unable to take oral medications	ampicillin 2g IV at induction or IM 30 minutes before procedure
Patients unable to take oral medications who are penicillin allergic or on long-term penicillin prophylaxis	clindamycin 600mg IV given in 50ml over 10 minutes at induction or up to 30 minutes before procedure

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
or
doxycycline 100mg daily
or
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

Generic Name	**Dose**		**Route**	**Duration [Days]**
	Adults	*Children*		
Rifampicin	600mg bd.	10mg/kg bd.	PO	2 days
Ciprofloxacin	500mg	10mg/kg	PO	Single Dose
Ceftriaxone	250mg	<15 years 125mg	IM	Single Dose

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 emtracitabine (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.*

Exposure	HIV status of source patient	
	Positive or Unknown*	Negative
Intact skin	No PEP	No PEP
Mucosal splash/ Non-intact skin	3 Drugs	No PEP
Percutaneous injury	3 Drugs	No PEP

*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 (Healtcare 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, twicea 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 immunecompromised persons and on day 0, 3, 7, and 14 for immunecompetent 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
doxycycline
tetracyclines
erythromycin estolate
streptomycin

TRY TO AVOID, USE ONLY IF ESSENTIAL

amikacin
aminoglycosides
chloramphenicol*
ciprofloxacin (avoid during 1st trimester)
colistin
co-trimoxazole*
fluconazole (dose-dependent toxicity)
ganciclovir
gentamicin
griseofulvin
imipenem
itraconazole
ketoconazole
linezolid
mebendazole (avoid during 1st trimester)
nalidixic acid
ofloxacin (avoid during1st trimester)
pentamidine
piperacillin/tazobactam
praziquantel (avoid during 1st trimester)
primaquine
pyrimethamine
quinine
quinolones (avoid during 1st trimester)
sulphonamides*
trimethoprim/sulfamethoxazole*
vancomycin

PROBABLY SAFE, USE WHEN CLEARLY INDICATED

acyclovir
amoxicillin
ampicillin
amphotericin B
cefazolin
cefotaxime
cefoxitin
ceftazidime
ceftriaxone
cephalosporins
clindamycin
cloxacillin
co-amoxiclav
efavirenz (try to avoid in 1st trimester)
ertapenem
erythromycin (avoid estolate derivative)
ethambutol
ethionamide
isoniazid
methenamine mandelate
metronidazole (avoid during 1st trimester)
nitrofurantoin*
nystatin
penicillins
piperacillin
pyrazinamide
rifampicin (Vit K needed at birth)
tenofovir (limited data, concern about bone and renal toxicity)
zidovudine

*contraindicated near term

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
cloxacillin
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*
vancomycin
* avoid in infants with G6PD deficiency

NO HUMAN DATA – PROBABLY COMPATIBLE

albendazole (in normal doses)
ethionamide

LIMITED HUMAN DATA – PROBABLY COMPATIBLE

ciprofloxacin
clindamycin
colistin
imipenem
meropenem
kanamycin
ketoconazole
mefloquine
methenamine
nitrofurantoin*
ofloxacin
ertapenem
pyrazinamide
primaquine

NO HUMAN DATA – POTENTIAL TOXICITY

griseofulvin
linezolid

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

chloramphenicol
clindamycin
cotrimoxazole
dapsone
sulfonamides
ethionamide
griseofulvin
indinavir
ketoconazole
miconazole
nalidixic acid
nitrofunantoin
pyrazinamide
sulfonamides
trimethoprim

MAY PROVE TO BE UNSAFE: USE WITH EXTREME CAUTION

albendazole
amprenavir
doxycycline
efavirenz
fluconazole
isoniazid
itraconazole
metronidazole
minocycline
nelfinavir
nevirapine
rifabutin
rifampicin
ritonavir
tetracyclines
zidovudine

USE WITH CAUTION

abacavir
azithromycin
cephalosporins (other)
ciprofloxacin
clarithromycin
didanosine
foscarnet
lamivudine
linezolid
mebendazole
mefloquine
moxifloxacin
ofloxacin
pentamidine
saquinavir
stavudine
zalcitabine

THOUGHT TO BE SAFE

acyclovir
amikacin
aminoglycosides
amoxicillin
amphotericin
ampicillin
ceftazidime
ceftriaxone
cefuroxime
cloxacillin
co-amoxiclav
didanosine
ertapenem
ethambutol
famciclovir
flucloxacillin
fusidic acid
ganciclovir
gentamicin
imipenem
methenamine
mandelate
natamycin
neomycin
niclosamide
nystatin
penicillin
piperacillin
primaquine
proguanil
pyrimethamine
quinine
streptomycin
valaciclovir
valganciclovir
vancomycin

INSUFFICIENT DATA FOR A RECOMMENDATION (AVOID IF POSSIBLE)

colistin
clofazimine
emtricitabine
framycetin
praziquantel
tazobactam
terizidone

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.**