ANTIBIOTIC GUIDELINE

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PREFACE to second edition

The first edition of "Antibiotic Guidelines" was published in 1997. The response was generally positive and the original authors are grateful to those users, particularly clinicians and other colleagues, who have provided suggestions, constructive criticism and other comments. We hope that most of these have been incorporated into this edition.

The second edition is a response to various pressures and requests for an updated version of the original. The original format has been retained and, as before, the content is the product of on-going efforts of the authors to keep abreast of new antibiotics, changing resistance patterns and the literature. The number of authors have been increased, both to spread the load and broaden the input.

It remains a concern that antibiotic prescribing is still often inappropriate. The discerning reader will recognise that there is little relationship between the recommendations contained in this publication and the "top-selling antibiotics" - all expensive - on the South African market. Hopefully this booklet will indeed assist clinicians and promote appropriate antibiotic therapy and prophylaxis.

As with the previous edition, this book is not intended to be a comprehensive reference text - it is a guideline document only, as its title indicates. It is therefore inevitable that there will be omissions and some content which may be contentious.

Again we will welcome constructive comments and suggestions for improvement.

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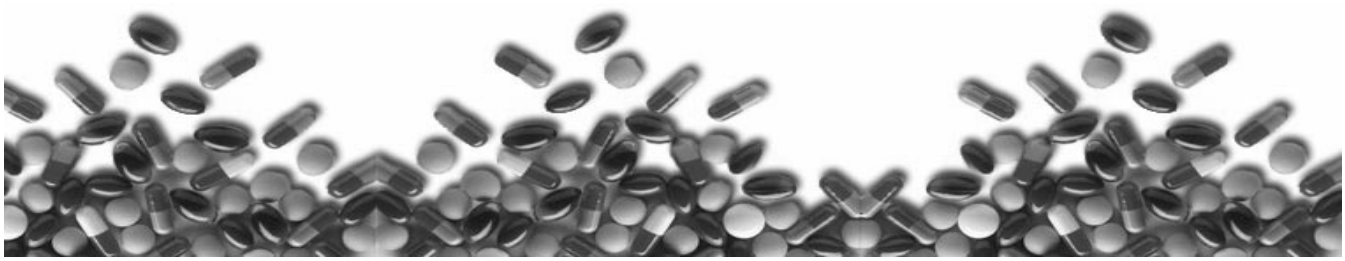

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Chapter 1: Principles of Diagnosis of Infectious Diseases and Antimicrobial Therapy

There are certain aspects which deserve special consideration when treating patients with antimicrobial agents.

Need for representative specimen collection before starting therapy

It is important to obtain adequate and representative specimens from all potentially infected sites prior to the initiation of antimicrobial therapy. Appropriate antimicrobial therapy is based on definitive identification of pathogenic organisms, which usually requires culture. Once antimicrobial therapy has been started, cultures often are rendered sterile, even though viable organisms may remain in the host. It is also important to avoid or minimize contamination by surface contaminants and commensals when collecting specimens.

Initial empirical choice

(i.e. informed guess) based on the most likely pathogens and suceptibilities

In most cases, it may be impossible to determine the exact nature of the infecting organisms before institution of antimicrobial therapy. Initial therapy must therefore be empirical - to make a rational choice from the many currently available antimicrobial agents, the clinician must be able to predict or "guess" infecting microorganism(s) and the antimicrobial susceptibility thereof. In these cases, the use of "bacteriological statistics" i.e. an awareness of those microorganisms most likely to cause infection in a given clinical setting, in conjunction with the local antibiotic resistance patterns, may be particularly helpful in choosing an empiric antimicrobial agent.

Subsequent need to adjust antimicrobial therapy in light of the laboratory results

Since different organisms vary in their susceptibility to antimicrobial agents, it is imperative that we have some means for determining the antimicrobial susceptibility of the infecting organism(s). Once the pathogen has been isolated, it can be subjected to susceptibility testing.

The commonly used disc-diffusion method is relatively simple to perform and is the most widely employed method. It provides semiquantitative or qualitative data about the susceptibility of a given organism to a given agent. The qualitative assessment of susceptibility is generally categorised as sensitive or resistant; however, some laboratories also report an intermediate category.

Quantitative data are also provided by methods that incorporate serial dilutions of antimicrobials in agar-containing or broth culture media. The lowest concentration of the antimicrobial agent which inhibits visible growth after an 18 - 24 hour incubation

period is known as the minimal inhibitory concentration (MIC). The minimal bactericidal concentration (MBC) is determined in broth dilution tests by subculturing samples without visible growth; this is based on 99.9% killing after 18 to 24 hours of incubation.

Testing the ability of the cultured pathogen to grow or not at a critical concentration (chosen to distinguish between sensitive and resistant bacteria), is a modification known as "breakpoint" testing. A recently described modification of the classical MIC test, the E-test, uses diffusion of a continuous concentration gradient of an antimicrobial agent from a plastic strip into an agar medium to yield quantitative measurements of antimicrobial susceptibility.

Monitoring Therapeutic response

In many patients, it is possible to monitor the therapeutic response on clinical grounds alone. Thus the subsidence of fever, the return of well-being, and the disappearance of both local and systemic signs of infection in the patient, all signify an appropriate response. No further formal monitoring is necessary in most cases.

An apparent failure to respond clinically may be due to either ineffectiveness of antimicrobial agent(s) (due to resistance or inappropriate route of administration) or to other reasons e.g. a localised infection that requires surgical drainage, or a superinfection etc. Careful reassessment is recommended when considering changes of antimicrobial therapy.

In certain situations, measurement of antimicrobial activity may be useful in predicting clinical response, e.g. determination of serum bactericidal activity (Schlichter test) in cases of infective endocarditis.

Assays for drugs with narrow Therapeutic:toxic ratio

For antibiotics such as the aminoglycosides and vancomycin, the measurement of their concentrations in serum/plasma or other body fluids is often useful to avoid excessive levels which are associated with toxicity, yet ensure that adequate (therapeutic) levels are achieved.

Pharmacokinetic properties of antibiotics

Knowledge of the pharmacodynamic and kinetic properties of antibiotics is imperative in choosing the correct antibiotic and correct dose.

In order for antibiotics to exert their bactericidal or bacteriostatic activity, a few important principles pertain:

1. Microbiological activity - antibiotic must bind to a specific binding site (e.g. ribosome or penicillin binding protein).
2. Concentration of the antibiotic at the site of the infection is important (the higher the concentration the more binding sites are occupied on/in the bacterial cells).
3. The antibiotics also have to remain on these binding sites for a sufficient period of time.

4. Minimum inhibitory concentration (MIC): This concentration represents the minimum amount of drug with which the bacteria have to come into contact, in order for the antibiotic towork.

Clinically speaking, 2 distinct groups of antibiotics are recognised:

Time dependant killing: (penicillins, cephalosporins, macrolides / azalides) The time that the antibiotic exceeds the MIC is crucial in predicting clinical outcome and cure. Concentrations of members of this group of antibiotics are required to be above the MIC for at least 50% of the dosing interval. If the bacterium is more resistant, the MIC is higher with subsequent reduction in time that the antibiotic concentration exceeds the MIC and therefore higher dosages of the drug may be required.

Concentration dependant antibiotics: (quinolones, aminoglycosides). The more the antibiotic concentration exceeds the MIC, the more killing will take place (irrespective and independent of the time the concentration exceeds the MIC). For this group of antibiotics a ratio of concentration: MIC 10 is required. This implies that a dose regimen should be chosen which results in a serum or tissue concentration of at least 10 times the MIC. Failure to achieve this concentration at the site of infection will lead to clinical and bacteriological failure, and is likely to induce resistance to the entire class of antibiotic.

Chapter 2: Notes on Selected Antibiotics

Beta-Lactams

This important group of cell wall-active antibiotics includes the penicillins, cephalosporins, carbapenems and some beta-lactamase inhibitors. They all contain an active beta-lactam ring in their chemical structure - from which their collective name is derived.

Penicillins

Penicillin V and Penicillin G are active against most aerobic Gram-positive organisms. Ampicillin and amoxycillin have some activity against several Gram-negative rods, and the Gram-negative spectrum is increased with piperacillin. Most anaerobes are susceptible to penicillin, with the notable exception of Bacteroides fragilis.

- Benzylpenicillin (Penicillin G) remains the antibiotic of choice for infections due to streptococci, susceptible staphylococci, meningococci, susceptible gonococci, Treponema pallidum, Pasteurella, Actinomyces and Clostridium perfringens. It is used in combination with aminoglyco-sides for enterococcal infections and endocarditis.
- Procaine penicillin G is a longer-acting, intramuscular alternative to benzylpenicillin, given 12 hourly. Levels achieved are lower than those for benzylpenicillin and it should therefore not be used to treat meningitis.
- Benzathine penicillin G is the longest acting form and provides very low levels for 3 weeks or more. It is used almost exclusively in the prevention of streptococcal pharyngitis (hence the prevention of rheumatic fever) and in the treatment of syphilis, other than neurosyphilis.
- Phenoxymethylpenicillin (Penicillin V) is administered orally and achieves much lower levels than parenteral benzylpenicillin. It is used primarily against Streptococcus pyogenes in the treatment of pharyngitis and the prevention of rheumatic fever. In other situations it has tended to be replaced by amoxycillin, whose oral absorption is more reliable and less dependent on an empty stomach.
- Cloxacillin has the exclusive role of treating beta-lactamase producing strains of staphylococci i.e. penicillin-resistant strains. Flucloxacillin is equivalent, but is better absorbed after oral administration. Both cloxacillin and flucloxacillin are examples of penicillinase-resistant penicillins. Methicillin or oxacillin is used to test susceptibility to these anti-staphylococcal penicilins.
- Amoxycillin and Ampicillin are equivalent, but amoxycillin is better absorbed after oral administration. These penicillins are effective against penicillin-susceptible organisms and more effective than penicillin against Enterococcus, Listeria, beta-lactamase negative Haemophilus influenzae, Salmonella typhi, Proteus mirabilis and some Escherichia coli. Ampicillin, but not amoxycillin, can be used to treat sensitive gastrointestinal Shigella infection. Amoxycillin is widely used to treat infectious exacerbations of chronic bronchitis but phen-oxymethylpenicillin is preferred for pharyngitis, not least because amoxycillin may cause a rash in patients with infectious mononucleosis.

- Amoxycillin plus Clavulanate: Combination with clavulanate (a beta-lactamase inhibitor) extends the spectrum of amoxycillin to include otherwise resistant strains of Haemophilus influenzae, Moraxella catarrhalis, some Enterobacteria-ceae and most anaerobes including Bacteroides fragilis. However, uncertain CSF penetration by clavulanate precludes the use of this antibiotic in meningitis and brain abscesses.
- Piperacillin: Piperacillin has the most extensive Gram-negative activity of the penicillins. Its activity spectrum is that of amoxycillin or ampicillin plus activity against many strains of Pseudomonas aeruginosa. Since they are often synergistic with the aminoglycosides, a combination may be used in life-threatening infections in neutropenic patients or patients with proven pseudomonas infection.
- Piperacillin plus Tazobactam: This combination uses another beta-lactamase inhibitor (tazobactam) which enhances the activity of piperacillin against plasmid-mediated (TEM, SHV types) beta-lactamase-producing Gram-negative bacilli such as Klebsiella spp and some E. coli strains. However, this combination is not able to fully overcome the enormous concentrations of chromosomally-mediated beta-lactamase produced by derepressed mutant strains of Enterobacter spp., Citrobacter freundii, Acinetobacter spp., and other Gram-negative bacilli, and therefore combined therapy with an aminoglycoside may be indicated in more serious infections.
- Piperacillin plus Tazobactam:

Cephalosporins

The cephalosporins are a group of broad-spectrum antibiotics, which are conveniently grouped into 3 generations, with increasing activity against Gram-negative aerobes, and somewhat decreasing Gram-positive activity. The table below shows a simplistic grouping based on their spectra of activity.

Generation	Spectrum	Parenteral	Oral
1st	Staphylococci (except MRSA) Streptococci (not Enterococci) E coli, Proteus Klebsiella	Cephalothin Cefazolin	Cephalexin Cephradine Cefadroxil
2nd	As for 1st generation plus Haemophilus (including beta-lactamase producers)	Cefamanole Cefuroxime	Cefaclor Cefprozil Cefuroxime Loracarbef
2nd	As for above plus Bacteroides	Cefoxitin	
3rd	As for 2nd generation plus most other Gram-negative bacilli except Pseudomonas	Cefotaxime Ceftriaxone	Cefpodoxime Ceftibuten Cefixime
3rd/4th	As for above plus Pseudomonas	Ceftazidime Cefepime Cefpirome	

General Notes

All are active against most streptococci, except Enterococcus spp. (which are all intrinsically resistant). Importantly, they also have no activity against Listeria or methi-

cillin-resistant staphylococci. Most penicillin-allergic patients will tolerate cephalosporins, but this group of antibiotics should be avoided if there is a definite history of anaphylaxis after penicillin administration. In general, the third-generation cephalosporins are significantly less active against staphylococci than the first- and second-generation cephalosporins.

First-generation cephalosporins

The first-generation cephalosporins are effective alternatives for treating staphylococcal and streptococcal infections. They are therefore alternatives for skin and soft-tissue infections, as well as for streptococcal pharyngitis. It is important to stress that the members of this generation are not indicated for empiric treatment of otitis media or sinusitis. Although these agents have some activity against E. coli, Klebsiella and Proteus, their use is limited to urinary tract infections caused by susceptible strains of these organisms.

Second-generation cephalosporins

The second-generation cephalosporins have increased activity against Gram-negative bacteria, including H. influenzae, N. meningitidis and M. catarrhalis. They are therefore useful agents for treating upper and lower respiratory tract infections, sinusitis and otitis media. These agents are also active against E. coli, Klebsiella and Proteus, which makes them potential alternatives for treating urinary tract infections caused by these organisms. Cefoxitin is a second-generation cephalosporin with anaerobic activity, and although seldom used as a therapeutic agent, it may have a role for prophylaxis in gastrointestinal surgery.

Third-generation cephalosporins

The third-generation cephalosporins are active against most enteric Gram-negative organisms, including beta-lactamase producers, salmonellae and shigellae; but have less activity against staphylococci. The parenteral third-generation cephalosporins (ceftriaxone and cefotaxime) have excellent activity against most strains of Streptococcus pneumoniae, including the vast majority of those with intermediate and high level resistance to penicillin. These agents also have activity against N. gonorrhoeae. Their use should be limited to infections resistant to first choice agents, gonococcal infections and infections caused by penicillin-resistant pneumococci. Ceftazidime has useful antipseudomonal activity.

Oral third-generation cephalosporins

Those available in South Africa include cefixime, cefpodoxime and ceftibutin. These agents have greater efficacy against Gram-negative organisms than the first- and second-generation cephalosporins, but are less effective against Staphylococcus aureus. They are also active against penicillinase-producing strains of Neisseria gonorrhoeae. They have no activity against Pseudomonas aeruginosa, enterococci or Campylobacter jejuni/coli. They offer no significant advantage over amoxycillin for otitis media and sinusitis, or over penicillin for pharyngotonsillitis. None of the oral cephalosporins are more active than amoxycillin against penicillin-resistant pneumococci.

Fourth-generation cephalosporins

These drugs have a spectrum of activity, which includes the antipseudomonal activity of ceftazidime and the Gram-positive activity of cefotaxime and ceftria-xone. Cefepime is a more Gram-negative drug with somewhat enhanced acti-vity against pseudomonas but slightly lesser activity against pneumococci, while cefpirome is more active against pneumococci and has somewhat lesser activity against pseudomonas. These drugs also have activity against nosocomial pathogens such as Enterobacter and Acinetobacter and their use should therefore be restricted to the setting of nosocomial sepsis.

Carbapenems

- Imipenem/cilastatin: Impenem is one of the broadest spectrum antibiotics available. It is combined with cilastatin to prevent its degradation by renal tubular dehydropeptidase. Its spectrum covers the Enterobacteriaceae, pseudomonas, Bacteroides fragilis and most Gram-positive cocci. However, it lacks activity against methicillin-resistant staphylococci, Enterococcus faecium, Corynebacterium jeikeium, Listeria, Clostridium difficile and Stenotrophomonas maltophilia. Seizures have been reported, especially with higher doses and in patients with impaired renal function. The use of this agent should be restricted to the treatment of life-threatening infections caused by highly resistant bacteria.
- Meropenem: Meropenem is a similar drug to imipenem but does not require combination with a dehydropeptidase inhibitor. It gives up a little activity against Gram-positive pathogens compared to imipenem. This drug has been suggested as an alternative for cefotaxime or ceftriaxone for management of meningitis, caused by penicillin-resistant Streptococcus pneumoniae.

Aminoglycosides

This group includes:

- Amikacin
- Kanamycin
- Gentamicin
- Neomycin
- Netilmicin
- Framycetin
- Tobramycin
- Streptomycin
- Spectinomycin

The aminoglycosides are active against aerobic Gram-negative bacilli, including pseudomonas. These antibiotics have no activity against anaerobes, and alone they are inactive against streptococci. When the aminoglycosides are used in combination with penicillin or ampicillin, a synergistic effect is obtained against most streptococci, including enterococci. Although the aminoglycosides are active against most staphylococci, they should not be considered first choice agents and should not be used alone to treat staphylococcal infections.

These agents are thus used in the treatment of serious infections with aerobic Gram-negative bacilli, including pseudomonas, complicated urinary tract infections, enterococcal endocarditis (in combination with a penicillin). Amikacin can also be used in combination therapy in the treatment of resistant tuberculosis. Amikacin is particularly effective when used against bacteria that are resistant to other aminoglycosides, since its chemical structure makes it less susceptible to several inactivating enzymes. Depending on local patterns of resistance, amikacin may therefore be the preferred agent for serious infections caused by Gram-negative bacilli.

Streptomycin is now seldom used except in antituberculous therapy, whereas spectinomycin is used only to treat gonorrhoea caused by penicillin-resistant gonococci.

The principal side effects of the aminoglycosides are otovestibular- and nephrotoxicity. They should be avoided when possible in the elderly and those with impaired renal function. Serum/plasma levels should be monitored in all patients receiving treatment for longer than 2 days. Once daily administration is as effective as divided doses and is the regimen of choice as the aminoglycosides' ability to kill microorganisms effectively is "concentration dependent".

* See annexure A regarding desirable therapeutic levels.

Quinolones

The classification of the quinolones into "generations" on the basis of microbiological activity is controversial, but is useful for practising clinicians.

According to this classification, nalidixic acid is a first-generation quinolone. Because of its reliable activity against most Enterobactericeae, it became a popular choice for the treatment of uncomplicated urinary tract infections. Nalidixic acid is also used to treat shigellosis in children. It requires dosing four times a day and is available only as an oral agent and does not achieve significant tissue levels. It has no activity against Pseudomonas aeruginosa, anaerobes, chlamydiae, mycoplasmas or Gram-positive bacteria.

The second-generation quinolones expanded the bacterial coverage to include Pseudomonas aeruginosa and staphylococci. These quinolones have modest-to-poor activity against streptococci (notably Streptococcus pneumoniae and enterococci) and anaerobes. They exhibit high intracellular penetration, allowing for therapy against intracellular organisms like chlamydiae, mycoplasmas and legionellae.

A significant problem has been the emergence of resistance during therapy for infections caused by Staphylococcus aureus and Streptococcus viridans. The second-generation quinolones can be divided into two subgroups. One group contains ciprofloxacin and ofloxacin, which are available in both oral and parenteral formulation, and can be used to treat minor and severe infections such as urinary tract infections, severe enteric infections caused by salmonellae or shigellae, gonorrhoea and typhoid fever. The other group contains agents available only as oral formulations (e.g. enoxacin, lomefloxacin, norfloxacin), which are used primarily for urinary tract infections. In general, these agents should be reserved for treatment of significant infections caused by Pseudomonas aeruginosa or other Gram-negative bacteria which are resistant to conventional antibiotics.

Generation	Generic name	Microbiological activity
1st	Nalidixic acid	Enterobacteriaceae, including Shigella
2nd	Ciprofloxacin Ofloxacin Enoxacin Lomefloxacin Norfloxacin	As above + Pseudomonas Chlamydia Mycoplasma Legionella
3rd	Levofloxacin Sparfloxacin	As above + Streptococcus pneumoniae (borderline activity)
4th	Moxifloxacin Gatifloxacin	As above + Streptococcus pneumoniae + Anaerobes

The third-generation quinolones have similar activity to the second-generation quinolones, plus increased activity against Streptococcus pneumoniae. However, they are less active than the second-generation quinolones against Gram-negative bacteria. Activity against anaerobes is modest-to-poor. Levofloxacin and sparfloxacin belong to this group of quinolones. These quinolones should ideally be reserved for use as alternatives to other agents for acute exacerbations of chronic bronchitis and bacterial pneumonia in elderly patients.

Moxifloxacin and gatifloxacin can be considered fourth-generation quinolones owing to their activity against anaerobes, and significantly increased activity against Streptococcus pneumoniae. Hence, these might be considered for the treatment of intra-abdominal infections (of intestinal or pelvic origin) in addition to repiratory tract infections (as for the third generation quinolones).

Tetracyclines

- Tetracycline
- Doxycycline
- Minocycline

The antimicrobial spectra of all tetracyclines are nearly identical. They have activity against Gram-positive cocci, Escherichia coli, Neisseria gonorrhoeae, Brucella spp., vibrios, rickettsiae, mycoplasmas, chlamy-diae and spirochaetes, including Treponema pallidum and Borrelia burgdorferi.

This is the treatment of choice for chlamydial, rickettsial, brucella and ureaplasma infections and is an alternative to erythromycin for Mycoplasma pneumoniae. Tetracyclines are also used for the treatment of inflammatory acne. Both doxycycline and minocycline have long half-lives and are therefore given once daily or twice daily. Unlike most other tetracyclines, they are reliably absorbed in the presence of food. Tetracyclines are contraindicated in children less than 8 years of age and in pregnancy (except for serious rickettsial and brucella infections) as they discolour developing teeth and may depress skeletal growth in premature infants. Only doxycycline can be used safely in renal insufficiency, and this agent is also less likely to stain the teeth. Gastrointestinal side effects and photosensitivity are relatively uncommon with all tetracyclines; vertigo is common with minocycline.

Macrolides

- Erythromycin: This is the treatment of choice for Legionella, Campylobacter, and Mycoplasma pneumoniae infections and for the treatment and prevention of whooping cough. It is used to treat chlamydial and ureaplasma infections in pregnancy or childhood, when tetracycline is contraindi-cated. Erythromycin has only marginal activity against Haemophilus influenzae. It is a useful drug in the treatment of infections caused by Streptococcus pyogenes and pneumococci in patients allergic to penicillin.
- Roxithromycin has similar antibacterial activity to erythromycin but has a longer half-life and has improved activity against Haemophilus influenzae. It is given twice a day.
- Clarithromycin has significantly increased activity against organisms traditionally considered susceptible to erythromycin, plus good activity against Mycobacterium avium and Helicobacter pylori. The major advantage over erythromycin includes better gastrointestinal absorption and tolerance and activity against Haemophilus influenzae. It is given once or twice twice a day.
- Azithromycin is less active than erythromycin against staphylococci and streptococci but more active against Haemophilus influenzae. It has a long half-life, allowing once daily dosing.

Clindamycin

Clindamycin is active against Gram-positive bacteria such as staphy-lococci, pneumococci, Streptococcus pyogenes, and against most anaerobes including Bacteroides fragilis. It is considered by some to be superior to penicillin in anaerobic pulmonary infections. It is an alternative to metronidazole for anaerobic infections (except those in the CNS), and bacterial vaginosis (topical) in pregnant women. Principal adverse effects are allergy (rash), antibiotic-associated diarrhoea including pseudomembranous colitis and rarely, hepatotoxicity.

Chloramphenicol

This agent is active against salmonellae, Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis, rickettsiae, and anaerobic bacteria (including Bacteroides fragilis). Now seldom used because of rare irreversible marrow aplasia (approximately 1 per 20000) and dose-related reversible circulatory collapse in infants ("grey baby syndrome"). Chloramphenicol is well absorbed, has broad spectrum activity and excellent CSF penetration. Chloramphenicol has a place in the treatment of brain abscess, meningitis in those allergic to beta-lactams, and is also effective in typhoid fever. It is a reasonable alternative to tetracycline for rickettsial infections in children less than 8 years of age.

Glycopeptides

- Vancomycin: Vancomycin is active against Staphylococcus aureus, Staphylococcus epidermidis, including strains resistant to methicillin (therefore also oxacillin and cloxacillin). Other Gram-positive bacteria such asStreptococcus pyogenes, Streptococcus pneumoniae, enterococci, Corynebacterium jeikeium, and Clostridium difficile are all sensitive to vancomycin. Ototoxicity, nephrotoxicity, allergy and,

when infused rap-idly, "red-man syndrome" (erythroderma and hypotension), are principal adverse effects. Vancomycin is not absorbed from the gastrointestinal tract. As an IV infusion, it is the antibiotic of choice for the treatment of serious methicillin/oxacillin-resistant staphylococcal infections. In the penicillin-allergic patient it is used in combination with an aminoglycoside for the treatment of enterococcal endocarditis. Given orally,vancomycin is an alternative to metronidazole for the treatment of pseudomembranous colitis (see under gastrointestinal infections).

* See annexure A regarding desirable therapeutic ranges.

- Teicoplanin: Teicoplanin is a glycopeptide antibiotic with a molecular structure related to that of vancomycin. Gram-positive bacteria such as staphylococci (including methicillin-resistant strains), streptococci, enterococci and many anaerobic Gram-positive bacteria are susceptible to teicoplanin invitro. Rare species of coagulase-negative staphylococci may be resistant to teicoplanin yet sensitive to vancomycin. Teicoplanin has an exceptionally long half-life, allowing once-daily intramuscular or intra-venous administration. Teicoplanin has been in clinical use for a shorter period than has been vancomycin, and is regarded by some as an alternative glycopeptide to vancomycin.

Cotrimoxazole (Trimethoprim + Sulphamethoxazole)

Cotrimoxazole is active against a broad spectrum of Gram-negative and Gram-positive bacteria, as well as Nocardia and Toxoplasma. This combination is used to treat Gram-negative urinary tract infections, and is the agent of choice for Nocardia infections. Cotrimoxazole is also used to treat and prevent Pneumocystis carinii and toxoplasma infection. Both the sulphonamide and trimethoprim may cause skin rashes, including Stevens-Johnson syndrome.

Fusidic acid

This is essentially an antistaphylococcal agent. It should always be used in combination with another antibiotic to prevent emergence of resistance e.g. cloxacillin, or in the case of MRSA/ORSA, rifampicin, cotrimoxazole or even a quinolone should be considered. Gastric irritation, when taken by mouth, and skin rashes are the only common side effects.

Metronidazole

Metronidazole has excellent activity against anaerobic bacteria, including Bacteroides fragilis and against several intestinal protozoa. It has no activity against aerobic or facultative anaerobic bacteria. It is the agent of choice for bacterial vaginosis, trichomoniasis, giardiasis, amoebiasis and balantidiasis. Nausea, metallic taste, and disulfiram-like effect with alcohol are side effects, which may be less common with the related agents tinidazole and nimorazole.

Nitrofurantoin

This orally administered agent does not achieve significant blood and tissue levels but is excreted in the active form in the urine. It is therefore only used for the treatment or

prophylaxis of uncomplicated lower urinary tract infections, due to most Gram-positive or Gram-negative bacteria. Pseudomonas aeruginosa and the Proteus group are intrinsically resistant. Pulmonary reactions may be problematic.

Rifampicin

Rifampicin is active against a wide range of microorganisms. Apart from its important role as an antituberculous and antilepromatous agent, rifampicin is used to eradicate nasopharyngeal carriage of Neisseria meningitidis and Haemophilus influenzae following meningitis, and as an adjunct to doxycycline (in brucellosis), and fusidic acid (in serious staphylococcal infection). Causes red discolouration of body fluids and occasional influenza-like symptoms and hepatotoxicity. Interferes with oral contraceptive metabolism. Due to its primary value as an antimycobacterial agent, its use for other purposes should be restricted.

Annexure A

Recommendations regarding “desirable” serum levels of the Amino-glycoside antibiotics and Vancomycin.

Both the aminoglycoside group of antibiotics and vancomycin have narrow therapeutic indices and monitoring of serum levels is essential to (i) assess adequacy of therapy and (ii) detect/avoid potential dose-related toxicity.

Aminoglycosides

These may be administered by the intravenous (IV) or intramuscular (IM) route. It should be noted that comparative studies have confirmed the efficacy of single daily dosage.

Intramuscular (IM) administration: Standard IM injection technique

Predose (trough) level: Take serum (clotted blood) specimen within 15 minutes before the next dose.

Postdose (peak) level: Take serum (clotted blood) specimen 1 hour (60 minutes) after IM administration.

Intravenous (IV) administration: Bolus (IV"push") is not recommended. The preferred practice is to infuse the aminoglycoside in 5% dextrose or 0.9% NaCl over 15 to 30 minutes.

Predose (trough) level: Take serum (clotted blood) specimen within 15 minutes before the next dose

Postdose (peak) level: Take serum (clotted blood) specimen 30 minutes after completion of the rapid IV infusion.

Note: Once daily dosing of aminoglycosides makes monitoring of peak levels unnecessary. The peak levels in the table refer to serum concentrations for 8 hourly dosing of gentamicin, netilmicin or tobramycin, and 12 hourly dosing of amikacin.

Vancomycin

The only parenteral route is intravenous (IV) administration. Bolus (IV "push") administration is contraindicated. The recommended practice is to infuse the vancomycin in 100 - 250 ml 5% dextrose or 0.9% NaCl over at least 60 minutes.

Predose (trough) level: Take serum (clotted blood) samples within 15 minutes before the next dose.

Postdose (peak) level: Take serum (clotted blood) samples 30 minutes after completion of IV infusion.

IT IS IMPORTANT THAT THE SPECIMENS ARE CLEARLY IDENTIFIED AND LABELLED AS "PEAK" OR "TROUGH" AS APPROPRIATE.

	PEAK	THROUGH	INCREASED RISK OF TOXICITY
Gentamicin	6 - 12	< 1.5	Trough > 2
Tobramycin	6 - 12	< 1.5	Trough > 2
Netilmicin	6 - 12	< 1.5	Trough > 2
Amikacin	15 - 30	< 1.5	Trough > 5
Vancomycin	20 - 40	5 - 10	Trough > 10

Peak levels transiently in excess of these levels are not considered to be associated with significant risk of toxicity.

Chapter 3: Generic/Trade Name Lists

B = antibacterial
F = antifungal
M = antimycobacterial
P = antiparasitic

GENERIC NAME	TRADE NAME	CLASS	PRICE*
Acyclovir	Activir	V	
	Adco-acyclovir		
	Zovirax		
Amantidine	Symmetrel	"V	"
Amikacin	Amikin	B	
	Kacinth-A		
Amorolfine	Loceryl	F	
Amoxycillin	Acucil	B	
	Adco-amoxycillin		
	Amocillin		
	Amoxil		
	Amoxyfizz		
	Arcanacillin		
	Betamox		
	C-mox		
	Hiconcil		
	Ipcamox		
	Maxcil		
	Moxan		
	Norimox		
	Penmox		
	Promoxil		
	Ranmoxy		
	Rocillin		
	Saltermox		
	Spectramox		
	Ultramox		
	Xeracil		
	Xillin		
	Zoxil		
Amoxycillin-clavulanate	Augmentin	B	
	Clamentin		
Amphotericin B	Fungizone	F	
Ampicillin	Acupillin	B	
	Ampipen		
	Ampimax		
	Be-ampicil		
	Co-cillin		
	Dyna-ampil		
	Excillin		
	Penbritin		

GENERIC NAME	TRADE NAME	CLASS	PRICE*
	Penrite		
	Petercillin		
	Ranamp		
	Spectracil		
Ampicillin+cloxacillin	Ampiclox	B	
	Apen		
	Cloxam		
	Intramed ampicillin + cloxacillin		
	Megamox		
Atovaquone	Wellvone	P	
Azithromycin	Zithromax	B	
Benzathine penicillin	Bicillin-LA	B	
	Intramed benzathine penicillin		
	Penilente		
	Ultracillin		
Cefaclor	Adco-cefaclor	B	
	Apo-cefaclor		
	CEC		
	CeClor		
	Cloracef		
	Lilly-cefaclor		
	Rolab-cefaclor		
	Vercef		
Cefamandole	Mandokef	B	
Cefepime	Maxipime	B	
Cefixime	Fixime	B	
Cefodroxil	Cefadrox	B	
	Cipadur		
	Duracef		
	Dacef		
Cefotaxime	Claforan	B	
Cefpirome	Cefrom	B	
Cefoxitin	Mefoxin	B	
Cefpodoxime	Orelox	B	
Cefprozil	Prozef	B	
Ceftazidime	Fortum	B	
Ceftibutin	Cedax	B	
	Sepexin		
Ceftriaxone	Rocephin	B	
Cefuroximeaxetil	Zinnat	B	
Cefuroximesodium	Zinacef	B	
	Intracef		
Cephalexin	Cerexin	B	
	Fexin		
	Keflex		
	Lenocef		
	Lilly-cephalexin		
	Ranceph		
Cephalothin	Keflin	B	
Cephazolin	Cefacidal	B	
	Izacef		
	Kefzol		
	Ranzol		
Cephradine	Bactocef	B	
	Cefril		

GENERIC NAME	TRADE NAME	CLASS	PRICE*
Chloramphenicol	Chlorcol	B	
	Chloromycetin		
	Chlorphen		
Chloroquine sulphate/ phosphate	Anoclor	P	
	Daramal		
	Nivaquine		
	Plasmoquine		
Ciprofloxacin	Ciprobay	B	
Clarithromycin	Klacid	B	
Clindamycin	Clindac	B	
	Dalacin-C		
Clofazidime	Lamprene	M	
Clotrimazole	Adco-clotrimazole	F	
	Canalba		
	Candaspor		
	Candizole V		
	Canesten		
	Canex		
	Closcript		
	Covospor		
	Medaspor		
	Mycoban		
	Normospor		
	Xeraspor		
Cloxacillin	Clocillin	B	
	Cloxin		
	Orbenin		
Cotrimoxazole	Acuco	B	
	Adco-cotrimoxazole		
	Bactrim		
	Bencole		
	Cocydal		
	Cotrivan		
	Cozole		
	Doctrim		
	Durobac		
	Dynazole		
	Fabubac		
	Norisep		
	Purbac		
	Q-med cotrimoxazole		
	Septran		
	Spectrim		
	Trimethox		
	Trimoks		
	Trimzole		
	Ultrasept		
	Ultrazole		
	Xeroprim		
	Xerazole		
Dapsone	Lennon-Dapsone	M,P	
Didanosine (ddI)	Videx	V (HIV)	
Diethylcarbamazine	Hetrazan (?availability)	P	
Doxycycline	Cyclidox	B,P	

GENERIC NAME	TRADE NAME	CLASS	PRICE*
	Doryx		
	Doxytabs		
	Dumoxin		
	Thedox		
	Vibramycin		
Econazole	Gyno-pevaryl	F	
Enoxacin	Bactidron	B	
Ethambutol	Myambutol	M	
	Rolab-ethambutol		
Ethambutol + isoniazid	Mynah	M	
	Tuberol		
Ethionamide	Ethatyl	M	
Erythromycin	Acu-erylate	B	
	Adco-erythromycin		
	Betamycin		
	E-mycin		
	Eromel		
	Erymax		
	Erymycin		
	Erythromid		
	Erythromycin		
	Erythroped		
	Estomycin		
	Ethimycin		
	Ilosone		
	Purmycin		
	Ryped		
	Spectrasone		
	Succilate		
	Succin		
	Xeramel		
Famciclovir	Famvir	V	
Flucloxacillin	Floxapen	B	
	Flucillin		
Flucloxacillin+amoxycillin	Flumox	B	
	Macropen		
	Megamox		
	Megapen		
	Suprapen		
Fluconazole	Diflucan	F	
Fusidic acid	Fusidin	B	
Ganciclovir	Cymevene	V	
Gentamicin	Cidomycin	B	
	Fermentmycin		
	Garamycin		
	Gencin		
	Q-med gentamicin		
Griseofulvin	Fulcin	F	
	Microcidal		
Halofantrine	Halfan	P	
Hydroxyurea	Hydrea	"V" (HIV)	
Imipenem	Tienam	B	
Indinavir	Crixivan	V (HIV)	
Interferon-alpha-2B	Intron-A	V	
INH-rifampicin	Rifinah	M	

GENERIC NAME	TRADE NAME	CLASS	PRICE*
INH-rifampicin-ethambutol	Myrin	M	
INH-rifampicin- pyrizinamide	Rifater	M	
Isoniazid	Isoniazid (Lennon)	M	
Itraconazole	Sporanox	F	
Kanamycin	Kanamycin-Novo	B	
Ketoconazole	Nizoral	F	
Lamivudine(3-TC)	3-TC Epivir	V (HIV)	
Levofloxacin	Tavanic	B	
Lomefloxacin	Maxaquin Uniquin	B	
Loracarbef	Lorabid	B	
Mebendazole	Anthex D-worm Vermox Wormgo	P	
Mefloquine	Lariam Mefliam	B	
Melarsoprol	Arsobal	P	
Meropenem	Meronem	B	
Metronidazole	Acuzole Adco-metronidazole Ambral Bemetrazole Berazole Dynametron Flagyl Medamet Metazol Narobic Trichozole Zagyl Zobacide Zolerol	B,P	
Miconazole	Daktarin Gyno-Daktarin Gynospor	F	
Minocycline	Apo-minocycline Cyclimycin Minomycin Minotabs Romin Triomin	B	
Mupirocin	Bactroban	B	
Nalidixic acid	Winlomylon Puromylon	B	
Natamycin	Natacin	F	
Nelfinavir	Vira-cept	V (HIV)	
Neomycin	Mycifradin	B	
Netilmicin	Netromycin	B	
Nevirapine	Viramune	V (HIV)	
Niclosamide	Yomesan	P	
Nimorazole	Naxogin	P	

GENERIC NAME	TRADE NAME	CLASS	PRICE*
Nitrofurantoin	Macrodantin	B	
Norfloxacin	Noroxin	B	
	Utin		
Nystatin	Canestat	F	
	Mycostatin		
	Nystacid		
Ofloxacin	Tarivid	B	
Penicillin G	Benzatec	B	
	Intramed-benzylpenicillin		
	Novopen		
Penicillin V	Betapen	B	
	Deltacillin		
	Len-VK		
	Novo-VK		
	V-cil-K		
Pentamidine	Pentacarinat	P	
Pipemidic acid	Deblaston	B	
	Septidron		
Piperacillin	Pipril	B	
Piperacillin-tazobactam	Tazocin	B	
Piperazine	Pipralen	P	
	Piprine		
Praziquantel	Biltricide	P	
Primaquine	Primaquine (Zeneca)	P	
Procaine penicillin	Hostacillin	B	
	Novocillin		
	Procillin		
Proguanil	Paludrine	P	
Pyrantel	Combantin	P	
Pyrazinamide	Pyrazide	M	
	Rozide		
Pyrimethamine	Daraprim	P	
Quinine dihydrochloride	Adco-quinine	P	
Quinine sulphate	Quinine sulphate (Lennon)	P	
Rifabutin	Mycobutin	M	
Rifampicin	Rifcin	M	
	Rifadin		
	Rimactane		
Ritonavir	Norvir	V	
Roxithromycin	Rulide	B	
Saquinavir	Fortovase	V (HIV)	
	Invirase		
Sparfloxacin	Zagam	B	
Stavudine (d4T)	Zerit	V (HIV)	
Streptomycin	Novostrep	B,M	
Sulphadoxine-pyrimethamine	Fansidar	P	
Teicoplanin	Targocid	B	
Terbinafine	Lamisil	F	
Tetracycline	Achromycin	B	
	Acu-oxytet		
	Be-oxytet		
	Dynoxytet		
	Hostacycline		

GENERIC NAME	TRADE NAME	CLASS	PRICE*
	Ledermycin		
	Megamycin		
	O-4cycline		
	O-tet		
	Oxypan		
	Riostatin		
	Roxy		
	Spectatet		
	Terramycin		
	Tetracem		
	Tetralysal		
	Tetramel		
	Tetrex		
	Viacin		
Thiabendazole	Mintezol	P	
Tinidazole	Fasigyn	P	
Tioconazole	Gyno-trosyd	F	
Tobramycin	Mytobrin	B	
	Nebcin		
Trimethoprim	Triprim	B	
Valaciclovir	Zelitrex	V	
Vancomycin	Vancocin	B	
	Vancomycin-HCL (Lederle)		
Zalcitabine (ddC)	Hivid	V (HIV)	
Zidovudine (AZT)	Retrovir	V (HIV)	

* PRICE TO BE UPDATED BY USER

Chapter 4: Trade/Generic Name Lists

TRADE NAME	GENERIC NAME	PRICE*
Achromycin	Tetracycline	
Activir	Acyclovir	
Acucil	Amoxycillin	
Acuco	Cotrimoxazole	
Acu-erylate	Erythromycin	
Acupillin	Ampicillin	
Acu-oxytet	Tetracycline	
Acuzole	Metronidazole	
Adco-acyclovir	Acyclovir	
Adco-amoxycillin	Amoxycillin	
Adco-cefaclor	Cefaclor	
Adco-clotrimazole	Clotrimazole	
Adco-cotrimoxazole	Cotrimoxazole	
Adco-erythromycin	Erythromycin	
Adco-metronidazole	Metronidazole	
Adco-quininedihydrochloride	Quininedihydrochloride	
Ambral	Metronidazole	
Amikin	Amikacin	
Amocillin	Amoxycillin	
Amoxil	Amoxycillin	
Amoxyfizz	Amoxycillin	
Ampiclox	Ampicillin+cloxacillin	
Ampimax	Ampicillin	
Ampipen	Ampicillin	
Anthex	Mebendazole	
Anoclor	Chloroquine	
Apen	Ampicillin+cloxacillin	
Apo-minocycline	Minocycline	
Arsobal	Melarsoprol	
Augmentin	Amoxycillin-clavulanate	
Bactidron	Enoxacin	
Bactocef	Cephradine	
Bactrim	Cotrimoxazole	
Bactroban	Mupirocin	
Be-ampicil	Ampicillin	
Be-oxytet	Tetracycline	
Bemetrazole	Metronidazole	
Bencole	Cotrimoxazole	
Benzatec	PenicillinG	
Berazole	Metronidazole	
Betamox	Amoxycillin	
Betamycin	Erythromycin	
Betapen	PenicillinV	
Bicillin-LA	Benzathinepenicillin	
Biltricide	Praziquantel	
Canestat	Miconazole	
Canalba	Clotrimazole	

TRADE NAME	GENERIC NAME	PRICE*
Candaspor	Clotrimazole	
CandizoleV	Clotrimazole	
Canesten	Clotrimazole	
Canex	Clotrimazole	
CEC	Cefaclor	
CeClor	Cefaclor	
Cedax	Ceftibutin	
Cefadrox	Cefodroxil	
Cefacidal	Cefazolin	
Cefril	Cephradine	
Cefrom	Cefpirome	
Cerexin	Cephalexin	
Chlorcol	Chloramphenicol	
Chloromycetin	Chloramphenicol	
Chlorphen	Chloramphenicol	
Cidomycin	Gentamicin	
Cipadur	Cefadroxil	
Ciprobay	Ciprofloxacin	
Claforan	Cefotaxime	
Clamentin	Amoxycillin-clavulanate	
Clindac	Clindamycin	
Clocillin	Cloxacillin	
Cloracef	Cefaclor	
Closcript	Clotrimazole	
Cloxin	Cloxacillin	
C-mox	Amoxycillin	
Cocillin	Ampicillin	
Cocydal	Cotrimoxazole	
Combantin	Pyrantel	
Cotet	Tetracycline	
Cotrivan	Cotrimoxazole	
Covospor	Clotrimazole	
Cozole	Cotrimoxazole	
Crixivan	Indinavir	
Cyclidox	Doxycycline	
Cyclimycin	Minocycline	
Cymevene	Ganciclovir	
D-worm	Mebendazole	
Dacef	Cefadroxil	
Daktarin	Miconazole	
Dalacin-C	Clindamycin	
Daraprim	Pyrimethamine	
Daramal	Chloroquinesulphate	
Deblaston	Pipemidicacid	
Deltacillin	PenicillinV	
Diflucan	Fluconazole	
Doctrim	Cotrimoxazole	
Doryx	Doxycycline	
Doxitab	Doxycycline	
Doxycyl	Doxycycline	
Dumoxin	Doxycycline	
Duracef	Cefadroxil	
Durobac	Cotrimoxazole	
Dyna-ampil	Ampicillin	

TRADE NAME	GENERIC NAME	PRICE*
Dynametron	Metronidazole	
Dynazole	Cotrimoxazole	
Dynoxytet	Tetracycline	
E-mycin	Erythromycin	
Epivir(3-TC)	Lamivudine	
Eromel	Erythromycin	
Erymax	Erythromycin	
Erymycin	Erythromycin	
Erythrocin	Erythromycin	
Erythromid	Erythromycin	
Erythroped	Erythromycin	
Estomycin	Erythromycin	
Ethatyl	Ethionamide	
Ethimycin	Erythromycin	
Excillin	Ampicillin	
Fabubac	Cotrimoxazole	
Famvir	Famciclovir	
Fansidar	Sulfadoxine-Pyrimethamine	
Fasigyn	Tinidazole	
Fermentmycin	Gentamicin	
Fexin	Cephalexin	
Fixime	Cefixime	
Flagyl	Metronidazole	
Floxapen	Flucloxacillin	
Flumox	Amoxycillin+flucloxacillin	
Fortovase	Saquinavir	
Fortum	Ceftazidime	
Flucillin	Flucloxacillin	
Fucidin	Fusidicacid	
Fulcin	Griseofulvin	
Fungizone	AmphotericinB	
Garamycin	Gentamicin	
Gencin	Gentamicin	
Gyno-Daktarin	Miconazole	
Gyno-pevaryl	Econazole	
Gynospor	Miconazole	
Gyno-trosyd	Tioconazole	
Halfan	Halofantrine	
Hetrazan	Diethylcarbamazine(?availability)	
Hiconcil	Amoxycillin	
Hivid	Zalcitabine(ddC)	
Hostacycline	Tetracycline	
Hydrea	Hydoxyurea	
Ilosone	Erythromycin	
Intracef	Cefuroximesodium	
Intramed-ampicillin-cloxacillin	Ampicillin-cloxacillin	
Intramedbenzylpenicillin	Benzylpenicillin	
Intramedbenzathinepenicillin	Benzathinepenicillin	
Intron-A	Interferon-alpha2B	
Invirase	Saquinavir	

TRADE NAME	GENERIC NAME	PRICE*
Ipcamox	Amoxycillin	
Izacef	Cefazolin	
Kacinth-AAmikacin		
Kanamycin-Novo	Kanamycin	
Keflin	Cephalothin	
Keflex	Cephalexin	
Kefzim	Ceftazidime	
Kefzol	Cephazolin	
Klacid	Clarithromycin	
Lamisil	Terbinafine	
Lamprene	Clofazimine	
Lariam	Mefloquine	
Ledermycin	Tetracycline	
Len-VK	PenicillinV	
Lennon-Dapsone	Dapsone	
Lennon-quininesulphate	Quininesulphate	
Lenocef	Cephalexin	
Lilly-cefaclor	Cefaclor	
Lilly-cephalexin	Cephalexin	
Loceryl	Amorolfine	
Lorabid	Loracarbef	
Lovire	Acyclovir	
Macrodantin	Nitrofurantoin	
Macropen	Amoxycillin+cloxacillin	
Mandokef	Cefamandole	
Maxcil	Amoxycillin	
Maxaquin	Lomefloxacin	
Maxipime	Cefepime	
Medamet	Metronidazole	
Medaspor	Clotrimazole	
Mefliam	Mefloquine	
Megamox	Ampicillin+cloxacillin	
Megapen	Amoxycillin+flucloxacillin	
Mefoxin	Cefoxitin	
Meronem	Meropenem	
Metazol	Metronidazole	
Microcidal	Griseofulvin	
Minomycin	Minocycline	
Minotabs	Minocycline	
Moxan	Amoxycillin	
Myambutol	Ethambutol	
Mycoban	Clotrimazole	
Mycobutin	Rifabutin	
Mycostatin	Nystatin	
Mynah	Ethambutol+isoniazid	
Myrin	INH-rifampicin-ethambutol	
Mytobrin	Tobramycin	
Narobic	Metronidazole	
Natacin	Natamycin	
Naxogin	Nimorazole	
Nebcin	Tobramycin	

TRADE NAME	GENERIC NAME	PRICE*
Netromycin	Netilmicin	
Nidatron	Metronidazole	
Nivaquine	Chloroquinesulphate	
Nizoral	Ketoconazole	
Norimox	Amoxycillin	
Norisep	Cotrimoxazole	
Noritet	Doxycycline	
Noroxin	Norfloxacin	
Norvir	Ritonavir	
Novo-VK	PenicillinV	
Novocillin	Procainepenicillin	
Novopen	PenicillinG	
Novostrep	Streptomycin	
Nystacid	Nystatin	
O-4cycline	Tetracycline	
O-tet	Tetracycline	
Orbenin	Cloxacillin	
Orelox	Cefpodoxime	
Oxypan	Tetracycline	
Paludrine	Proguanil	
Penbritin	Ampicillin	
PenilenteLA	Benzathinepenicillin	
Penilenteforte	Benzathinepenicillin+procainepenicillin+ benzylpenicillin	
Penmox	Amoxycillin	
Penrite	Ampicillin	
Pentacarinat	Pentamidine	
Petercillin	Ampicillin	
Pipralen	Piperazine	
Pipril	Piperacillin	
Piprine	Piperazine	
Plasmaquine	Chloroquinesulphate	
Primaquine(Zeneca)	Primaquine	
Procillin	Procainepenicillin	
Promoxil	Amoxycillin	
Prozef	Cefprozil	
Purbac	Cotrimoxazole	
Purmycin	Erythromycin	
Puromylon	Nalidixicacid	
Pyrazide	Pyrazinamide	
Q-medcotrimoxazole	Cotrimoxazole	
Q-medgentamicin	Gentamicin	
Ranamp	Ampicillin	
Ranceph	Cephalexin	
Ranmoxy	Amoxycillin	
Ranzol	Cefazolin	
Retrovir	Zidovudine(AZT)	
Rifadin	Rifampicin	
Rifater	INH+rifampicin+pyrazinamide	
Rifcin	Rifampicin	
Rifinah	Rifampicin+INH	

TRADE NAME	GENERIC NAME	PRICE*
Rimactane	Rifampicin	
Riostatin	Tetracycline	
Rocephin	Ceftriaxone	
Rocillin	Amoxycillin	
Rolab-cefaclor	Cefaclor	
Rolab-ethambutol	Ethambutol	
Romin	Minocycline	
Roxy	Tetracyline	
Rozide	Pyrazinamide	
Rulide	Roxithromycin	
Ryped	Erythromycin	
Saltermox	Amoxycillin	
Sepexin	Ceftibutin	
Septidron	Pipemidicacid	
Septran	Cotrimoxazole	
Soframycin	Framycetin	
Spectracil	Ampicillin	
Spectramox	Amoxycillin	
Spectrim	Cotrimoxazole	
Sporanox	Itraconazole	
Succin	Erythromycin	
Succilate	Erythromycin	
Suprapen	Amoxycillin+flucloxacillin	
Symmetrel	Amantadine	
Targocid	Teicoplanin	
Tarivid	Ofloxacin	
Tavanic	Levofloxacin	
Terramycin	Tetracycline	
Tetracem	Tetracycline	
Tetralysal	Tetracycline	
Tetramel	Tetracycline	
Tetrex	Tetracycline	
Thedox	Doxycycline	
Tienam	Imipenem	
3-TC	Lamivudine	
Tobrex	Tobramycin	
Trichozole	Metronidazole	
Trimethox	Cotrimoxazole	
Trimoks	Cotrimoxazole	
Trimzole	Cotrimoxazole	
Triomin	Minocycline	
Triprim	Trimethoprim	
Ultracillin	Benzathinepenicillin	
Ultramox	Amoxycillin	
Ultrazole	Cotrimoxazole	
Ultrasept	Cotrimoxazole	
Uniquin	Lomefloxacin	
Utin	Norfloxacin	
V-cil-K	PenicillinV	
Vancocin	Vancomycin	
Vancomycin-HCL-Lederle	Vancomycin	

TRADE NAME	GENERIC NAME	PRICE*
Vercef	Cefaclor	
Vermox	Mebendazole	
Vibramycin	Doxycycline	
Videx	Didanosine(ddI)	
Viramune	Nevirapine	
Vira-cept	Nelfinavir	
Wellvone	Atovaquone	
Winlomylon	Nalidixicacid	
Wormgo	Mebendazole	
Xeracil	Amoxycillin	
Xeramel	Erythromycin	
Xeroprim	Cotrimoxazole	
Xerazole	Cotrimoxazole	
Xillin	Amoxycillin	
Yomesan	Niclosamide	
Zagam	Sparfloxacin	
Zagyl	Metronidazole	
Zelitrex	Valaciclovir	
Zentel	Albendazole	
Zerit	Stavudine(d4T)	
Zinacef	Cefuroxime	
Zinnat	Cefuroxime	
Zithromax	Azithromycin	
Zobacide	Metronidazole	
Zolerol	Metronidazole	*PRICE TO BE
Zovirax	Acyclovir	UPDATED BY
Zoxil	Amoxycillin	THE USER

Chapter 5: Antibiotics in Pregnancy

PROBABLY SAFE	MAY BE HARMFUL USE ONLY IF ESSENTIAL	CONTRAINDICATED
Amoxycillin	Acyclovir	Amantadine
Amoxycillin-clavulanate	Amikacin	Ciprofloxacin
Ampicillin	Aminosalicylic acid	Clarithromycin
Cefadroxil	Amphotericin B	Doxycycline
Cefamandole	Azithromycin	Enoxacin
Cefazolin	Cefepime	Erythromycin estolate
Cefotaxime	Chloramphenicol[1]	Fluconazole
Cefoxitin	Clindamycin	Flucytosine
Cefpodoxime	Cotrimoxazole[1]	Ganciclovir
Ceftazidime	Ethambutol	Griseofulvin
Ceftriaxone	Ethionamide	Lomefloxacin
Cefuroxime	Famciclovir	Minocycline
Cephalexin	Gentamicin	Nalidixic acid
Cephalothin	Itraconazole	Norfloxacin
Cephradine	Mebendazole	Ofloxacin
Chloroquine	Mefloquine	Primaquine
Cloxacillin	Metronidazole	Tetracyclines
Erythromycin (not estolate)	Netilmicin	
Imipenem	Niclosamide	
Isoniazid	Nitrofurantoin[1]	
Loracarbef	Pentamidine	
Nystatin	Piperacillin-tazobactam	
Piperacillin	Praziquantel	
Piperazine	Pyrantel	
Rifampicin	Pyrazinamide	
	Pyrimethamine	
	Quinine	
	Streptomycin	
	Sulphonamides[1]	
	Thiabendazole	
	Tobramycin	
	Trimethoprim	
	Trimethoprim-sulfamethoxazole[1]	
	Valaciclovir	
	Vancomycin	
	Zidovudine	

[1] Contraindicated at term

Chapter 6: Antibiotic Prophylaxis In Surgery

Fundamental principles of Surgical Prophylaxis

- The antibiotic must be in the tissue before the bacteria are introduced i.e. antibiotic must be given intravenously shortly before surgery to ensure high blood / tissue levels. Prophylaxis failure may be due to antibiotics given too late or more often, given too early. The half-life of the particular antibiotic is therefore important.
- There is no data to support more than a single dose. Further doses generally constitute treatment. Note the waste of resources, the in-creased risk of complications and the fact that multiple doses are not associated with increased efficiency.
- The chosen antibiotics must be active against the most common ex-pected pathogens.
- Deviations from these guidelines may be warranted in certain situations, e.g. MRSA outbreak in an individual hospital.
- High risk patients, e.g. patients with jaundice or diabetics, or patients who undergo any procedures to insert prosthetic devices, generally warrant antibiotic prophylaxis.

N.B. There are no convincing statistical differences in efficacy between the 1st, 2nd or 3rd generation cephalosporins, therefore a 1st generation cephalosporin MUST be the preferred option.

For which type of operations?

Antibiotic prophylaxis is generally indicated for patients undergoing the following types of operations:

- All clean-contaminated procedures; these include penetration of the gastrointestinal tract, whether by penetrating trauma or related to a pathological organ event (e.g. ruptured appendix, perforated colonic diverticulum) prior to the development of clinical peritonitis.
- Clean operations with foreign body implant (e.g. vascular, cardiac and orthopaedic operations), and those without foreign body implants especially hernia repair, breast surgery, median sternotomy, vascular surgery involving the aorta and the lower extremities, and craniotomy.

The use of antibiotics in operations classified as contaminated or dirty/infected should be considered as therapeutic and is clearly not prophylactic i.e. treatment should be given for a longer duration. Operations for acute cholecystitis, empyema of the gallbladder, ascending cholangitis or liver abscess require antibiotic treatment rather than prophylaxis (see under gastrointestinal infections). The same applies to operations for a perforated appendix with evidence of local or generalised peritonitis and/or intraabdominal abscess, and penetrating abdominal trauma where significant gastrointestinal leakage with peritoneal soiling is identified at the time of the operation.

Timing of antibiotic prophylaxis

Current recommendations are that the parenteral antibiotics used in prophylaxis should be given in sufficient dosage within 30 minutes preceding incision. This results in near maximum drug levels in the wound and the surrounding tissues during the operation. This can be facilitated by having the anaesthetist administer the antibiotic in the operating room when the intravenous lines are inserted shortly before operative incision. A single preoperative dose of antibiotic has the same efficacy as multiple doses and the current recommendation is to administer a second dose only if the operation lasts for longer than 2 - 3 hours. With the oral preoperative antibiotic preparation commonly used before elective colonic resection, the chosen agents should be given during the 24 hours before the operation in order to attain significant intraluminal (local) and serum (systemic) levels.

Route of administration of prophylactic antibiotics

Intravenous administration of the prophylactic antibiotic is preferred for most patients undergoing an operative procedure. Oral antibiotics currently play a major role only in the preparation of patients before elective colon surgery.

Antibiotic prophylaxis for common surgical operations

1. CARDIAC, THORACIC AND VASCULAR SURGERY

   Antibiotic prophylaxis in cardiovascular surgery has proven beneficial only in the following procedures :

   - Reconstruction of the abdominal aorta
   - Procedures on the leg which involve a groin incision
   - Any vascular procedure with insertion of a prosthesis / foreign body
   - Lower extremity amputation for ischaemia
   - Cardiac surgery

   Cardiac: prosthetic valve insertion, coronary artery bypass graft, other open heart surgery, pacemaker implant, median sternotomy.

   1st generation cephalosporins e.g. cefazolin 1 - 2 g pre-induction
   OR
   2nd generation cephalosporins e.g. cefuroxime 1.5 g IV

   Note:

   - During prolonged operations, additional intraoperative doses every 4 - 8 hours are indicated.
   - Some authors recommend continuing the antibiotic for up to 48 hours after the procedure (e.g. 1 - 2 g 8 hrly).
   - Vancomycin, only if there is a high rate of documented MRSA infections in the unit.

   Non-cardiac vascular: e.g. aortic resection, prosthesis, groin incision, lower extremity amputation.

Cefazolin 1 g pre-induction. Additional intraoperative doses at 4 - 8 hour intervals during prolonged operations
OR
Vancomycin, for MRSA outbreaks only

Note:

- The value of antibiotics in carotid or brachial artery surgery has not been established, unless prosthetic material is used.
- To cover for Gram-negative coliform bacteria during groin incisions, a 2nd generation cephalosporin can be considered, only if high resistance rates to cefazolin are present in a specific community.

2. GENERAL THORACIC: PULMONARY, OESOPHAGEAL

1st generation cephalosporins e.g. cefazolin 1 - 2 g pre-induction
OR
2nd generation cephalosporins e.g. cefuroxime 1,5 g IV.

Note: Some authors recommend continuing the antibiotic for up to 48 hrs after the procedure to prevent empyema or pneumonia.

3. ORTHOPAEDIC SURGERY

Arthroplasty of joints, and/or joint replacement.

1st generation cephalosporins eg. cefazolin 1 - 2 g pre-operatively. If the operation is longer than 3 hours, give a second dose. Some authors recommend continuing the antibiotic for up to 48 hours after the procedure (e.g. cefazolin 1 - 2 g 8 hrly).

Open reduction of fracture
1st generation cephalosporin eg. cefazolin 1 - 2 g IV pre-op.

Laminectomy, spinal fusion
Prophylactic antibiotics have not been proved to be beneficial.

Lower limb amputation

1st generation cephalosporins eg. cefazolin 1 - 2 g IV.
OR
cefoxitin 2 g IV.

Note:

- The use of a 2nd generation cephalosporin may be considered in cases of possible Gram-negative bacterial contamination (e.g. hip surgery), but is dictated by high incidence of resistance to the 1st generation cephalosporins.
- Data regarding prophylactic antibiotics in arthroscopic surgery is not available.

- Compound (open) fractures are considered contaminated, so antibiotics are essentially therapeutic in such situations.

4. GASTRODUODENAL SURGERY

Antibiotics are indicated in high risk patients only, i.e. patients with bleeding ulcer, obstructive duodenal ulcer, gastric ulcer, low gastric acidity, decreased GI motility, malignancy or morbid obesity.

a. 1st generation cephalosporins e.g. cefazolin 1 g IV pre-op.

b. For beta-lactam allergy, gentamicin 120 mg plus clindamicin 600 mg IV preop.

5. BILIARY TRACT SURGERY

Most studies show that achieving adequate drainage will prevent post-procedural cholangitis or sepsis and there is no further benefit from prophylactic antibiotics. With inadequate drainage, antibiotics may be of value. The American Society for GI Endoscopy recommends prophylaxis for known or suspected biliary obstruction. The value of prophylaxis for ERCP is controversial.

Note that cephalosporins are not active against the enterococci, yet are clinically effective as prophylaxis in biliary surgery. With cholangitis, treat as infection, not prophylaxis. High risk patients include those >70 years of age, acute cholecystitis, non-functioning gall-bladder, obstructive jaundice or common duct stones.

a 1st generation cephalosporins e.g. cefazolin 2 g pre-op as a single dose
OR
b cefoxitin 2 g pre-op as a single dose.

6. INGUINAL HERNIA REPAIR

Available data is limited, routine use is not recommended. For a mesh implant, give prophylaxis e.g. 1st generation cephalosporin as a single dose.

7. COLON SURGERY

Recommended approach for preoperative preparation before elective colon surgery and terminal ileal surgery:

Second day prior to surgery (at home)

- Dietary restriction - low residue or liquid diet.
- Magnesium sulphate, 30 ml of a 50% solution (15 g) orally at 10h00, 14h00 and 18h00.
- In the evening, enemas until clear.

<u>Day of hospitalisation (preoperative day)</u>

- Admit in the morning.
- Clear liquid diet, IV fluids as needed.
- Magnesium sulphate in dosage as above at 10h00 and 14h00.

OR

- Whole-gut lavage with polyethylene glycol electrolyte solution 1L/h for 2 - 4 hours, or 10% mannitol until diarrhoea effluent is clear.
- Neomycin and erythromycin base, 1 g each orally at 13h00, 14h00 and 23h00. Alternative oral antibiotics include metronidazole plus kanamycin or neomycin.

Day of surgery

- Cefoxitin 2 g pre-op and every 6 hours for 3 doses OR
- Metronidazole 500 mg IV pre-op single dose OR
- Ampicillin plus metronidazole plus aminoglycoside all as single doses

OR

- 3rd generation cephalosporin plus metronidazole as a single dose

OR

- for patients with beta-lactam allergy, give metronidazole 500 mg IV and gentamicin 3 mg/kg IV pre-operatively, both as single doses.

For non-elective colorectal surgery, give cefoxitin 1 g IV pre-operatively and then 1 g 8 hourly for 3 doses.

8. APPENDICECTOMY

- Cefoxitin 2 g IV pre-op and for up to 3 doses. If perforated, continue for 3 - 5 days.
- For patients with beta-lactam allergy, give metronidazole 500 mg IV pre-operatively or use metronidazole in form of suppository.

9. PENETRATING ABDOMINAL TRAUMA

Any antibiotic cover can be considered as treatment and not as prophylaxis.

Cefoxitin 2 g IV on admission, continue q.i.d. for 2 - 5 days for intestinal perforation
OR
Metronidazole 500 mg IV and gentamicin 1.7 mg/kg IV.

10. ABDOMINAL SURGERY NOT INVOLVING A VISCUS

Data to support recommendations for prophylaxis not available.

11. OBSTETRICS AND GYNAECOLOGY

- Vaginal hysterectomy and emergency caesarian section
  1st generation cephalosporin eg. cefazolin 1 - 2 g IV, as a single dose.
- Abdominal hysterectomy, cervical cerclage after 18 weeks, induced abortion with risk factors, (e.g. history of previous PID, multiple partners, young, known gonococcal or chlamydia infections) - antibiotic is probably indicated. 1st generation cephalosporin eg. cefazolin 1 - 2 g IV.

- Elective caesarian section
  Prophylactic antibiotics are not indicated.
- Insertion of IUCD
  Prophylactic antibiotics are not indicated.

12. UROLOGICAL SURGERY
    - Prostatectomy
      Prophylaxis only in high risk patients viz. uraemia, diabetes, neurological bladder, large residual volume, cardiac disease or previous UTI.
    - quinolones as a single oral pre-operative dose e.g. ciprofloxacin 500 mg PO stat or
    - aminoglycosides as a single IV pre-operative dose.
    - Transrectal prostate biopsy
      The quinolones have been shown to reduce bacteraemia from 37% to 7%.

    Note:
    - Dilatation of urethra, endoscopic diagnostic procedures, needle biopsy or lithotripsy with sterile urine: prophylactic antibiotics are not indicated.
    - Antimicrobials are not recommended prior to urological procedures in patients with sterile urine.
    - Prophylaxis is supported if catheter has been present for > 24 hours.
    - Ideally the catheter should be inserted two hours or less, prior to surgery.
    - If the urine is infected, it is preferable to sterilize it before beginning an elective procedure.

13. HEAD AND NECK SURGERY
    - Tonsillectomy with/without adenoidectomy
      Data regarding prophylaxis are not available.
    - Major head, neck and oral surgery
      If incision is through oral or oropharyngeal mucosa:

      Cefazolin 2 g IV as single dose
      OR
      Amoxycillin-clavulanate IV 1,2 g as single dose
      OR
      Gentamicin 80mg PLUS clindamycin 600mg IV as single doses
    - Rhinoplasty
      Prophylactic antibiotics have not proved effective.

Surgical procedure	Predominant infecting microorganism(s)	Recommended agent	Dose	Route
Cardiothoracic	Staphylococci	Cefazolin OR Cefuroxime OR Vancomycin (see text)	1 - 2 g 1.5 g	IV IV
Non-cardiac vascular surgery	Staphylococci	Cefazolin or Cefuroxime	1 - 2 g 1.5 g	IV IV
Arthroplasty of joints, joint replacement Open reduction of fractures Lower limb amputation	Staphylococci	Cefazolin	1- 2 g	IV
Gastroduodenal	Streptococci, coliforms, anaerobic bacteria incl. Bacteroides spp.	Cefazolin	1 g	IV
Biliary tract For high risk only: > 70 years Obstructive jaundice Acute cholecystits Acute cholangitis Common duct stone Low risk:	Coliforms, enterococci, anaerobic bacteria incl. Bacteroides, clostridia	Cefazolin or Cefoxitin No prophylaxis	2 g 2 g	IV IV
Colon/small bowel	Coliforms, anaerobic bacteria incl. Bacteroi-des fragilis	Cefoxitin see text for alteratives.	2 g	IV
Appendectomy	Coliforms, anaerobic bacteria incl. Bacteroi-des fragilis	Cefoxitin	2 g	IV
Penetrating abdominal trauma	Coliforms, anaerobic bacteria incl. Clostridia, Bacteroides fragilis	Cefoxitin	2 g	IV
Vaginal or abdominal hyster-ectomy	Coliforms, enterococci group B streptococci	Cefazolin	1 - 2 g	IV
Caesarian section with high risk e.g. premature rupture of membranes Low risk - elective	as for hysterectomy	Cefazolin or Cefoxitin No prophylaxis	1 g 2 g	IV IV
Abortion	as for hysterectomy	Cefazolin	1 g	IV
Prostatectomy	Coliforms	Ciprofloxacin or gentamicin	500 mg 1,5 mg/kg	PO IV
CNS shunts	Staphylococci	Cefazolin	1 g	IV

Chapter 7: Antibiotic Prophylaxis for Non-surgical Conditions

Bacterial endocarditis

Prevention of infective endocarditis in persons with certain underlying cardiac conditions is important since this infection continues to cause serious morbidity and mortality despite advances in diagnosis and treatment.

A. Cardiac conditions for which antibiotic prophylaxis is indicated include:

- Prosthetic cardiac valves
- Most congenital abnormalities
- Rheumatic and other acquired valvular abnormalities
- Previous bacterial endocarditis
- Hypertrophic cardiomyopathy
- Mitral valve prolapse with valvular regurgitation

Procedures for which Endocarditis Prophylaxis in the abovementioned patients is necessary, include:

- Dental procedures known to cause mucosal or gingival bleeding e.g.extractions, dental implant placement and reimplantation of avulsed teeth, root canal instrumentation or surgery, professional cleaning
- Tonsillectomy and/or adenoidectomy
- Surgical conditions that involve penetration of intestinal or respiratory mucosa
- Bronchoscopy with a rigid bronchoscope
- Sclerotherapy for oesophageal varices
- Biliary tract surgery
- Cystoscopy
- Urethral dilatation
- Urethral catheterisation, if infection is present
- Prostatic surgery
- Incision and drainage of infected tissue

Procedures where antibiotic prophylaxis is not necessary for the abovementioned patients include:

- Dental procedures not likely to induce bleeding e.g. adjustment of orthodontic appliances, shedding of primary teeth, taking of oral radiographs, injection of intraoral anaesthetic
- Endotracheal intubation
- Bronchoscopy with a flexible bronchoscope, with or without biopsy
- Tympanostomy tube insertion
- Cardiac catheterisation
- Upper gastrointestinal endoscopy with or without biopsy

- Caesarian section
- Abdominal hysterectomy
- Uncomplicated vaginal delivery
- Dilatation and curettage
- Therapeutic abortion
- Insertion or removal of intrauterine devices
- Urethral catheterisation without evidence of infection
- Circumcision

B. Antibiotic prophylaxis is not recommended for patients with:
- Cardiac pacemakers and implanted defibrillators
- Previous rheumatic fever without valvular dysfunction
- Physiological, functional or innocent murmurs
- Previous coronary artery bypass surgery
- Uncomplicated atrial septal defect
- Isolated secundum atrial septal defect
- Mitral valve prolapse without valvular regurgitation
- Surgical repair of atrial septal defect, ventricular septal defect or patent ductus arterious
- Previous Kawaski disease without valvular dysfunction

Prophylactic regimens

A. Dental, oral, respiratory tract or oesophageal procedures

Streptococcus viridans is the most common cause of endocarditis following dental, oral, respiratory tract, or oesophageal procedures.

Amoxycillin 2 g PO (50 mg/kg in children) 1 hour before the procedure. A second dose is not necessary.

- If allergic to penicillin/amoxycillin:

  Cephalexin or cefadroxil 2 g PO (50 mg/kg in children) 1 hour before the procedure.
  OR
  Clindamycin 600 mg PO or IV (20 mg/kg in children) 1 hour before the procedure.
  OR
  Azithromycin or clarithromycin 500 mg PO (15 mg/kg in children) 1 hour before the procedure.
- If unable to take oral medications:

  Ampicillin 2 g IV (50 mg/kg in children) 30 minutes before the procedure.
  OR
  Clindamycin 600 mg IV (20 mg/kg in children) 30 minutes before the procedure.

A second dose of antibiotic is not necessary because the abovementioned antibiotic dosages achieve prolonged serum levels above the MICs of most oral streptococci and prolonged serum inhibitory concentrations.

Erythromycin is no longer included because of gastrointestinal upset.

B. Genitourinary and gastrointestinal procedures

The relevant organisms are usually enterococci, and rarely Gram-negative bacilli.

Ampicillin 2 g IV (50 mg/kg in children) PLUS gentamicin 1.5 mg/kg IV (1.5 mg/kg in children) 30 minutes before the procedure followed by one dose of amoxycillin 1 g PO (25 mg/kg in children) 6 hours after the initial dose OR one dose of ampicillin 1 g IV (25 mg/kg in children) 8 hours after the initial dose.

If allergic to ampicillin/penicillin or unable to take oral medication:

Vancomycin 1 g IV (20 mg/kg in children) PLUS gentamicin 1.5 mg/kg IV (2 mg/kg in children) 30 minutes before the procedure, as single dose only.

Contacts of invasive Haemophilus influenza type b and meningococcal infections

The purpose of chemoprophylaxis in contacts is to eradicate nasopharyngeal colonisation by Neisseria meningitidis or Haemophilus influenzae type b and thus reduce both the risk of disease in contacts and the transmission to nonimmune susceptible people.

Haemophilus influenzae contacts

Rifampicin prophylaxis should be prescribed promptly for all household contacts of patients with severe invasive Haemophilus influenzae infections (e.g. meningitis and epiglottitis) especially if the contact is less than 4 years old. Prophylaxis for infants and young children (less than 4 years old) with day-care exposure is also appropriate. The dosage of rifampicin is 600 mg PO daily x 4 doses for adults (20 mg/kg/day x 4 doses in children older than 1 month, and 10 mg/kg/day x 4 doses in children younger than 1 month).

Meningococcus contacts

Household contacts, day-care contacts, and only health-care workers with direct exposure to oral secretions (e.g. mouth-to-mouth resuscitation) of patients with invasive meningococcal infection, require prophylaxis. The index case also requires an agent to eradicate nasopharyngeal carriage, prior to discharge from hospital (unless treated with ceftriaxone or cefotaxime) since therapy with penicillin may not eliminate nasopharyngeal carriage of the organism.

The recommended chemoprophylactic agents include:

Rifampicin 20 mg/kg (to a maximum of 600 mg) given 12 hourly PO x 4 doses
OR
Ceftriaxone 250 mg (in adults) or 125 mg (in children) IM as a single dose
OR
Ciprofloxacin 500 mg PO as a single dose in adults and older children

Influenza A

Amantadine is effective against influenza A but not against influenza B. In outbreak situations, it can be used as supplement or in addition to vaccine in those at high risk e.g. elderly persons, health-care providers, and those with chronic disease. It provides temporary protection for those at immediate risk, until immunisation has stimulated immunity 2 weeks after immunisation. Dose of amantadine: 100 mg PO daily.

Pertussis exposure

Erythromycin may be given to household contacts in doses of 50 mg/kg/day in 4 divided doses for 14 days.

Post-splenectomy

Asplenic patients are more prone to invasive infection by capsulated bacterial pathogens, such as Streptococcus pneumoniae, Haemophilus influenzae type b, and Neisseria meningitidis. Ideally, patients should receive pneumococcal polyvalent, Haemophilus influenzae type b, and meningococcal vaccines at least 2 weeks before splenectomy. Thereafter, revaccinate every 5 - 6 years. In addition, benzathine penicillin G 1.2 mU IM should be administered once monthly for 2 - 3 years after splenectomy. Alternative antibiotic chemotherapy includes penicillin V 250 mg PO 12 hourly daily (125 mg PO 12 hourly in children less than 5 years). For sophisticated patients, the "amoxycillin in pocket" approach is recommended; patients take amoxycillin 250 mg 8 hourly at the first sign of an upper respiratory tract infection.

Rheumatic fever

Chemoprophylaxis is usually started after the first episode of rheumatic fever and continued for 5 years, or up to the age of 18 years, which ever is the longer. The aim is to maintain antibiotic levels sufficient to prevent pharyngeal infection with Streptococcus pyogenes.

The recommended agents include:

Benzathine penicillin G 1.2 mU IM once monthly (900000 U for children less than 9 years)
OR
Penicillin V 250 mg PO 12 hourly (125 mg PO 12 hourly in children less than 5 years)
OR
Erythromycin 250 mg PO 12 hourly (10 mg/kg/day if less than 40 kg)

Chapter 8: Bone and Joint Infections

Osteomyelitis

Intravenous treatment should be given until the patient has been afebrile for several days, when carefully monitored oral treatment can be substituted. The duration of antibiotic treatment is usually 6 weeks in adults and at least 3 weeks in children.

A. Acute haematogenous osteomyelitis

Empiric antibiotic therapy for presumed bacterial osteomyelitis should only be given after obtaining blood cultures.

Adults and children over 5 years

The usual organisms involved are Staphylococcus aureus and Streptococcus spp.

Empiric treatment:

Cloxacillin 100 - 200 mg/kg/day up to 12 g/day IV divided 6 hourly
OR
Cefazolin100 mg/kg/day up to 4 g/day IV divided 6 hourly

In patients allergic to beta-lactams:

Vancomycin 1 g IV 12 hourly (40 mg/kg/day in children)
OR
Clindamycin 16 mg/kg/day up to 1200 mg/day IV divided 6 hourly
OR
Fusidic acid 30 mg/kg/day up to 1500 mg/day IV divided 8 hourly.

It is ideal to combine clindamycin or fusidicacid with a second antistaphylococcal agent such as rifampicin.

Enterobactericeae are occasional causes of acute haematogenous osteomyelitis in adults. In such cases, ceftriaxone 2 g IV once daily OR ciprofloxacin 200 - 300 mg IV 12 hourly OR 500 - 750 mg orally 12 hourly is suggested.

Children under 5 years

Consider Haemophilus influenzae in addition to Staphylococcus aureus and Streptococcus spp.

Empiric treatment:

Cefotaxime 50 mg/kg IV 8 hourly
PLUS
Cloxacillin 50 - 150 mg/kg/day IV divided 6 hourly for 3 weeks.

B. Osteomyelitis following penetrating injuries of the foot

Pseudomonas aeruginosa infection commonly follows penetrating injuries of the foot. Gentamicin OR amikacin OR tobramycin PLUS piperacillin OR ceftazidime are suggested.

Septic arthritis

Empiric antibiotic therapy for presumed bacterial arthritis should only be given after obtaining blood cultures and withdrawing synovial fluid for microscopy and culture. The common causes of septic arthritis in various age groups are similar to those of acute haematogenous osteomyelitis (see above). The same antibiotic regimens may be used but in the case of septic arthritis a 3-week course is usually adequate. Prompt aspiration and irrigation is indicated and may need to be repeated several times until the infection is controlled. Occasionally open surgical drainage is required. Most agents used to treat septic arthritis reach sufficient levels in the joint when given intravenously, and therefore, intra-articular injections of antibiotics, or inclusion of antibiotics in solutions used to irrigate the joint, are unnecessary.

Prosthetic joint infection

Diagnosis and treatment are commonly difficult. The usual infecting organisms are Staphylococcus aureus, coagulase-negative staphylococci; or less commonly, bacteria such as Pseudomonas aeruginosa, E coli, Klebsiella species.

Successful treatment involves both surgical intervention and antibiotic therapy. Close co-operation between the orthopaedic surgeon and the microbiology laboratory is essential. It is strongly recommended that deep representative tissue specimens be obtained for culture, prior to initiation of any antimicrobial therapy.

Treatment plans are usually individualised. Surgical options include (1) soft tissue debridement, with retention of prosthetic components; (2) debridement and removal of all prosthetic components and cement, with immediate or delayed reimplantation of a new prosthesis; and (3) debridement and removal of all prosthetic components and cement, without reimplantation.

Antibiotics are usually given intravenously for 4 - 6 weeks:

Cloxacillin 100 - 200 mg/kg/day up to 12 g/day divided 6 hourly
OR
Cefazolin 2 g IV every 12 hours
OR
Vancomycin 1 g IV 12 hourly (40 mg/kg/day) - vancomycin should NOT be used to treat oxacillin-(cloxacillin) susceptible staphylococci.

Preliminary data indicate that combinations including an oral quinolone, such as ciprofloxacin, PLUS an antistaphylococcal agent, such as rifampicin or fusidic acid or clindamycin, may be a useful outpatient regimen after 2 weeks of IV antibiotic therapy.

Septic bursitis

It is almost always due to Staphylococcus aureus and should be treated by aspiration and cloxacillin or a first-generation cephalosporin or clindamycin or fusidic acid for 3 weeks. Note: fusidic acid or clindamycin should be combined with a second antistaphylococcal agent such as rifampicin and should be restricted to patients who are allergic to penicillin or infections caused by methicillin-(oxacillin) resistant Staphylococcus aureus.

Causative Organism and / or Illness type	Drug of Choice	Adult Dose	Dose in Children	Alternative
Osteomyelitis Acute haematogenous osteomyelitis				
Adults and children > 5 yr	Cloxacillin OR Cefazolin	2 - 3 g 6hrly IV 1.5 g 8 hrly IV	100 - 200 mg/ kg/day 100 mg/ kg/ day	Clindamycin or Fusidic acid PLUS Rifampicin
Children < 5 yrs	Cefotaxime PLUS Cloxacillin		50 mg/kg 8 hrly IV 100 - 200 mg/ kg/day	Amoxycillin+ clavulanate
Following penetrating injuries of the foot	Gentamicin OR Amikacin PLUS Piperacillin OR Ceftazidime	5 mg/kg IV/IM once daily 15 mg/kg IV/ IM once daily 3 - 4 g 4 - 6 hrly IV/IM 0.5 - 2 g 8 – 12 hrly IV/IM	1 - 2.5 mg/ kg 8 hrly 15 mg/kg IV/ IM once daily 50 mg/kg 4 - 6 hrly 30 - 50 mg/ kg 8 hrly	
Septic arthritis	see acute haematogenous osteomyelitis			
Septic bursitis	Cloxacillin OR Cefazolin	2 - 3 g 6hrly IV 1.5 g 8 hrly IV	100 - 200 mg/ kg/day 100 mg/kg/ day	Clindamycin or Fusidic acid PLUS Rifampicin

Chapter 9: Cardiovascular Infections

Infective endocarditis

Before antibiotic therapy is initiated, multiple blood cultures (3 sets, collected from different sites, within a 24 hour interval) MUST be obtained in any patient in whom infective endocarditis is suspected.

1. Native valve endocarditis

   Empiric treatment for native valve endocarditis

   Penicillin G 20 mU per day given in equally divided doses every 4 hours by IV bolus injection PLUS gentamicin 80 mg IV 12 hourly. If there is a strong possibility of staphylococcal infection – eg., in intravenous drug users and patients on haemodialysis - vancomycin 1 g IV 12 hours should be used instead of penicillin G.

   When the results of the blood cultures are known and the antibiotic sensitivity of the organism has been determined, the treatment can be modified and decisions made about its duration.

   If the patient's haemodynamic condition deteriorates despite appropriate antibiotic treatment, the opinion of a cardiac surgeon should be sought.

   Definitive treatment of viridans streptococcal and Streptococcus bovis endocarditis.

   The regimen used will depend on the precise penicillin sensitivity of the isolate, as determined by the MIC.

   A. Fully sensitive to penicillin (MIC < 0.1 mg/l)

      Penicillin G 20 mU per day given in equally divided doses every 4 hours by IV bolus injection for 14 - 28 days PLUS gentamicin 80 mg IV twice daily for 14 - 28 days.

      Conditions to be met for a two week treatment regimen:
      - Native valve infection.
      - No evidence of thromboembolic disease.
      - No vegetations more than 5 mm diameter on echocardiogram.
      - No cardiovascular risk factors such as heart failure, aortic insufficiency or conduction abnormalities.
      - Clinical response within 7 days. Temperature should return to normal, patient should feel well and appetite should return.

   B. Reduced sensitivity to penicillin (MIC > 0.1 mg/ml)

      Penicillin G 20 mU per day given in equally divided doses every 4 hours by IV bolus injection for 28 days PLUS gentamicin 80 mg IV twice daily for 28 days.

Definitive treatment of Enterococcal endocarditis

Enterococcus faecalis and Enterococcus faecium are more resistant to penicillin than the viridans streptococci. Most strains are killed by a combination of either ampicillin or amoxycillin plus gentamicin. Some strains exhibit high level gentamicin resistance and cannot be killed with the combination; some of these high level gentamicin resistant enterococci may be sensitive to streptomycin, therefore streptomycin sensitivity should be determined for these strains.

A. Gentamicin-sensitive or low level resistant (MIC < 100 mg/ml)

   Ampicillin 3 g 6 hourly by IV bolus injection PLUS gentamicin 80 mg IV/IM twice daily for 28 days.

B. Gentamicin highly resistant (MIC > 2000 mg/ml)

   Ampicillin 3 g 6 hourly by IV bolus injection for a minimum of 6 weeks. Streptomycin can be added, if the strain is sensitive.

Definitive treatment of endocarditis caused by Staphylococcus aureus or coagulase-negative staphylococci

Staphylococci may be (i) penicillin-sensitive non-beta-lactamase producers, (ii) beta-lactamase producers resistant to penicillin but sensitive to methicillin (or oxacillin) and hence sensitive to cloxacillin, or (iii) both penicillin- and methicillin-resistant and hence resistant to all beta-lactam antibiotics. Thus, the definitive regimen to be used depends on the sensitivity results.

A. Penicillin-sensitive:

   Penicillin G 20 mU per day in equally divided doses every 4 hours by IV bolus injection for 28 days PLUS gentamicin 80 – 120 mg IV 8 hourly for 28 days.

B. Penicillin-resistant, methicillin-(oxacillin/cloxacillin) sensitive:

   Cloxacillin 2 g 4 hourly by IV bolus injection for 28 days PLUS gentamicin 80 – 120 mg IV 8 hourly for the initial 7 days of therapy.

C. Penicillin- and methicillin-resistant:

   Vancomycin 1 g by IV infusion over at least 100 minutes twice daily for 28 days PLUS gentamicin 80 – 120 mg IV 8 hourly for 7 days.

   There is insufficient data to support the use of teicoplanin as an alternative to vancomycin for staphylococcal endocarditis.

Definitive treatment of endocarditis due to viridans streptococci, or enterococci or staphylococci, in patients allergic to penicillin:

Penicillins are fundamental to the antibiotic treatment of endocarditis; hypersensitivity to them may occasionally be associated with hypersensitivity to cephalosporins and other beta-lactams. Penicillin hypersensitivity therefore seriously compromises the range of antibiotics that can be used. For this reason, patients who claim to be allergic to penicillins, should be closely questioned about the nature of the penicillin hypersensitivity reaction.

Where the alleged manifestations of penicillin hypersensitivity are of a vague or minor nature e.g. gastrointestinal disturbance, and do not indicate an immediate-type hypersensitivity, treatment with a penicillin is justified.

Treatment with penicillin, ampicillin, amoxycillin, or cephalosporins is unjustifiable in patients with a history of immediate-type hypersensitivity reaction e.g. anaphylaxis or urticarial rashes. In such patients, vancomycin should be substituted for penicillin or ampicillin, and combined with gentamicin.

2. Prosthetic Valve Endocarditis

The same choice of empiric and definitive antibiotic regimens are recommended for native and prosthetic valve endocarditis. The duration of therapy for prosthetic valve endocarditis is usually 4 to 6 weeks.

In cases of staphylococcal endocarditis in the presence of a prosthetic value, the American Heart Association recommends that rifampicin be added to the cell wall active agent (i.e. cloxacillin or vancomycin) for a full 6-week period, and that gentamicin be administered for the first 2 weeks.

Note: Gentamicin levels must be monitored in all patients where gentamicin is used in the treatment of bacterial endocarditis (twice a week if serum

Intravascular catheter-related infection

creatinine levels are normal, and daily if serum creatinine is raised).

Draw blood cultures by venepuncture from a separate vein and not from the vascular line; this is to avoid contamination from the catheter hub. The value of comparing quantitative cultures from a vein with those drawn through the catheter is controversial and not routinely performed. Peripheral catheters should be removed and sent to the laboratory for culture of the distal 2 - 5 cm of the catheter tip. Meticulous aseptic technique is essential when removing the catheter, to avoid confusing contamination. Central lines may be changed and the removed tip sent to the laboratory for culture. Some laboratories perform semi-quantitative counts in an attempt to distinguish between colonisation/infection and contamination. If infection is confirmed, removal of the new catheter, which is likely to be contaminated, should be considered.
If a catheter-related bloodstream infection is confirmed, treatment is selected on the basis of the culture and sensitivity results, and the clinical condition of the patient:

1. Coagulase - negative staphylococci:

Antistaphylococcal therapy for 7 days, provided the patient responds clinically in 48 to 72 hours. The catheter may be "saved" in the majority, but a recurrence rate of approximately 20% can be expected.

2. Staphylococcus aureus:

Uncomplicated: Antistaphylococcal therapy for 14 days. Complicated (e.g. septic thrombophlebitis): antistaphylococcal therapy for 4 weeks.

3. Candida spp.:

Fluconazole 400mg daily for 14 days.

Chapter 10: Central Nervous System Infections

Acute Bacterial Meningitis

Meningitis may be fulminant. The aetiology is established by examination of cerebrospinal fluid (CSF) obtained by lumbar puncture and sometimes by blood culture. When such specimens cannot be collected (obtained) immediately, empiric treatment should be started without delay. The standard recommendations for the empiric treatment of bacterial meningitis have undergone some significant changes in the last decade. The emergence of beta-lactamase-producing strains of Haemophilus influenzae, which now account for approximately 10% of community-acquired strains, has dictated against the use of ampicillin alone as empiric therapy for meningitis in infants and children less than 5 years old. In addition, there is an increasing prevalence of Streptococcus pneumoniae strains which are either highly- or intermediately-resistant to penicillin. This has led most authorities to now recommend one of the third-generation cephalosporins (i.e. ceftriaxone or cefotaxime) as the empiric agent of choice for bacterial meningitis in all age groups. Furthermore, some authorities re-commend the addition of vancomycin to the third-generation cephalosporin as empiric therapy, in areas where resistance to the third-generation cephalosporins amongst strains of Streptococcus pneumoniae occurs. In all situations, therapy must be reviewed once identification and sensitivities of the causative organism become available.

Therefore, it is now imperative that CSF isolates be tested for susceptibility to appropriate antimicrobials, including the performance of minimum inhibitory concentration (MIC) determinations for key agents and tests for beta-lactamase production.

EMPIRIC TREATMENT

Neonates

Group B streptococci, Enterobactericeae, or rarely Streptococcus pneumoniae, Haemophilus influenzae or Listeria monocytogenes are the usual causes.

Cephalosporins are ineffective against Listeria monocytogenes. Therefore, ampicillin must be added to the initial (empiric) regimen.
Cefotaxime 100 - 200 mg/kg/day IV divided 12 hourly
OR
Ceftriaxone 100 mg/kg/day divided 12 - 24 hourly
PLUS
Ampicillin 100 - 200 mg/kg/day IV divided 6 - 12 hourly.

Children aged 2 months to 5 years of age

Haemophilus influenzae is still more common than Streptococcus pneumoniae or Neisseria meningitidis.

Ceftriaxone 100 mg/kg/day, up to 2 g/day IV, as a single daily dose
OR
Cefotaxime 150 - 200mg/kg/day, up to 6 g/day IV, divided 6 - 12 hourly

Note: Ampicillin, amoxycillin or chloramphenicol are not adequate and should only be used in emergency situations if the preferred agents are unavailable.

Adults and children over 5 years of age

Streptococcus pneumoniae and Neisseria meningitidis account for the majority of cases. Penicillin-resistant and intermediately-resistant strains of Streptococcus pneumoniae now occur widely in South Africa. These strains are almost invariably sensitive to cefotaxime, ceftriaxone and vancomycin. However, strains with reduced susceptibility to the third-generation cephalosporins, although rare, have been described in many of the major centres in South Africa.

Ceftriaxone 100 mg/kg/day, up to 2 g/day IV, as a single daily dose
OR
Cefotaxime 150 - 200 mg/kg/day, up to 6 g/day IV, divided 6 - 12 hourly.

SPECIFIC TREATMENT

Meningococcal meningitis

Benzylpenicillin 250000 units/kg/day IV divided 4 hourly for 7 days; up to 20 - 24 million units per day in adults

Pneumococcal meningitis

Benzylpenicillin 250000 units/kg/day IV divided 4 hourly for 7 - 10 days if the isolate is known to be susceptible to penicillin; up to 20 - 24 million units per day in adults. If the strain shows intermediate susceptibility or is fully resistant to penicillin, then treat with ceftriaxone or cefotaxime, if sensitive. If the strain is intermediately- or fully resistant to cefotaxime or ceftriaxone, vancomycin and/or rifampicin may be added.

Haemophilus influenzae meningitis

Ceftriaxone 100 mg/kg/day, up to 2 g/day, IV as a single daily dose for 10 days
OR
Cefotaxime 150 - 200 mg/kg/day, up to 6 g/day, IV divided 6 - 12 hourly for 10 days.

Ampicillin or amoxycillin 200 mg/kg/day IV divided 6 hourly OR chloramphenicol 12.5 - 25 mg/kg 6 hourly IV can be used if the isolate is shown to be susceptible.

ROLE OF DEXAMETHASONE

It has become apparent that the reduction of the host inflammatory response is necessary for optimal management of some forms of acute bacterial meningitis. Dexamethasone in doses of 0.15 mg/kg every 6 hours for the first 4 days of antibiotic treatment of bacterial meningitis has been shown to reduce the frequency of hearing loss and other neurological sequelae, especially in children with Haemophilus influenzae meningitis. The effect in adults and in children with meningitis due to other pyogenic bacteria remains controversial. The first dose of dexamethasone MUST be given 30 minutes before the first dose of antibiotic.

Note: It must not be given after the onset of antibiotic therapy.

Brain abscess

Usual pathogens include Streptococcus milleri, Enterobacteriaceae, Staphylococcus aureus and anaerobes (often polymicrobic).

Empirical treatment:	Penicillin PLUS ceftriaxone PLUS metronidazole
Dose:	Penicillin G 5 mU 4 hourly (adults)
	Ceftriaxone 1 - 2 g 12 - 24 hourly (adults)
	Metronidazole 750 mg 8 hourly (adults)

Definitive treatment depends on the causative organism and results of susceptibility testing:

Nocardia	Cotrimoxazole PLUS amikacin PLUS imipenem OR cefotaxime for 2 months, then cotrimoxazole alone for a total of 12 months
Dose:	Cotrimoxazole (TMP/SMX) 2.5 - 10 mg/kg TMP/ 12.5 - 50 mg/kg SMX 12 hourly
	Amikacin 15mg/kg IV or IM daily
Staphylococcus aureus	Cloxacillin for 3 - 6 weeks
Dose:	2 g 6 hourly (adults), 200 mg/kg/day (children)
Pseudomonas	Ceftazidime PLUS amikacin for 4 - 16 weeks
	OR
	Piperacillin PLUS amikacin for 4 - 16 weeks
Dose:	Ceftazidime 2 g 8 hourly (adults)
	Amikacin 15 mg/kg daily (adults)
	Piperacillin 4 g 8 hourly (adults)

Causative Organism and / or Illness type	Drug of Choice	Adult Dose	Dose in Children	Alternative
Acute bacterial meningitis:				
Neonates	Cefotaxime OR Ceftriaxone PLUS Ampicillin		100 - 200 mg/kg/ day IV 100 mg/kg day IV 100 - 200 mg/ kg/day IV	
Children 2 months - 5 years	Ceftriaxone OR Cefotaxime		100 mg/kg/day IV 150 - 200 mg/kg/ day IV	Ampicillin OR Chloramphenicol
Adults and children > 5 years	Ceftriaxone OR Cefotaxime	100 mg/kg/day IV 150 - 200 mg/kg/ day IV	100 mg/kg/day IV 150 - 200 mg/ kg/day IV	
Meningococcal meningitis		Penicillin G 250000 U/kg/ day IV in 4 - 6 divided doses (up to 20 - 24 million U/day)	250000 U/kg/day	Ampicillin OR Chloramphenicol
Pneumococcal meningitis	Penicillin G	250000 U/kg/ day IV in 4 - 6 divided doses (up to 20 - 24 million U/day)	250 000 U/kg/ day	Cefotaxime OR Ceftriaxone - if not fully sensitive to penicillin PLUS Vancomycin and/ or rifampicin if not fully sensi- tive to third generation cephalosporins
Haemophilus influenzae meningitis	Ceftriaxone OR Cefotaxime	100 mg/kg/ day IV 150 - 200 mg/ kg/day IV in 2 - 4 divided doses	100 mg/kg/ day IV 150 - 200 mg/ kg/day IV	Ampicillin 200 mg/ kg/day IV in 4 divided doses OR Amoxycillin (same dose as ampicillin) only if sensitive OR Chloramphenicol
Brain abscess	Penicillin G PLUS Ceftriaxone PLUS Metronidazole	5 mU 4 hrly 1 - 2 g 12 – 24 hrly 750 mg 8 hrly		

Chapter 11: Ear, Nose and Throat Infections

Otitis media

Acute suppurative otitis media

Usual pathogens: Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis. Occasional pathogens include Streptococcus pyogenes and Staphylococcus aureus.

The usual course of acute otitis media is spontaneous resolution for the majority of patients within 1 – 2 days. The routine use of antibiotics for this condition is based largely on the fear of complications, if antibiotics are not used.

Because Streptococcus pneumoniae is the most common cause of acute otitis media and the least likely to resolve on its own, therapy must be effective against this organism. Strains of Streptococcus pneumoniae throughout South Africa have shown rapid changes in their resistance patterns, and hence the recommendations in this guideline are based on surveillance data on antimic-robial susceptibilities, especially for penicillin. Of those strains showing resis-tance to penicillin, the vast majority (95 – 99 %) are partially- (intermediately-) resistant on MIC testing, and hence amoxycillin remains the preferred oral antimicrobial because it is highly effective against strains of Streptococcus pneumoniae which are both fully susceptible, and partially- (intermediately-) resistant to penicillin. Amoxycillin also demonstrates better pharmacodynamics to these strains than does any other commonly available oral agent. At present, no other oral agent is likely to eradicate penicillin non-susceptible Streptococcus pneumoniae more consistently in upper respiratory sites.

The standard dose of amoxycillin is 40 - 50 mg/kg/day in three divided doses. Higher doses (80 - 100 mg/kg/day) produce concentrations in the middle ear which are sufficient to treat penicillin non-susceptible strains of Streptococcus pneumoniae and hence these higher doses are recommended for empiric therapy of acute otitis media.

It should be noted that although 12% of strains of Haemophilus influenzae and 90% of Moraxella catarrhalis produce beta-lactamase, acute otitis media associated with these microbes almost invariably resolves without treatment.

When clinical failure occurs, other alternative agents should be considered. These include amoxycillin-clavulanate, cefuroxime axetil and intramuscular ceftriaxone.

The newer quinolones (including levofloxacin, moxifloxacin and gatifloxacin), although approved for respiratory tract infections in adults, are not approved for routine paediatric use.

Treatment is for at least 5 days (similar expected results as the 7 - 10 day re-commendation) in children 2 years or more: A 7 - 10 day course is recommended for children less than 2 years of age.

Persistent effusion

Persistent effusion following acute otitis media is seen in 40% of children after 1 month and in 10% after 3 months. The continued use of antibiotic because of effusion, is not indicated: refer for consideration of tympanostomy tube placement.

Mastoiditis

Pathogens and treatment are as for otitis media. An urgent specialist ENT opinion is advisable, as surgery may be necessary.

Otitis externa

Most are due to so-called "swimmer's ear" and the pathogens involved are us-ually Pseudomonas aeruginosa, Proteus mirabilis or other Gram-negative bacteria. Treat-ment: Clean the external ear canal with an acidic solution, such as 2% acetic acid. After cleaning the canal, initiate ototopical therapy with ciprofloxacin drops or gen-tamicin ophthalmic solution or tobramycin drops. Systemic antibiotics play little role in treating acute otitis externa; they are reserved for patients who have concomitant cellulitis of the auricle or periauricular structures, or invasive infections.

Malignant otitis

Malignant otitis externa is an uncommon syndrome, which usually occurs in el-derly diabetic patients or debilitated patients, where Pseudomonas aeruginosa invades the soft tissue, cartilage and bone. This condition is best treated with parenteral antip-seudomonal agents e.g. piperacillin or ceftazidime or imipenem PLUS an aminoglyco-side, and followed with an oral quinolone e.g. cipro-floxacin, when appropriate. Surgical debridement is often required.

Sinusitis

Common pathogens: Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis. Anaerobes play a significant role in adult sinusitis especially if persistent - so-called "chronic sinusitis".

Treatment: Topical decongestant for 5 days (systemic decongestants are not recom-mended). Amoxycillin 500 mg three times daily (80 - 100 mg/kg/day in children) for 10 - 14 days is the treatment of choice for acute sinusitis. Alternative, but significantly more expensive treatment includes amoxycillin- clavulanate 500 - 875 mg (amoxycillin dose) 8 OR 12 hourly (80 - 100 mg/kg/day in children) for 10 - 14 days OR cefuroxime axetil 500 mg 12 hourly (125 mg 12 hourly in children < 2 years, and 250 mg in chldren 2 – 12 years) for 10-14 days. If the patient responds poorly to your first choice of therapy, consider treatment which includes anaerobes in its spectrum of activity.

Pharyngitis/Tonsillitis

The most common and important bacterial cause is Streptococcus pyogenes (= Lancefield group A beta-haemolytic streptococcus).

Penicillin VK 250 - 500 mg 6 hourly (50 mg/kg/day in children) for 10 days
OR
Amoxycillin 250 - 500 mg 8 hourly (25 - 50 mg/kg/day in children) for 10 days.

For the penicillin-allergic patient, erythromycin 500 mg 8 hourly (30 - 50 mg/kg/day) for 10 days.

Penicillin is the only agent conclusively shown to prevent rheumatic fever. The expense of the new macrolides and the cephalosporins do not warrant their use as first line agents.

Oral thrush (Candidiasis)

Swish with 5 - 10 ml of oral nystatin suspension (100000 units/ml) three times per day. Oral ketoconazole 200 - 400 mg/day is also effective in oral candidiasis. In HIV-infected patients, treatment with fluconazole 150 mg PO daily x 5 days is recommended.

Causative Organism and/ or type of Illness	Drug of Choice	Adult Dose	Dose in Children	Alternative
Acute suppurative otitis media	Amoxycillin	80 - 100 mg/kg/ day PO in 3 divided doses x 5 days	80 - 100 mg/kg/ day PO in 3 divided doses x 5 days	Amoxycillin- clavulanate OR Cefuroxime axetil OR Ceftriaxone
Mastoiditis	Amoxycillin	As for otitis media	As for otitis media	As for otitis media
Otitis externa	Gentamicin OR Tobramycin OR Ciprofloxacin	Topically 2 - 4 drops 4 hrly Topically 2 - 4 drops 4 hrly Topically 2 - 4 drops 4 hrly	Topically Topically	
Sinusitis	Amoxycillin	500 mg PO 8 hrly x 10 - 14 days	80 - 100 mg/kg/ day PO x 10 -14 days	Amoxycillin- clavulanate OR Cefuroxime axetil
Pharyngitis/ tonsillitis	Penicillin V OR Amoxycillin	250 - 500 mg PO 6 hrly x 10 days 250 - 500 mgPO 8 hrly x 10 days	50 mg/kg/day PO x 10 days 25 - 50 mg/kg/ day x 10 days	Erythromycin x 10 days OR Azithromycin x 5 days

Chapter 12: Eye Infections

Superficial eye infections such as blepharitis and conjunctivitis are generally treated adequately with antimicrobial agents applied topically. More serious infections may require subconjunctival injections.

Although it is always recommended that a swab be taken for culture and sensitivity, so that specific therapy may be instituted later if the infection does not respond to the drug used empirically (initially), this is not always practical for superficial infections. However, if an eye infection is at all serious and extends beyond the conjunctiva, specimen collection for culture and sensitivity tests is essential before commencing therapy.

Blepharitis

This is often seen as a chronic inflammatory process involving the eyelid margins and is usually due to Staphylococcus aureus.

Treatment: Lid hygiene is important. It involves cleaning the lid with diluted baby shampoo (one or two drops of baby shampoo in a bottle cap full of warm water), using a cotton-tip applicator or washcloth, two to three times daily PLUS topical anti-staphylococcal antibiotics e.g. topical bacitracin + neomycin solution (4 - 6 times a day for 1 - 2 weeks). Then reduce frequency to once daily before bedtime and continue for 4 - 8 weeks. Alternatives include fusidic acid drops 1 - 2 drops 4 - 6 times daily for 1 - 2 weeks.

Hordeola

- External hordeolum (Stye):

  Staphylococcus aureus is the predominant microbial pathogen. These lesions usually come to a head and rupture spontaneously within a matter of days. Application of warm compresses 4 - 6 times per day usually suffices for treatment of this condition. Resolution can be hastened if the pointing lesion is pricked with a sterile needle.

  Topical antibiotic therapy is unnecessary unless there are multiple styes, when topical fusidic acid or bacitracin PLUS neosporin or framycetin may be warranted.

- Internal hordeolum: (acute meibomianitis):

  Staphylococcus aureus is the major microbial pathogen. Treatment require warm compresses PLUS an oral antistaphylococcal agent e.g. cloxacillin or flucloxacillin. If the condition does not respond to this regimen, incision and drainage are indicated and the patient should be referred to an ophthalmologist.

Conjunctivitis

Both infectious (viral, bacterial, chlamydial) and noninfectious (allergy, foreign body) should be considered. Watery discharge may be associated with upper respiratory infection or adenovirus. Hallmarks of viral conjunctivitis are a follicular reaction and preauricular lymphadenopathy.

Purulent or mucopurulent discharge suggests a bacterial or chlamydial cause.

- Viral conjunctivitis ("pink-eye"):

  Treatment is supportive. The use of topical corticosteroid therapy is controversial. Children are generally kept out of school for up to 2 weeks after the onset of the infection.

- Bacterial conjunctivitis:

  Acute bacterial conjunctivitis in the adult is most often due to staphylo-cocci and/or streptococci. Haemophilus influenzae is more common in children. Topical antibiotics usually suffice. Topical chloramphenicol may rarely cause idiosyncratic bone marrow suppression. Alternative agents include gentamicin or tobramycin eye drops (for adults) and ointment (for children), or fusidic acid eye-drops.

- Conjunctivitis in the newborn (ophthalmia neonatorum):

  Due to Chlamydia trachomatis or Neisseria Gonorrhoeae. Note: The best form of prophylaxis is 2.5% aqueous povidone-iodine solution.
  - Chlamydia trachomatis: Erythromycin syrup (40 - 50 mg/kg/ day) in 4 divided doses for 14 days. Investigate and treat parents for genital infection.
  - Neisseria gonorrhoeae: Ceftriaxone 25 - 50 mg/kg IM as a single dose. Investigate and treat parents for genital infection.
  - Chlamydial disease in the adult: Oral tetracycline (500 mg 8 hourly) or doxycycline (100 mg 12 hourly) or erythromycin (500 mg 6 hourly) for 7 days, or azithromycin 1 g PO as a single dose.
  - Gonococcal conjunctivitis in adults: Ceftriaxone 1 g IM as a single dose.

Lacrimal system infections

- Canaliculitis:

  This is usually caused by Actinomyces, and rarely by Propionibacterium spp., Nocardia or Bacteroides. Treatment consists of mechanical expression of the exudative or granular material from the canaliculi, combined with probing and irrigation of the nasolacrimal system with a penicillin G (100000 U/ml) eyedrop solution. Patients should be referred to an ophthalmologist for definitive treatment.

- Dacrocystitis (infection of the nasolacrimal sac):

  Usually due to streptococci (including Streptococcus pneumoniae) or Staphylococcus aureus but culture should guide definitive therapy.

Acute infections: Treat with oral amoxycillin-clavulanate or cefuroxime.

Chronic infections: Irrigate the outflow tract with an antibiotic solution such as penicillin G (100000 U/ml) as a temporary measure. Definitive surgical decompression ultimately rests with the ophthalmologist.

Keratitis (Infection of the cornea)

Causes include bacteria, fungi, Herpes simplex virus or rarely, acanthamoeba. Keratitis is a sight-threatening ocular emergency and requires prompt recognition and immediate referral to an ophthalmologist.

- Herpes simplex keratitis:
  - Epithelial disease: Topical antiviral agents e.g. acyclovir ointment applied to eye five times a day, continued for at least 3 days after healing.
  - Stromal disease: Complex - combination of antiviral therapy and topical corticosteroids.
- Bacterial keratitis:

  Usually due to Pseudomonas aeruginosa, Streptococcus pneumoniae and rarely Staphylococcus aureus. Cefazolin eye drops (100 mg/ml; parenteral cefazolin mixed with tears naturale) and either gentamicin or tobramycin eye drops (3 mg/ml) or ciprofloxacin instilled every 15 - 60 minutes around the clock for the first 24 - 72 hours, with a slow reduction in dosing over a period of several weeks.
- Fungal keratitis:

  Usually due to Fusarium, Aspergillus or Candida. Treat empirically with natamycin (5%) eyedrops; administer every 30 - 60 minutes around the clock for the first 24 - 72 hours. Alternative agents include amphotericin B in a concentration of 0.15% (to be made up by a pharmacist) or miconazole.

Causative Organism	Drug of choice	Dosage
Blepharitis	Topical Bacitracin + Neomy-cin OR Topical Fusidic acid	4 - 6 times per day x 1 – 2 weeks and then once nocte x 4 - 8 weeks 1 -2 drops 12 hourly x 1 - 2 weeks
Hordeola		
External hordeolum(styes)	No antibiotics	
Internal hordeolum	Cloxacillin	500 - 1000 mg PO 8 hrly x 5 days
Conjunctivitis		
Viral conjunctivitis	No antibiotics	
Bacterial conjunctivitis	Chloramphenicol OR Gentamicin OR Tobramycin OR Fusidic acid	Topical Topical Topical Topical
Chlamydia (adults)	Tetracycline OR Doxycycline OR Erythromycin OR Azithromycin	500 mg PO 8 hrly x 7 days 100 mg PO 12 hrly x 7 days 500 mg PO 6 hrly x 7 days 1 g PO as a single dose
Gonococcus (adults)	Ceftriaxone	1 g1M as a single dose
Ophthalmia neonatorum:		
Chlamydia trachomatis	Erythromycin	40 - 50 mg/kg/day PO in 4 divided doses x 14 days
Neisseria gonorrhoeae	Ceftriaxone	25 - 50 mg/kg IM single dose only
Keratitis		
Herpes simplex	Acyclovir	Apply ointment 5 x/day and continue for 3 days after healing
Bacterial	Gentamicin OR Tobramycin OR Ciprofloxacin PLUS Cefazolin	Instill eyedrops every 15 -60 min. for 24 - 72 hours and then slowly increase interval

Chapter 13: Gastrointestinal Infections

Helicobacter pylori-associated peptic ulceration/gastritis

All patients with peptic ulceration who are also infected with H. pylori should receive antibiotic therapy. The diagnosis of H. pylori infection is best made by histological examination of gastric antral biopsy samples. Effective treatment regimens include a proton pump inhibitor plus at least two antibiotics:

Omeprazole 20 mg 12 hourly
OR
Lansoprazole 30 mg once daily
PLUS
Amoxycillin 1000 mg 12 hourly
OR
Metronidazole 400 mg 12 hourly
PLUS
Clarithromycin 500 mg 12 hourly

All agents should be given for 7 days.

Infectious Diarrhoea

The first priority in management is to ensure adequate fluid and electrolyte replacement.

- Campylobacter jejuni/coli

  Usually susceptible to erythromycin, which eradicates the organism from the stool within 48 hours. The illness, however, is usually self limiting. Generally, antibiotics should only be prescribed if the patient is acutely ill, has persistent fever, has bloody diarrhoea or is deteriorating.

  The drug of choice is erythromycin 250 mg orally 6 hourly (children 30 - 50 mg/kg/day in divided doses) for 5 - 7 days.

  Erythromycin resistance is rare (5%) - for these isolates, the recommended treatment is:

  Ciprofloxacin 200 mg orally 12 hourly for 5 days
  OR
  Norfloxacin 400 mg 12 hourly for 5 days
  OR
  Doxycycline 100 mg 12 hourly (in adults) for 5 days.

  In children, amoxycillin-clavulanate (6.6 – 13.3 mg/kg PO 8 hourly) is recommended for erythromycin-resistant strains.

- Shigella species

  Shigella gastroenteritis is essentially self-limiting and antibiotics are probably only indicated for severely ill patients, those with dysentery, and the very young or old.

  Ampicillin (not amoxycillin) 250 - 500 mg 6 hourly or 4 g as a single oral dose (in adults) and 12.5 – 25 mg/kg PO 6 hourly in children
  OR
  Ciprofloxacin 500 mg 12 hourly (in adults)
  OR
  Norfloxacin 400 mg 12 hourly
  OR
  Nalidixic acid 1 g 6 hourly (for adults) and 55 mg/kg/day in 4 divided doses in children.

  Nalidixic acid for children is effective and safe. Ciprofloxacin 1 g PO as a single dose is effective for shigellosis, other than Shigella dysenteriae.

  Amoxycillin should not be substituted for ampicillin, as it is not effective for shigellosis. Antibiotics should be given for 3 - 5 days.

- Salmonella species

  Antibiotics are usually not indicated for salmonella gastroenteritis except in the very young or elderly, debilitated patients or those with evidence of systemic infection. Antibiotics may prolong salmonella excretion, and probably do not significantly reduce symptoms or shorten the duration of the illness.

  Amoxycillin 500 mg orally 8 hourly (40 - 50 mg/kg/day in children)
  OR
  Cotrimoxazole 1 DS 12 hourly (4 - 5 mg TMP/kg/day and 20 - 25 mg SMX/kg/day in children) for 10 days.

  Oral chloramphenicol is an effective alternative agent. For resistant strains, ciprofloxacin 500 mg 12 hourly or norfloxacin 400 mg BD for 5 days. Cefotaxime/ceftriaxone are alternatives for systemic infection caused by resistant strains.

- Cholera

  Tetracycline 40 mg/kg/day PO in 4 divided doses (maximum of 4 g/day) x 2 days. Alternatives include ofloxacin, ciprofloxin, norfloxacin, doxycycline and cotrimoxazole.

- Plesiomonas and Aeromonas

  These are relatively rare causes of gastroenteritis and antibiotic therapy is usually not indicated unless there is evidence of systemic infection.

- Traveller's diarrhoea

  Usually due to enterotoxigenic Escherichia coli or Giardia lamblia. However, any enteric pathogen can cause traveller's diarrhoea. It is therefore necessary that stool samples be submitted for microbiological examination. Treat empirically with a 3 - 5 day course of a quinolone e.g. ciprofloxacin, ofloxacin or norfloxacin.

For those patients who do not respond to a quinolone, an empiric trial of metronidazole should be given for 7 - 10 days. If the diarrhoea continues, endoscopic evaluation should be considered.

Clostridium difficile

Usually associated with post-antibiotic diarrhoea, confirmed by demonstrating Clostridium difficile toxin in stool.

Metronidazole 400 mg orally 8 hourly for 5 - 10 days
OR
Vancomycin 125 mg orally 6 hourly for 5 - 10 days.

There is an increasing tendency to prefer metronidazole before vancomycin, not only because of major cost savings, but also due to concern over selection of vancomycin resistance amongst enterococci. If the patient has an ileus or is vomiting, metronidazole can be given intravenously (500 mg IV 8 hourly) since it is excreted in bile.

Entamoeba histolytica, Balantidium coli, Blastocystis hominis, Cryptosporidium, Giardia lamblia and Isospora belli - see under TREATMENT OF PROTOZOAL INFECTIONS.

Typhoid fever

Despite apparent in vitro sensitivity to a variety of antibiotics, Salmonella typhi has been documented to respond to only 6 chemotherapeutic agents:

Ampicillin 1 g IV 6 hourly (25 - 50 mg/kg/day in children)
OR
Amoxycillin 1 g PO or IV 8 hourly (40 - 50 mg/kg/day in children)
OR
Chloramphenicol 1 g PO IV 6 hourly (50 - 100 mg/kg/day in children)
OR
Cotrimoxazole 1 DS tablet PO 12 hourly (4 - 5 mg PO TMP/kg/day and 20 - 25 mg SMX/kg/day in children)
OR
Quinolones (eg ciprofloxacin 500 mg PO 12 hourly)
OR
Third-generation cephalosporins (eg ceftriaxone 1 g daily IMI (25 – 50 mg/kg/day in children).

Treat for 2 weeks with all these agents, except for ceftriaxone which is only given for 5 days, and ciprofloxacin which is given for 7 days.

Multiresistant strains of Salmonella typhi are increasingly common in India and some parts of Africa. Most remain susceptible to the quinolones and the 3rd-generation cephalosporins. It has been recommended that amoxycillin be used as the first-line agent in those who cannot afford ciprofloxacin (adults) and ceftriaxone (children).

Cholecystitis, Cholangitis, Diverticular disease and Intra-abdominal infections, including secondary Peritonitis

Management of the patient with intra-abdominal infection often includes surgical intervention, supportive measures, and antibiotic therapy. Enterobacteriaceae, enterococci and anaerobes are the usual pathogens. Antibiotic regimens used for initial treatment must include agent(s) effective against the common enteric aerobes and anaerobes. Numerous options are available including:

Ampicillin PLUS metronidazole PLUS amikacin
OR
Ampicillin PLUS metronidazole PLUS ceftriaxone
OR
Ampicillin PLUS metronidazole PLUS cefotaxime
OR
Ampicillin PLUS clindamycin PLUS amikacin
OR
Ampicillin PLUS clindamycin PLUS cefotaxime
OR
Ampicillin PLUS clindamycin PLUS ceftriaxone
OR
Cefoxitin alone
OR
Piperacillin/tazobactam alone

Doses:

Amikacin: 15 mg/kg once daily (adults), 15 mg/kg/day (children)
Ampicillin: 1 - 2 g IV 6 hourly (adults), 25 - 50 mg/kg/day (children)
Cefoxitin: 2 g IV 8 hourly (adults), 80 - 160 mg/kg/day (children)
Ceftriaxone: 1 - 2 g IM daily (adults), 25 - 50 mg/kg/day (children)
Cefotaxime: 2 g IV 8 hourly (adults), 100 - 200 mg/kg/day(children)
Clindamycin: 600 - 900 mg IV 6 - 8 hourly (adults)
Metronidazole: 1 g IV 8 hourly (adults), 30 mg/kg/day (children)
Piperacillin/tazobactam: 4.0/0.5 g IV 8 hourly (adults)

Antibiotics should be adjusted according to sensitivities of the implicated strain(s). Although there is no consensus on the duration of therapy, 5 - 7 days therapy is usually adequate for generalised peritonitis or a localised abscess. Antibiotics, however, should be continued until temperature and peripheral white cell count are normal.

Causative Organism and/or type of Illness	Drug of Choice	Adult Dose	Dose in Children	Alternative
Helicobacter peptic ulcer	Omeprazole OR Lansoprazole Plus Clarithromycin PLUS Amoxycillin OR Metronidazole	20 mg PO 12 hrly 30 mg PO once daily 500 mg PO 12 hrly 1000 mg PO 12 hrly 400 mg PO 12 hrly All given for 7 days		Bismuth citrate120 mg PO 6 hrly PLUS Metronidazole 400 mg PO 8 hrly PLUS Tetracycline 500 mg PO 6 hourly All given for 14 days
Campylobacter jejuni/ coli	Erythromycin	250 mg PO 6 hrly x 5 - 7 days	30 - 50 mg kg/ day PO	Ciprofloxacin OR Norfloxacin OR Doxycycline
Shigella species	Ampicillin OR Nalidixic acid (children)	250 - 500 mg 6 hrly PO x 3 - 5 days 1 g PO 6 hrly 3 - 5 days	12.5 - 25 mg/ kg PO 6 hrly 55 mg/kg/day	Norfloxacin 400 mg PO 12 hrly x 3 - 5 days OR Ciprofloxacin 500 mg PO 12 hrly x 3 - 5 days
Salmonella species	Amoxycillin	500 mg PO 8 hrly x 10 days	40 - 50 mg/kg/ day PO	Cotrimoxazole OR Ciprofloxacin OR Norfloxacin
Clostridium difficile	Metronidazole	400 mg PO 8 hrly x 5 - 10 days	15 mg/kg/day PO	Vancomycin 125 mg PO x 5 - 10 days
Cholera	Tetracycline	40 mg/kg/day x 2 days		Norfloxacin OR Doxycycline OR Cotrimoxazole
Plesiomanas/ Aeromonas	No antibiotics			
Traveller's diarrhoea	Ciprofloxacin If no response ADD Metronidazole	500 mg 12 hrly PO x 3 - 5 days 400 mg 12 PO hrly x 7 - 10 days		Norfloxacin
Typhoid fever	Amoxycillin OR Ciprofloxacin OR Ceftriaxone	1 g PO or IV 8 hrly x 14 days 500 mg PO 12 hrly x 7 days 1 g IM/IV daily x 5 days	40 - 50 mg/kg/ day 25 - 50 mg/kg/ day	Ampicillin OR Chloramphenicol OR Cotrimoxazole
Cholecystitis, Cholangitis, diverticular disease, intra-abdominal infections (e.g. secondary peritonitis)	Ampicillin PLUS Metronidazole PLUS Amikacin OR Ceftriaxone OR Cefotaxime	1 - 2 g IV 6 hrly 1g IV 8 hrly 15 mg/kg IV daily 1 - 2 g IV/IM daily 2 g IV 8 hrly	25 - 30 mg/kg/ day 30 mg/kg/day 15 mg/kg IV 25 - 50 mg/kg/ day 100 - 200 mg/ kg/day	Cefoxitin 2 g IV 8 hrly OR Piperacillin/tazobactam 4.0/0.5 g IV 8 hrly

Chapter 14: Genital Tract Infections

Where possible, a definitive laboratory diagnosis should be established since:

- aetiological diagnosis on the grounds of clinical examination is unreliable,
- multiple pathogens may be present,
- antibiotic resistance is common, and
- investigation and treatment of the sexual partner is invariably necessary.

A "syndromic" approach to therapy can be adopted while waiting for definitive laboratory diagnosis, or in situations where laboratory confirmation is not possible.

Acute Urethritis in males

Usually caused by Neisseria gonorrhoeae and Chlamydia trachomatis.

Empiric treatment:

Cefotaxime 1 g IM as a single dose
OR
Ceftriaxone 250 mg IM as a single dose
OR
Ciprofloxacin 500 mg orally as a single dose
OR
Ofloxacin 400 mg PO as a single dose
PLUS
Doxycycline 100 mg 12 hourly for 7 days
OR
Minocycline 100 mg 12 hourly for 7 days
OR
Azithromycin 1 g orally as a single dose

Vaginal discharges

The discharge arises from the:

1. Vaginal wall (True Vaginitis)

   Trichomoniasis

   Metronidazole 400 mg orally 12 hourly for 7 days or 2 g orally as a single dose. Alternative therapy includes tinidazole 2 g orally as a single dose. Treatment of sexual partner(s) is also recommended to prevent reinfection.

   Candidiasis:

   - <u>Nonpregnant women</u>

     Topical agents eg. clotrimazole 1 single 500 mg vaginal tablet OR 2 x 100 mg vaginal tablets nocte for 3 nights OR vaginal cream nocte for 6 nights

(miconazole, tioconazole and terconazole are alternative topical preparations)
OR
Fluconazole 150 mg PO as a single dose
OR
Itraconazole 200 mg PO12 hourly for 2 doses

- Pregnant women

  Only topical azole therapies (clotrimazole, miconazole, tioconazole or terconazole) should be used to treat pregnant women. Treat for 7 days.

- Recurrent infection

  Ketoconazole 100 mg orally daily
  OR
  Ketoconazole 400 mg orally for 5 days at the onset of menses
  OR
  Fluconazole 150 mg orally as a single dose given monthly

- Gardnerella vaginalis (Bacterial vaginosis) :

  Metronidazole 400 mg 12 hourly for 7 days
  OR
  Metronidazole 2 g orally one dose only In pregnant women 1% clindamycin lotion is the preferred form of therapy. Sexual partners should be treated in patients with recurrent infections.

2. Endocervix (Endocervicitis)

Caused by Neisseria gonorrhoeae and Chlamydia trachomatis. Treat as for urethritis in the male.

- Chlamydia trachomatis urethritis/cervicitis

  Treatment: Azithromycin 1 g orally once only
  OR
  Tetracycline 500 mg 6 hourly for 7 days
  OR
  Doxycycline or minocycline 100 mg 12 hourly for 7 days
  OR
  Erythromycin 500 mg 6 hourly for 7 days

Sexual partner(s) should also be treated unless shown to be free from infection.

- Neisseria Gonorrhoeae urethritis/cervicitis

  Treatment: Ceftriaxone 125 mg IM once
  OR
  Ciprofloxacin 500 mg PO single dose
  OR
  Ofloxacin 400 mg PO single dose
  OR
  Spectinomycin 2 g IM single dose

  Sexual partner(s) should also be treated unless shown to be free from infection.

Genital ulceration

Causes include syphilis, chancroid, Herpes simplex virus, and rarely lymphogranuloma venereum (LGV) and granuloma inguinale. In the majority of these patients, diagnosis is made on clinical grounds (poor accuracy) and treatment is given empirically because mixed infections are commonly encountered. Sexually transmitted genital ulceration is associated with increased susceptibility to HIV infection, and it is therefore recommended that a serological test for HIV be performed on every patient with a genital ulcer.

Empiric treatment:

Benzathine penicillin (2.4 mU IM)
PLUS
Erythromycin (500 mg 8 hourly for 14 days)
OR
Azithromycin 1g orally as a single dose

This will provide "cover" for early syphilis and chancroid.

1. SYPHILIS
   - Primary or secondary syphilis: Benzathine penicillin G 2.4 mU IM as a single dose. For patients allergic to penicillin, doxycycline 100 mg 12 hourly for 14 days OR tetracycline 500 mg 6 hourly for 14 days. Children should be treated with benzathine penicillin G 50000 U/kg (up to 2.4 mU) IM as a single dose.
   - Latent or tertiary syphilis: Benzathine penicillin G 2.4 mU IM weekly for 3 weeks. For patients allergic to penicillin, doxycycline 100 mg 12 hourly for 28 days OR tetracycline 500 mg 6 hourly for 28 days.
   - Neurosyphilis:

     Benzylpenicillin G 2 - 4 mU IV 4 hourly for 10 - 14 days
     OR
     Procaine penicillin 2. 4 mU IM daily for 10 - 14 days
     PLUS
     Probenecid 500 mg orally 6 hourly for 10 - 14 days

     Note: Benzathine penicillin is not adequate therapy for syphilis if there is neurological involvement, irrespective of the stage of the disease.
   - Congenital syphilis:

     Benzylpenicillin G 100000 to 150000 U/kg/day in two divided doses for 10 days
     OR
     Procaine penicillin G 50000 U/kg/dose IM as a single daily dose for 10 days.

2. Genital Herpes
   - First episode:
     Acyclovir 400 mg PO three times a day for 7 -10 days
     OR
     Acyclovir 200 mg PO five times a day for 7 - 10 days

OR
Famciclovir 250 mg PO three times a day for 7 - 10 days
OR
Valaciclovir 1000 mg PO twice a day for 7 - 10 days

- Recurrent episodes: When treatment is started during the prodrome or within 1 day after onset of lesions, many patients who have recurrent disease benefit from episodic therapy.

  Acyclovir 400 mg PO three times a day for 5 days
  OR
  Acyclovir 200 mg PO five times a day for 5 days
  OR
  Acyclovir 800 mg PO twice a day for 5 days
  OR
  Famciclovir 125 mg PO twice a day for 5 days
  OR
  Valaciclovir 500 mg PO twice a day for 5 days

Topical therapy with acyclovir is substantially less effective than the systemic (orally administered) drug, and its use is discouraged.

3. CHANCROID

   Ceftriaxone 250 mg IM as a single dose
   OR
   Azithromycin 1 g orally as a single dose
   OR
   Erythromycin 500 mg 6 hourly for 7 days
   OR
   Ciprofloxacin 500 mg orally 12 hourly x 3 days

   Azithromycin and ceftriaxone offer the advantage of single-dose therapy.

4. Lymphogranuloma Venereum (LGV)

   Doxycycline 100 mg orally 12 hourly for 21 days
   OR
   Erythromycin 500 mg orally 6 hourly for 21 days.

   Buboes may require aspiration through intact skin or incision and drainage to prevent the formation of inguinal or femoral ulceration.

5. Granuloma Inguinale (Donovanosis)

   Minocycline or doxycycline 100 mg PO 12 hourly
   OR
   Erythromycin 500 mg PO 6 hourly
   OR
   Cotrimoxazole 1 DS PO 12 hourly
   OR
   Tetracycline 500 mg PO 6 hourly.

Treatment should continue until complete epithelialisation has taken place, which may take several weeks.

Pelvic Inflammatory Disease (PID)

The organisms usually implicated in PID include Neisseria gonorrhoeae, Chlamydia trachomatis, Enterobacteriaeceae, Streptococcus spp., and anaerobes.

Treatment - outpatient:

Doxycyline or minocycline (100 mg 12 hourly for 14 days) PLUS metronidazole 400 mg 12 hourly for 14 days
OR
Ceftriaxone 250 mg IM OR cefoxitin 2 g IM as single doses PLUS doxycycyline 100 mg 12 hourly for 14 days
OR
Ofloxacin 400 mg orally 12 hourly for 14 days OR ciprofloxacin 500 mg orally 12 hourly for 14 days
PLUS
metronidazole 400 mg orally 12 hourly for 14 days

Hospitalisation is recommended when:

- the diagnosis is uncertain,
- the possibility of surgical emergencies such as appendicitis or ectopic pregnancy cannot be excluded,
- a pelvic abscess is suspected,
- the patient is pregnant,
- the patient is an adolescent,
- severe illness precludes outpatient management,
- the patient has not responded to outpatient therapy,
- the oman is knon to be infected ith HIV or
- clinical follow-up cannot be arranged ithin 72 hours of the initiation of antibiotic treatment.

Treatment - inpatient:

Cefoxitin 2 g IV 6 hourly PLUS doxycycline 100 mg IV or orally every 12 hours for at least 48 hours after substantial clinical improvement, after which doxycycline 100 mg orally 12 hourly plus metronidazole 400 mg 12 hourly should be given until day 14 of treatment.

Alternative therapy includes clindamycin 900 mg IV 8 hourly PLUS gentamicin 1.5 mg/kg IV/IM 8 hourly. This regimen is continued for at least 48 hours after the occurrence of substantial clinical improvement, after which doxycycline 100 mg PO 12 hourly OR clindamycin 450 mg PO 6 hourly, should be given until day 14 of treatment
OR
Ofloxacin 400 mg IV 12 hourly PLUS metronidazole 500 mg IV 8 hourly
OR

Ciprofloxacin 200 mg IV 12 hourly PLUS doxycycline 100 mg IV or PO 12 hourly PLUS metronidazole 500 mg IV 8 hourly.

In all patients with PID:

- endocervical specimens should be examined for Neisseria gonorrhoeae and Chlamydia trachomatis,
- a pregnancy test should be performed to minimise the possibility of overlooking a tubal pregnancy,
- intrauterine contraceptive devices, if present, should be removed once antimicrobial treatment has begun, and
- male sexual partners should be evaluated.

In severe cases, blood cultures should be obtained before therapy. If culdocentesis is performed, pus should be submitted (in a syringe) for microbiological investigations.

Epididymo-orchitis

- Men younger than 35 years: The usual cause is Chlamydia trachomatis or Neisseria gonorrhoeae. Treat with a single dose of ceftriaxone 250 mg IM followed by oral doxycycline 100 mg 12 hourly for 10 days.
- Men older than 35 years: The usual cause is one of the uropathogens e.g. Escherichia coli, Pseudomonas aeruginosa. Treat with:

  Cotrimoxazole 1 DS tablet 12 hourly
  OR
  Ofloxacin 300 mg 12 hourly
  OR
  Ciprofloxacin 500 mg 12 hourly
  OR
  Norfloxacin 400 mg 12 hourly for 2 - 3 weeks.

  Urine culture, urethral culture for Neisseria gonorrhoeae and a urine or urethral PCR or LCR for Chlamydia trachomatis are indicated.

Rape or high-risk sexual exposure

Send samples for detection of trichomonas, gonococci and chlamydiae. Obtain serum for baseline syphilis and HIV serology, and a pregnancy test.

Empiric treatment: cover for gonorrhoea, chlamydiae and incubating syphilis.

Ceftriaxone 125 mg IM as a single dose
PLUS
Metronidazole 2 g PO as a single dose
PLUS
Azithromycin 1 g PO as a single dose OR doxycycline 100 mg PO BD x 7 days.

Most experts also recommend postexposure hepatitis B vaccination (without HBIG) at the time of the initial examination, and then 1 and 6 months after the first dose.

Antiretroviral prophylaxis is contentious. We, however, would recommend antiretroviral prophylaxis to rape victims.

Causative Organism and/ or Illness type	Drug of Choice	Adult Dose	Alternative
Acute urethritis (males)	Cefotaxime OR Ceftriaxone OR Ciprofloxacin OR Ofloxacin PLUS Doxycycline OR Minocycline OR Azithromycin	1 g IM 250 mg IM 500 mg PO stat 400 mg PO stat 100 mg PO 12 hrly x 7 days 100 mg PO 12 hrly x 7 days 1 g PO stat	
Vaginal trichomoniasis	Metronidazole	400 mg PO 12 hrly x 7 days OR single dose	Tinidazole 2 g PO as a single dose
Vaginal Candidiasis: Non-pregnant	Clotrimazole OR Fluconazole	500 mg vaginal tab once OR2 x 100 mg vaginal tab nocte x 3 nights OR vaginal (1%) cream nocte x 6 nights 150 mg PO as a single dose	Miconazole OR Tioconazole OR Terconazole Itraconazole 200mg12 hrly x 2 doses
Pregnant women	Clotrimazole OR Miconazole OR Tioconazole OR Terconazole	Treat for 7 days	
Recurrent infection	Fluconazole	150 mg PO as a single dose given once monthly	Ketoconazole 100 mg PO daily OR 400 mg PO for 5 days at onset of menses
Bacterial Vaginosis	Metronidazole	400 mg PO 12 hrly x 7 days OR2 g PO x as a single dose	1% Clindamycin lotion 5 g daily x 7 days
Endocervicitis	As for acute urethritis in males		
Genital ulceration (Syndromic therapy)	Benzathine penicillin PLUS Azithromycin OR Erythromycin	2.4 mU IM as a single dose 1 g PO stat 500 mg PO 8 hrly x 14 days	
Chancroid	Ceftriaxone OR Azithromycin	250 mg Im stat 1 g PO as a single dose	Erythromycin 500 mg PO 6 hrly x 7 days OR Ciprofloxacin 500 mg PO 12 hrly x 3 days
Genital herpes:			

Causative Organism and/ or Illness type	Drug of Choice	Adult Dose	Alternative
First episode	Acyclovir OR	200 mg PO 5 times per day x7 - 10 days	Famciclovir 250 mg PO 3 times per day x 7 days
	Acyclovir	400 mg PO 3 times per day x7 - 10 days	OR Valaciclovir 1 g PO 12 hrly x 7 days
Recurrences	Acyclovir OR	200 mg PO 5 times per day x5 days	Famciclovir 125 mg PO 12 hrly x 5 days
		OR	OR
	Acyclovir OR	400 mg PO 3 times per day x5 days OR	Valaciclovir 500 mg PO 12 hrly x 5 days
	Acyclovir OR	800 mg PO 2 times per day x 5 days	
Lympho-granuloma venereum	Doxycycline	100 mg PO 12 hrly x 21 days	Erythromycin 500 mg PO 6 hrly x 21 days
Syphilis:			
Primary or secondary syphilis	Benzathine penicilin	2.4 mU IM as a single dose14 days OR	Doxycycline 100 mg PO 12 hrly x Tetracycline 500 mg PO 6 hrly x14 days
Latent or tertiary syphilis	Benzathine penicillin	2.4 mU IM weekly x 3 weeks	Doxycyline 100 mg PO 12 hrly x28 days OR Tetracycline 500 mg PO 6 hrly x 28 weeks
Neurosyphilis	Penicillin G	2 - 4 mU IV 4 hrly x10 - 14 days	Procaine penicillin 2.4 mU IM x 10 - 14 days PLUS Probenecid 500 mg PO 6 hrly
Congenital syphilis	Penicillin G	50000 U/kg IV12 hrly x 10 days	Procaine penicillin 50000 U/kg IM daily x10 days
Pelvic Inflammatory Disease			
Outpatient treatment	Doxycycline	100 mg PO 12	Ceftriaxone 250 mg
	OR	hrly x 14 days	IM once
	Minocycline	100 mg 12 hrly PO x	OR
	PLUS	14 days	Cefoxitin 2 g IM
	Metronidazole	400 mg PO 12 hrly x	once
	OR	14 days	PLUS
	Ciprofloxacin	500 mg PO 12 hrly x	Doxycycline 100 mg
	OR	14 days	PO 12 hrly x14 days
	Ofloxacin	400 mg PO 12 x 14 days	

Causative Organism and/ or Illness type	Drug of Choice	Adult Dose	Alternative
Inpatient	Cefoxitin PLUS Doxycyline	2 g IV 6 hrly 100 mg IV 12 hrly until clinical improvement, followed by Doxycycline 100 mg PO 12 hrly PLUS Metronidazole 400 mg PO 12 hrly to complete 10 -14 days	Ofloxacin 400 mg IV 12 hrly PLUS Metronidazole 500 mg IV 8 hrly OR Ciprofloxacin 200 mg IV 12 hrly PLUS Doxycycline 100 mg IV or PO 12 hrly PLUS Metronidazole 500 mg IV 8 hrly
Epididymo-orchitis Men < 35 years	Ceftriaxone PLUS Doxycycline	250 mg IM once 100 mg PO 12 hrly x 10 days	
Men > 35 years	Ofloxacin OR Ciprofloxacin	300 mg PO 12 hrly x 2 - 3 weeks 500 mg PO 12 hrly x 2 -3 weeks	Norfloxacin 400 mg PO 12 hrly x 2 - 3 weeks OR Cotrimoxazole1DS hrly PO x2 - 3 weeks
Rape or high- risk sexual exposure	Ceftriaxone PLUS Metronidazole PLUS Azithromycin OR Doxycycline	125 mg IM single dose 2 g PO single dose 1 g PO single dose100 mg PO 12 hrly x 7 days	

Chapter 15: Lower Respiratory Tract Infections

Acute Bronchitis

The vast majority of episodes of acute bronchitis infections are caused by viruses e.g. influenza viruses, RSV, adenoviruses, etc. There are no reports in the literature to suggest that such patients benefit from antibiotics; therefore therapy should be symptomatic. During outbreaks of Mycoplasma pneumoniae or Chlamydia pneumoniae infection, prescription of a macrolide or a tetracycline can be considered.

Acute exacerbations of Chronic bronchitis

Viruses are often implicated, at least initially. Secondary infections by bacteria such as Streptococcus pneumoniae, Moraxella catarrhalis and Haemophilus influenzae may be involved when sputum becomes purulent and increases in volume. Although most clinicians treat patients in this setting with antibiotics, most studies comparing antibiotics with placebo have shown little difference in the rate of resolution of symptoms. If antibiotics are prescribed, these should be based on the culture and sensitivity results and should be given for 7 - 10 days. Amoxycillin-clavulanate, cefuroxime axetil or loracarbef may be considered initially for empiric antibiotic therapy.

Pneumonia

When the cause of pneumonia is known, the clinician will seldom have difficulty in deciding what to prescribe; it is therefore recommended that in severe cases, blood cultures and sputum (or other respiratory secretions) be submitted for microscopy and culture. However empiric antibiotic therapy is usually given while waiting for laboratory results. The choice varies according to the age of the patient, the severity of the illness and presence of any underlying illness.

- Community-acquired pneumonia (CAP)
  - Outpatient and inpatient treatment in patients less than 60 years without underlying disease

    Streptococcus pneumoniae is by far the commonest cause of CAP. Amoxycillin 1000 mg orally 8 hourly (80 - 100 mg/kg/day in children)
    OR
    Ampicillin 1000 mg IV 6 hourly (200 mg/kg/day in children)
    OR
    Penicillin VK 1000 mg orally 6 hourly or penicillin G 2 - 4 mU 6 hourly IV (100000 units/kg/day in children)

    Treat for at least 5 days or 36 - 48 hours after the temperature has normalised.

Alternative, but more expensive agents are erythromycin, clarith-romycin, azithromycin (these agents should ideally be used during mycoplasma epidemics) OR cefuroxime axetil. In general, the use of macrolides for empiric therapy, should be discouraged since studies have documented similar outcomes in patients treated with penicillins compared to macrolides in the setting of large numbers of "atypical" infections. Suggestions that macrolides may be more attractive in the setting of penicillin-resistant pneumococci is unfounded, since macrolide resistance parallels penicillin resistance amongst pneumococcal isolates and may indeed by encountered in penicillin-sensitive isolates. There is little or no place for routine use of oral or parenteral third-generation cephalosporins such as cefpodoxime, ceftibutin or cefixime for CAP in this age group.

- Patients more than 60 years and/or those with underlying illness/comorbidity

  Cefuroxime +/- erythromycin
  OR
  Amoxycillin-clavulanate +/- erythromycin

  These agents should be given parenterally initially and replaced with oral agents once the temperature has settled. Treat for a total of 5 - 10 days. Although some authorities recommend the addition of an amino-glycoside in suspected Pseudomonas aeruginosa infections, studies in South Africa have shown that Pseudomonas aeruginosa is rarely encountered in this group of patients, while Klebsiella pneumoniae is more often seen. The majority of Klebsiella spp, especially in the com-munity setting, are susceptible to cefuroxime and amoxycillin-clavu-lanate.

- Severely ill patients

  As a generalisation, the presence of two or more of the parameters listed below indicate severe illness:

  Clinical features:

  * confusion/decreased consciousness
  * low blood pressure (systolic < 90 mmHg, diastolic < 60 mmHg)
  * respiratory rate > 30 breaths/minute
  * multilobar consolidation
  * extrathoracic systemic complications
  * comorbid disease

  Laboratory parameters:

  * hypoxaemia (pO2 < 8 kP)
  * white cell count < 4 or > 30 x 109/l
  * abnormal renal function (e.g. urea > 7 mmol/l)
  * abnormal liver function (e.g. albumin < 30 g/l)
  * rapidly expanding infiltrates
  * multilobar consolidation
  * cavitation.

Cefuroxime OR amoxycillin-clavulanate
PLUS
Amikacin
PLUS
Erythromycin
All agents are given parenterally for 2 - 3 weeks.

Note: Because Pseudomonas aeruginosa is infrequently encountered in community-acquired pneumonia, empiric treatment with fourth-generation cephalosporins or carbapenems is not necessary.

- "Atypical pneumonia"

  Usually caused by Mycoplasma pneumoniae, Chlamydia pneumoniae or rarely Legionella spp.

  Erythromycin 500 mg 6 hourly (30 - 50 mg/kg/day in children)
  OR
  Roxithromycin 150 mg 12 hourly (5 - 10 mg/kg/day in children)
  OR
  Clarithromycin 250 mg 12 hourly
  OR
  Azithromycin 250 mg daily
  OR
  Tetracycline 500 mg 6 hourly
  OR
  Doxycycline 100 mg 12 hourly.

  Treat for 7 - 10 days for mycoplasma and chlamydia, but for 21 days for legionella.

- Pneumonia during influenza epidemics

  Usually caused by Staphylococcus aureus, Streptococcus pneumoniae, or Haemophilus influenzae. Treat with amoxycillin-clavulanate OR cefuroxime axetil OR cephalexin. Adjust therapy once aetiology established.

- Aspiration pneumonia

  Usually due to anaerobes alone or with facultative or aerobic bacteria. The most common aerobes in community-acquired cases are Streptococcus spp., whilst Gram-negative bacilli and Staphylococcus aureus are prominent in Hospital-acquired aspiration pneumonia.

  Metronidazole orally, rectally or IV PLUS amikacin IV
  OR
  Metronidazole orally, rectally or IV PLUS amoxycillin-clavulanate
  OR
  Metronidazole orally, rectally or IV PLUS cefuroxime OR cefotaxime.

  Clindamycin can be used as an alternative to metronidazole. Duration of therapy is based on clinical grounds.

- Hospital-acquired pneumonia or pneumonia in the debilitated patient

  In addition to the usual pathogens, also consider Gram-negative bacilli such as Pseudomonas aeruginosa, Acinetobacter spp., Klebsiella spp., Serratia spp. and staphylococci.

  Empiric regimens include:

  Ceftriaxone 2 g IM once daily (25 - 50 mg/kg/day in children)
  OR
  Cefotaxime 1 g IV 8 hourly (150 - 200 mg/kg/day in children)
  OR
  Ceftazidime 1-2 g IV 8 hourly (90 - 150 mg/kg/day in children)
  OR
  Cefepime 1 - 2 g 12 hourly OR cefpirome 2 g 12 hourly
  PLUS
  Amikacin 15 mg/kg given IV once daily.

  Alternate regimens include imipenem alone. If the patient has notresponded within 48 hours to the above regimen, and there is a clinical suspicion of a staphylococcal infection, cloxacillin 2 g 4 hourly IV (150 - 200 mg/kg/day in children) or vancomycin 500 mg IV 12 hourly (40 mg/kg/day in children), should probably be added. Therapy should be adjusted once results of cultures are available.

- Pneumonia in the immunocompromised patient (e.g. AIDS)

  In addition to other causes, also consider Pneumocystis carinii, fungi and Cytomegalovirus. These patients require urgent specialist referral.

Causative Organism and / or Illness type	Drug of Choice	Adult Dose	Dose in Children
Acute bronchitis	No antibiotic		
Acute exacerbation of chronic bronchitis	Amoxycillin-clavulanate OR Cefuroxime axetil OR Loracarbef	250 - 500 mg PO 8 hrly 125 - 500 mg PO 12 hrly 200 - 400 mg PO 12 hrly	6.6 - 13.3 mg/kg PO 8 hrly 125 - 500 mg PO 12 hrly 7.5 - 15 mg/kg PO 12 hrly
Community-acquired pneumonia Patients < 60 years	Penicillin V OR Penicillin G OR Amoxycillin OR Ampicillin	1000 mg PO 6 hrly x 5 days 2 - 4 mU IV 6 hrly x 5 days 1000 mg PO 8 hrly x 5 days 1000 mg IV 6 hrly5 days	12.5 - 25 mg/kg 6 hrly PO 100000 U/kg/day IV 80 - 100 mg/kg/day PO 200 mg/kg/ day IV
Patients > 60 years and/or with underlying illness	Cefuroxime	0.75 - 1.5 g IV 8 hrly OR 0.5 g PO 12 hrly	

Causative Organism and / or Illness type	Drug of Choice	Adult Dose	Dose in Children
	PLUS		
	Erythromycin	0.25 - 0.5 g IV/PO 6 hrly	
Severely ill patient	Cefuroxime	0.75 - 1.5 g IV	
	OR	8 hrly x 2 - 3 wks	
	Amoxycillin clavulan-ate	500 mg IV 8 hrly x 2 - 3 wks	
	PLUS		
	Amikacin	15 mg/kg/day IV	
	PLUS	x 2 - 3 wks	
	Erythromycin	500 mg IV 6 hrly x 2 - 3 wks	
"Atypical pneumonia"	Erythromycin	500 mg IV 6 hrly	30 - 50 mg/kg/day
	OR	x 7 - 10 days	5 - 10 mg/kg/day
	Roxithromycin	150 mg PO 12	
	OR	hrly x 7 - 10 days	
	Azithromycin	250 mg PO daily	
	OR	x 7 - 10 days	
	Clarithromycin	250 mg PO 12 hrly x 7 - 10 days	
Pneumonia during influenza epidemics	Amoxycillin clavulan-ate	500 mg PO 8 hrly x 5 days	13.3 mg/kg PO 8 hrly x 5 days
	OR		0.125 - 0.5 g
	Cefuroxime axetil	500 mg PO	PO 8 hrly x 5 days
	OR	12 hrly x 5 days	PO 12 hrly
	Cephalexin	500 mg PO	25 mg/kg PO
		6 hrly x 5 days	6 hrly x 5 days
Aspiration pneumonia	Metronidazole	7.5 mg/kg IV	7.5 mg/kg IV/PO
	PLUS	PO 6 hrly	6 hrly
	Amikacin	15 mg/kg/day IV	15 mg/kg/day IV
Hospital-acquired pneumo-nia	Ceftriaxone	2 g IM/IV daily	25 - 50 mg/kg/day
	OR		
	Cefotaxime	1 g IV 8 hrly	150-200mg/kg/day
	OR		
	Ceftazidime	1 - 2 g IV 8 hrly	90 - 150mg/kg/day
	OR		
	Cefepime	1 - 2 g IV 12 hrly	
	OR		
	Cefpirome	2 g IV 12 hrly	
	PLUS		
	Amikacin	15 mg/kg/day	15 mg/kg/day

Chapter 16: Skin and Soft Tissue Infections

Acne

Topical benzoyl peroxide (Acnidazil, Benoxyl, Panoxyl, Quinoderm), tretinoin (Retin-A, Airol) or topical clindamycin. Systemic doxycycline and/or isotretinoin (Roaccutane) should be considered for severely inflamed or cystic cases.

Bite wounds

Pasteurella multocida (cats and dogs), Eikenella corrodens (humans), Staphylococcus aureus, Streptococcus spp., and/or oral anaerobes may be involved.

Amoxycillin/clavulanate OR ampicillin PLUS cloxacillin OR cefoxitin are appropriate empirical treatment and the duration should be clinically determined.

Doses:Ampicillin 500 mg 6 hourly (75 - 100 mg/kg/day in children)
Amoxycillin-clavulanate 500 mg 8 hourly (13.3 mg/kg 8 hourly in children)
Cloxacillin 1 - 2 gram 6 hourly (50 - 100 mg/kg/day in children)
Cefoxitin 1 - 2 g 8 hourly (80 - 160 mg/kg/day in children)

In those who have had a complete course of tetanus toxoid (3 or more doses), a booster should be given if it is more than 10 years since the last injection.

Passive immunisation with tetanus immune globulin (TIG), at least 250 units IM, is indicated in patients with dirty or neglected wounds who have not had at least 3 doses of tetanus toxoid (primary immunisation), or a booster within the last 10 years. Tetanus toxoid should be given at the same time but at a separate site.

Note:

- The tetanus prophylaxis outlined for bite wounds, also applies for traumatic wounds.
- The need for rabies vaccination should be assessed in each individual case of an animal bite

Breast abscess/Mastitis

Lactating: Usually due to Staphylococcus aureus: cloxacillin is first choice.

Nonlactating: Anaerobes and/or Staphylococcus aureus: amoxycillin-clavu-lanate is recommended.

Erysipelas

Usually due to Streptococcus pyogenes. Treat with benzylpenicillin initially IV and continue treatment with oral penicillin VK for 10 days.

Cellulitis

Usually due to Streptococcus pyogenes, but Staphylococcus aureus is often also involved.

When cellulitis is associated with an open wound, there is usually an exudate that can be obtained for culture. In the setting of cellulitis with unbroken skin, a needle aspiration from the advancing edge can sometimes yield a positive diagnosis. Blood cultures are also of diagnostic value.

Treat with amoxycillin-clavulanate OR a 1st-generation cephalosporin (cephalothin or cephalexin or cefazolin).

In young children with facial cellulitis, consider Haemophilus influenzae. In diabetics and debilitated patients, consider Staphylococcus aureus, Enterobactericeae and anaerobes.

Erythrasma

Caused by the bacterium Corynebacterium minutissimum. Treat with oral erythromycin 250 mg 6 hourly. A 5-day course is usually sufficient but occasionally 2 - 3 weeks treatment is required.

Furunculosis

Usually due to Staphylococcus aureus. No antibiotic therapy is necessary. The treatment of choice is surgical drainage.

In most persons with recurrent furunculosis (boils), the nares and the perineum are usually the sites of Staphylococcus aureus carriage. In such patients, diabetes mellitus should be excluded.

Therapeutic regimes which are effective for recurrent furunculosis include:

Mupirocin ointment or cream applied topically to the nares, axillae, and perineum for a 5 day period with or without one of the following oral antibiotics:

Oral clindamycin 150 mg daily (in adults) for a 3-month period
OR
Oral rifampicin 600 mg daily (in adults) for 7 - 10 days
OR
Oral cloxacillin 500 mg 6 hourly for 7 -10 days.

Best results have been obtained with clindamycin.

Necrotising cellulitis or fasciitis

Urgent surgical debridement in addition to broad spectrum antibiotics to cover Enterobacteriaceae, anaerobes, Streptococcus spp., Staphylococcus aureus, e.g. amoxycillin-clavulanate OR clindamycin PLUS amikacin, until culture results become available.

Impetigo

Usual pathogens are Streptococcus pyogenes with or without Staphylococcus aureus.

Treat with amoxycillin-clavulanate OR a 1st-generation-cephalosporin OR penicillin (ampicillin) PLUS cloxacillin. Topical mupirocin also results in high rates of cure.

Infected wounds

Treat according to the clinical condition, and the results of culture and sensitivity tests from representative specimens. It is important to distinguish between superficial wound colonisation and true infection, as antimicrobial therapy is generally not indicated for colonisation.

The need for tetanus prophylaxis should be evaluated in the case of traumatic wounds (see under bite wounds).

Nasal carriage of Staphylococcus aureus

In situations where eradication of nasal carriage of Staphylococcus aureus is required, mupirocin nasal ointment applied 2 to 4 times a day for 5 to 7 days, is recommended. Alternatives include local application of chlorhexidine or povidone iodine cream/ointment.

Chapter 17: Systemic Bacterial Infections

Brucellosis

Adults: Doxycycline 100 mg orally 12 hourly PLUS rifampicin 900 mg orally once daily for 6 weeks.

Children <8years: Cotrimoxazole (TMP 20 mg/kg/day + SMZ 100 mg/kg/day)

Tick-bite fever

Tetracycline 25 - 50 mg/kg/day orally in 4 divided doses for 5 - 7 days or for at least 48 hours after the resolution of the fever. Alternatively doxycycline 100 mg 12 hourly can be used. In children less than 8 years of age, and pregnant women tetracyclines are relatively contraindicated.

Chloramphenicol (50 mg/kg/day) orally in 4 divided doses is the drug advocated for children, whilst erythromycin (much poorer response compared to tetracycline) is the recommended agent in pregnant women. Alternatively one dose of doxycycline followed by erythromycin has been suggested in children less than 8 years, and in pregnant women.

Sepsis of unknown cause in the neutropenic patient

Usual organisms include Enterobactericeae, Pseudomonas aeruginosa, Staphylococcus aureus and streptococci. All these patients require an intensive diagnostic evaluation PRIOR to the institution of empiric antibiotic therapy, which is now accepted as the standard treatment for patients with febrile neutropenia.

Amikacin 500 mg IV 12 hourly PLUS Piperacillin 2 g IV 4 hourly
OR
Imipenem 500 mg IV 6 hourly
OR
Meropenem 1 g IV 6 hourly
OR
Piperacillin/tazobactam PLUS amikacin 500 mg IV 12 hourly
OR
Amikacin 500 mg IV 12 hourly PLUS cefepime 1 g IV 12 hourly
OR
Amikacin 15 mg/kg IV as a single daily dose PLUS cefpirome 1 - 2 g 12 hourly

Vancomycin should also be considered empirically if there is:

- severe mucositis
- obvious catheter-related infection
- hypotension
- colonisation with MRSA
- prior administration of a quinolone.

Consider addition of vancomycin PLUS amphotericin B (or fluconazole) if the patient remains culture negative and fails to respond within 3 - 5 days of empiric antibiotic therapy. Antibiotic treatment should ideally be given until the peripheral white cell count exceeds 500/mm3.

Typhoid fever

See under gastrointestinal infections.

Chapter 18: Urinary Tract Infections

Optimal therapy for urinary tract infection is based on results of susceptibility tests following culture of the causative organisms.

Acute uncomplicated Cystitis

This includes patients with asymptomatic bacteriuria.

These infections are typically community-acquired and are usually caused by Escherichia coli (90%), Staphylococcus saprophyticus (5%), or other Enterobactericeae (5%). Mixed infections are rare. In view of the high prevalence of resistance to ampicillin and cotrimoxazole, some authorities recommend amoxycillin-clavulanate, an oral first-generation cephalosporin (e.g. cephalexin), or a quinolone (ciprofloxacin, enoxacin, ofloxacin etc) as the empiric agents of choice. However, others advocate the use of either ampicillin or cotrimoxazole for uncomplicated UTI since these antibiotics frequently achieve concentrations in urine in excess of the MICs of resistant strains. This may explain why an uncomplicated UTI may apparently respond to an antibiotic even when the pathogen is judged resistant by laboratory tests. Quinolones should be avoided during pregnancy. A 3-day regimen achieves the best results in patients with uncomplicated UTI. This is considered as effective, costs less, and causes fewer side effects than 7-day regimens. One-day regimens are associated with higher recurrence rates. The antibiotics listed below are in order of cheapest to more expensive drugs.

Ampicillin or amoxycillin 250 mg 8 hourly for 3 days (50 mg/kg/day in children)
OR
Cotrimoxazole 1 double strength tablet 12 hourly for 3 days (8 mg/kg/day TMP + 40 mg/kg/day SMX)
OR
Enoxacin 400 mg 12 hourly for 3 days
OR
Fosfomycin 3 g orally stat dose
OR
Amoxycillin-clavulanate 1 tablet containing 250 mg amoxycillin 8 hourly for 3 days
OR
Ciprofloxacin 250 mg 12 hourly for 3 days
OR
Cephalexin 500 mg 12 hourly for 3 days (25 - 50 mg/kg/day in children)
OR
Ofloxacin 200 mg 12 hourly for 3 days
OR
Norfloxacin 400 mg 12 hourly for 3 days.

Single dose therapy is no longer favoured.

In pregnancy, consider a 7-day regimen of ampicillin, amoxycillin, cotrimoxazole (not in 3rd trimester), amoxycillin-clavulanate or cephalexin.

Acute Pyelonephritis

This is caused by the same range of pathogens as uncomplicated cystitis, except that Staphylococcus saprophyticus is a rare cause of pyelonephritis.

Pre- and post-treatment (10 - 14 days after discontinuation of treatment) cultures are strongly advised.

Treatment with appropriate antibiotics for 2 weeks is usually sufficient. The initial route of antibiotic administration (oral vs parenteral) and setting of treatment (outpatient vs inpatient) depends on the severity of the illness (mild to moderate vs moderate to severe), overall clinical condition, patient reliability and compliance, whether there is nausea and/or vomiting, and whether the patient is pregnant. Suggested empiric regimens include:

Mild-to-moderate illness:

Oral antibiotics:

Enoxacin 400 mg 12 hourly for 14 days
OR
Ciprofloxacin 250 mg 12 hourly for 14 days
OR
Amoxycillin/clavulanate 1 tablet containing 250 mg amoxycillin 8 hourly for 14 days.

Severe illness and possible urosepsis:

Parenteral therapy (e.g. ciprofloxacin OR amikacin with or without ampicillin OR a second- or third-generation cephalosporin) until the fever abates, then oral therapy (as for mild-to-moderate illness) for a total of 14 days.

Pregnancy:

Hospitalisation is recommended. Ceftriaxone (OR cefotaxime) OR amikacin IV until the fever abates, then oral therapy with amoxycillin-clavulanate OR cephalexin OR cefuroxime axetil for a total of 14 days.

Recurrent urinary infections

Continuous prophylactic antibiotic therapy should be considered in women with more than 3 UTI's/year. Antibiotics are given on a thrice-weekly basis and the choice of antibiotic is based on previous sensitivity results, and costs.

Postcoital prophylaxis if UTI is related to coitus:

Single dose of norfloxacin 400 mg OR ciprofloxacin 250 mg OR amoxycillin/clavulanate 1 tablet OR cephalexin 500 mg OR nitrofurantoin 100 mg OR trimethoprim 100 mg after coitus. Micturition to empty the bladder completely shortly after coitus should be strongly advocated.

Prevention of catheter-associated UTI:

Administration of antimicrobials is not of value in preventing colonisation/infection in patients with indwelling catheters. Furthermore, this has been shown to promote the selection of resistance.

Urinary tract infections in children

In general, children with urinary tract infections without obstruction or vesicoureteric reflux, have a very good prognosis. In the presence of obstruction (e.g. urethral valves), severe destruction of renal parenchyma can occur. Ultrasonography and voiding cystourethrography are therefore recommended in all boys after the first episode of urinary infection and in preschool girls at least after the second infection, in order to detect remediable causes timeously.

Prostatitis

Acute:

Ciprofloxacin 500 mg 12 hourly OR ofloxacin 300 mg 12 hourly OR norfloxacin 400 mg 12 hourly OR cotrimoxazole 1 DS tablet twice daily.

These antibiotics are given for 2 - 4 weeks.

Urine culture is necessary in the initial workup, and 10 – 14 days after completion of treatment.

Chronic:

Antibiotic as above for 4 weeks. If there is no response after 4 weeks, the same antibiotic should be given for 12 weeks.

Causative Organism and/or Illness type	Drug of Choice	Adult Dose	Dose in Children	Alternative
Acute uncomplicated UTI	Ampicillin OR Amoxycillin OR Cotrimoxazole OR Cephalexin	250 mg PO 8 hrly x 3 days 250 mg PO 8 hrly x 3 days 1 DS PO 12 hrly x 3 days 500 mg PO 12 hrly x 3 days	50 mg/kg/day 50 mg/kg/day 8 mg/kg/day TMP +40 mg kg/day SMX 25 - 50 mg/kg/ day	Amoxycillin-clavulanate 250 mg PO 8 hrly x 3 days OR Enoxacin 400 mg PO 12 hrly x 3 OR Ciprofloxacin 250 mg 12 hrly x 3 days OR Ofloxacin 200 mg 12 hrly x 3 days
Acute pyelonephritis: Mild-to-moderate illness	Ciprofloxacin OR	250 mg PO 12 hrly x 14 days		Enoxacin 200 mg 12 hrly PO x 14 days
	Ofloxacin OR Amoxycillin clavulanate	200 mg PO 12 hrly x 14 days 250 mg PO 8 hrly x 12 days kg	6.6 - 13.3 mg/ PO 8 hrly	

Causative Organism and/or Illness type	Drug of Choice	Adult Dose	Dose in Children	Alternative
Severe illness	Ciprofloxacin OR Amikacin	200 mg IV 12 hrly 15 mg/kg/day IV After fever abates, treat with oral agents Treat for a total of 14 days	 15 mg/kg/day IV	
Pregnancy OR	Ceftriaxone OR Cefotaxime THEN Amoxycillin-clavulanate OR Cephalexin 500 mg PO 12 hrly Cefuroxime	1 - 2 g/day IV 1 - 2 g IV 12 hrly 250 mg PO 8 hrly 250 mg PO 12 hrly	 	
Prostatitis: Acute: Chronic:	 Ciprofloxacin OR OR Ofloxacin Treat for up to 12 weeks	 500 mg PO 12 hrly x 2 - 4 weeks 300 mg PO 12 hrly x 2 - 4 weeks	 Norfloxacin 400 mg PO 12 hrly Cotrimoxazole 1DS PO 12 hrly	

Chapter 19: Treatment of Tuberculosis

The following core concepts underline the management of tuberculosis.

Initial diagnostic emphasis is on bacteriological methods, including direct microscopy and culture of representative sputum specimens (up to 3), collected prior to therapy.

Treatment regimens each consist of an initial intensive phase followed by a continuation phase, totalling 6 months in new cases, 8 months in retreatment patients and 4 months in children.

Individual drugs or tablets containing combinations of drugs are available.

The Department of Health encourages directly observed therapy (DOT) and a patient-centred approach. Emphasis is placed on the cure of new tuberculosis patients at the first attempt.

Treatment of new patients

Ideally susceptibility testing should be performed on all initial isolates. If this is not possible, susceptibility testing should be carried out on all patients who continue to have positive sputum in spite of correct treatment. Combination tablets are preferred. It is essential that the correct dose and duration of treatment are adhered to. Antituberculous drugs must be given five times per week, eg. Monday to Friday during the initial intensive phase; no treatment is necessary on the other two days. During the continuation phase, drugs can be taken three times per week.

A four drug regimen is preferred for initial therapy i.e. the first 8 weeks. This regimen includes:

Isoniazid (INH) 5 mg/kg PO daily (max 300 mg)
PLUS
Rifampicin 10 mg/kg PO daily (max 600 mg)
PLUS
Pyrazinamide 25 mg/kg PO daily (max 2 g)
PLUS
Ethambutol 15 mg/kg PO daily (max 2. 5g)

INH 80 mg/rifampicin 120 mg/pyrazinamide 250 mg is available in a combination tablet = RIFATER. Therefore in patients > 50 kg, 5 tablets of RIFATER PLUS ethambutol 1200 mg = 3 tablets should be given daily Monday to Friday for the first 2 months. Thereafter a combination of INH and rifampicin = RIFINAH, is used for the last 4 months in the recommended doses given Monday to Friday.

DOSAGE IN ADULTS

Intensive phase - 2 Months	Under 50 kg	Over 50 kg
INH + rifampicin + pyrazinamide [1]	4 tablets	5 tablets
Ethambutol 400 mg	2 tablets	3 tablets

Continuation phase - 2 Months	Under 50 kg	Over 50 kg
INH + rifampicin	3 tablets [2]	2 tablets [3]

1 Combination tablet INH/rifampicin/pyrazinamide 80/120/250 mg

2 Combination tablet INH/rifampicin 100/150 mg

3 Combination tablet INH/rifampicin 150/300 mg

DOSAGE IN CHILDREN

Intensive phase - 2 Months	5 - 10 kg	11 - 20 kg	21 - 30 kg
INH + rifampicin [4]	½ tablet	1 tablet	2 tablets
Pyrazinamide	½ tablet	1 tablet	2 tablets

Continuation phase 2 or 4* months	5 - 10 kg	11 - 20 kg	21 - 30 kg
INH + rifampicin 4	½ tablet	1 tablet	2 tablets

4 Combination INH/rifampicin tablet 100/150 mg

* 2 months - children with primary TB and/or effusion

4 months - children with progressive primary, cavitating or non-pulmonary TB

Retreatment of Tuberculosis in adults

This includes sputum positive patients who were:

1. Treated before and were shown to be sputum negative by smear and culture at the end of treatment (cured: now relapsed or reinfected)
2. Treated before, completed 6 months' treatment, but were not shown to be sputum negative at the end of treatment (failed).
3. Treated before, but whose treatment was interrupted by missing a total of 2 months' treatment during the 6 months' course.

Treat with a combination of MYRIN (150 mg rifampicin + 75 mg INH + 300 mg ethambutol/tablet) PLUS 500 mg pyrazinamide PLUS streptomycin 20 - 40 mg/kg IM 3 times per week for 2 months. In the 3rd month, treat with MYRIN PLUS pyrazinamide. Treat with MYRIN only for the next 5 months (i.e. month 4 - 8).

Intensive phase - 2 months 5 times per week	Under 50 kg	Over 50 kg
INH + rifampicin + ethambutol [5]	3 tablets	4 tablets
Pyrazinamide 500 mg	2 tablets	3 tablets
Streptomycin (3 times per week)	750 mg	1000 mg

Third month: 5 times per week	Under 50 kg	Over 50 kg
INH + rifampicin + ethambutol [5]	3 tablets	4 tablets

Third month: 5 times per week	Under 50 kg	Over 50 kg
Pyrazinamide 500 mg	2 tablets	3 tablets

Continuation phase 5 months3 times per week	Under 50 KG	Over 50KG
INH + rifampicin + ethambutol [5]	3 tablets	4 tablets

5 Use a combination tablet 75/150/300 mg

Treatment of multidrug resistant (MDR) TB

Multidrug resistant (MDR) TB refers to resistance to at least both INH and rifampicin.

If the isolate is resistant to rifampicin and INH, treat with:

ethambutol PLUS
ciprofloxacin OR ofloxacin PLUS
amikacin PLUS
pyrazinamide for 18 - 24 months.

If the isolate is resistant to rifampicin, INH and ethambutol, treat with

pyrazinamide PLUS
ciprofloxacin OR ofloxacin PLUS
amikacin PLUS
ethionamide OR cycloserine OR clofazimine for 24 months.

Dose of second-line agents:

Ciprofloxacin 500 - 750 mg PO 12 hourlyAmikacin 15 mg/kg IM daily
Ethionamide 250 - 500 mg PO 12 hourly
Clofazimine 100 - 200 mg PO daily
Cycloserine 250 - 500 mg PO 12 hourly

A detailed document "The South African Tuberculosis Control Programme: Practical Guidelines" (1996) is available from the Department of Health and is recommended for further reading.

Chapter 20: Antifungal Chemotherapy

Polyenes

Amphotericin B

Amphotericin B remains the mainstay of therapy for systemic mycoses against which all other parenteral antifungals are measured to assess efficacy. Side effects with conventional amphotericin B are common and include chills, fever, vomiting, pain, nephrotoxicity and anaemia. Daily doses range from 0.3 - 1.0 mg/kg/day given over 1 - 4 hours as an infusion in 5% dextrose.

Nystatin

This polyene does not have the patient compliance, potency or extended antifungal spectrum of the azoles, but remains an alternative for vaginal yeast infection during pregnancy. It is only available for topical application.

Natamycin

It is the therapy of choice for keratitis due to filamentous fungi. It is only available for topical application.

Azoles

Most of the imidazoles available in South Africa are topical agents and have few side effects. Those available in South Africa include:

- Clotrimazole
- Miconazole
- Econazole
- Tioconazole
- Intravenous miconazole is obsolete except for the treatment of Pseudoallescheria boydii infection.

Oral ketoconazole has potential hepatotoxicity and endocrine effects and is poorly absorbed in the absence of gastric acidity.

The triazoles, fluconazole and itraconazole, appear to be less hepatotoxic, do not affect cortisol and testosterone synthesis, and have fewer drug interactions than ketoconazole. These agents have significant activity against a broad spectrum of fungal pathogens causing infection in humans.

Fluconazole is water soluble and can be used IV as well as orally. It penetrates the CSF and is excreted in an active form in urine.

Terbinafine

This expensive antifungal can be given orally for the treatment of tinea (ringworm) involving the hands, feet and nails (preferred to griseofulvin). Side effects are uncom-

mon (gastrointestinal and skin reactions). The optimal clinical effect may be observed some weeks after completion of therapy. A topical preparation is also available for cutaneous infections. This is effective against pityriasis versicolor whereas the oral formulation is not.

Amorolfine

This topical compound has been used with reasonable success in the treatment of onychomycosis. Although it is not as effective as terbinafine, it has excellent patient compliance, tolerability and safety.

Griseofulvin

Griseofulvin at 10 mg/kg/daily with foods to a maximum of 1 g daily in 3 divided doses continued for 12 to 18 months, has in the past been used for difficult dermatophyte infections involving the hair shaft, feet and nails.

Potential teratogenicity and other adverse effects (eg. reduction in effectiveness of oral contraceptives, photosensitivity, neurological problems) and the availability of other drugs now limit its use.

Flucytosine

Flucytosine is seldom used alone because of the risk of emergence of resistance during monotherapy. It is usually combined with amphotericin B to treat invasive candida and cryptococcus infections. It is not readily available in South Africa.

The usual dose is 100 - 150 mg/kg/day in 4 divided doses.

Chapter 21: Treatment of Specific Fungal Infections

Aspergillosis

Treatment is reserved for invasive pulmonary or disseminated infection, although recent data indicates a role for itraconazole in allergic bronchopulmonary aspergillosis. High dose amphotericin B (at least 0.7 mg/kg/day) for 6 weeks or more. Itraconazole at 400 - 600 mg/day for 6 months is a possible alternative. Involved tissue may require surgical removal.

Candidiasis

Oral/vaginal: Topical clotrimazole, econazole, miconazole or tioconazole. Patient tolerance and compliance in vaginal infection is better with shorter courses of oral therapy (e.g. single oral dose 150 mg fluconazole).

During pregnancy: Only topical azole therapies (clotrimazole, miconazole, tioconazole or terconazole) should be used to treat pregnant women. Topical nystatin is an alternative.

Chronic/recurrent mucocutaneous: Fluconazole 400 mg daily for 2 days followed by 100 - 200 mg daily for 3 weeks.

Cystitis: Oral fluconazole 150 mg daily for 7 days OR 200 - 300 ml of amphotericin B solution, 5 - 10 mg/l (25 - 50 mg in 500 ml of 5% dextrose water), instilled by triple lumen catheter with cross-clamping for 60 - 90 minutes, twice daily for 2 days.

Candidaemia in post-surgical patients or infected vascular lines: Remove infected lines. Amphotericin B 0.7 - 1.0 mg/kg/day for 7 - 10 days or fluconazole orally at a dose of 400 mg per day for 14 days or more.

Invasive or systemic: Amphotericin B 0.7 - 1.0 mg/kg/day. Fluconazole, in doses of 400 mg/day IV, is an alternative treatment to amphotericin B in non-neutropenic patients.

Corneal infection (keratomycosis): Topical natamycin suspension (2.5%) 2 hourly or more frequently initially.

Cryptococcus infections

Amphotericin B 0.7 mg/mg IV for 2 weeks followed by fluconazole 400 mg PO daily for an additional 8 weeks is the recommended regimen for cryptococcal meningitis. The addition of flucytosine (not available in South Africa) in doses of 100 mg/kg/day in conjunction with the amphotericin B phase of treatment, does not dramatically improve immediate outcome. Initial therapy with fluconazole (400 - 800 mg PO) is associated with a 50% relapse rate; this regimen may be considered in patients with very mild disease and those who present with cryptococcosis without meningeal

involvement. In HIV-infected patients, fluconazole in doses of 200 - 400 mg PO daily should be prescibed as mainten-ance therapy.

Dermatophyte infections (Ringworm or Tinea)

Topical imidazoles for uncomplicated ringworm of the body or groin twice daily for at least 10 days after clearance of lesions. Alternatives include terbinafine (1% cream twice daily), amorolfine (0.25% cream once daily). For infection involving scalp or beard, oral itraconazole (100 mg once daily for 2 - 4 weeks) or terbinafine (250 mg/ day for 3 - 6 weeks) together with a topical imidazole. Chronic hand/foot lesions, including nails, require oral itraconazole (6 months) or terbinafine (6 weeks to 3 months) or possibly 5% amorolfine nail lacquer (twice daily for 6 - 12 months).

Pityriasis versicolor

A single oral dose of 400 mg ketoconazole or two weeks of topical treatment with an imidazole.

Chapter 22: Treatment of Protozoal Infections

Amoebiasis

Metronidazole 400 - 800 mg orally 3 times daily for 5 - 10 days (children 35 mg/kg/day)
OR
Tinidazole 2 g orally once daily for 3 days (children 50 - 60 mg/kg/day); up to 5 days in hepatic involvement.

Follow-up stool examination is always necessary because no regimen is completely effective in eradicating intestinal infection.

Balantidium coli

Metronidazole 400 - 800 mg orally 3 times daily for 5 - 10 days
OR
Tetracycline 500 mg 4 times daily for 10 days

Blastocystis hominis

Anecdotally, response to metronidazole 400 mg three times daily has been reported (children 35 mg/kg/day) – usually for 5 days.

Blastocystis hominis is often considered to be a commensal. Treatment can be considered when other causes of gastroenteritis have been excluded and high counts are present in stools, in the presence of persistent symptoms.

Cryptosporidium

There is currently no known effective treatment for cryptosporidiosis. Fluid and electrolyte replacement is of prime importance in the management of this infection, which is usually self-limiting in immunocompetent individuals.

Giardiasis

Metronidazole 2 grams PO as a single dose OR 400 mg PO 12 hourly for 7 days (children 15 mg /kg/day in three divided doses orally for 7 days) OR tinidazole 2 g PO as a single dose.

A recently described alternative is albendazole 400mg once daily for 5 days in, adults and children older than 2 years

Isospora belli

Oral cotrimoxazole 1 double strength tablet 6 hourly for 10 days, then 12 hourly for 3 weeks.

Trichomoniasis

Metronidazole 2 g as a single oral dose or 400 mg 12 hourly for 7 days. Metronidazole has been used extensively in pregnancy for the treatment of trichomoniasis. The teratogenic effect appears to be minimal and if present, greatest during the first trimester, when the drug should not be used. If therapy cannot be avoided, then it can probably be used safely in the last two trimesters of pregnancy.

The sexual partner(s) should also be treated to prevent reinfection.

Malaria

Treatment:

In South Africa, the overwhelming majority of cases (> 90%) are caused by Plasmodium falciparum, whereas P. ovale and P. malariae are less common. P. vivax is extremely uncommon in Africa, but imported cases do occur. Chloroquine resistance is widespread in P. falciparum – distribution includes all of sub-Saharan Africa including South Africa. It is therefore important to consider ALL malaria patients potential cases of chloroquine-resistant P. falciparum malaria in view of the consequences of inappropriate therapy. The drug of choice for all other forms of malaria (i.e. other than P. falciparum) remains chloroquine (see tables on pages 135 - 137).

For patients with P. ovale and P. vivax infection, primaquine phosphate should also be considered after clinical cure with chloroquine, to eradicate residual hypnozoites from the liver.

Primaquine is contraindicated in pregnancy and in children under the age of 1 year.

Uncomplicated P. falciparum malaria can be treated with oral sulphadoxine-pyrimethamine (single dose) or oral quinine (7 days) (see page 134). Halo-fantrine is an alternative therapy, but a second course is required one week after the first.

Quinine is indicated for complicated or severe malaria caused by P. falciparum and should be given intravenously if the patient is vomiting or otherwise unable to take oral medication. Administration should be changed to the oral route as soon as possible, and quinine therapy should be continued for at least a total of 7 days.

There is no evidence to support the use of an additional agent (e.g. doxycycline, sulphadoxine-pyrimethamine) to quinine therapy for P. falciparum acquired in southern Africa (although this may be indicated for P. falciparum infections acquired in South East Asia or South America where quinine resistance is described).

P. falciparum infection in pregnancy or in children aged less than one year of age should be regarded as complicated malaria and should be treated with quinine as first choice.

Recommended Drug	Dose in Adults	Dose in Children
Sulphadoxine-pyrimethamine*	3 tablets PO as a single dose	Contraindicated if < 1 years 6 - 10 kg = ½ tablet 11 - 20 kg = 1 tablet
OR	> 65 kg = 4 tablets	21 - 30 kg = 1½ tablets 31 - 40 kg = 2 tablets 50 - 60 kg = 3 tablets 41 - 50 kg = 2½ tablets
Quinine (oral)	2 tablets (600 mg quinine salt) 8 hrly x 7 days or until blood smear is negative	10 mg/kg 8 hrly x 7 days
OR Halofantrine**	500 mg 6hrly for 3 doses. Repeat after one week	8 mg/kg 6 hrly for 3 doses. Repeat after one week

* Non-immunes (eg. travellers) often respond slowly to sulphadoxine-pyrimethamine.

** Avoid if mefloquine taken within previous two weeks.

Treatment of complicated Plasmodium falciparum malaria

If: Parasitaemia > 5%
Hb < 6 g/dl
Spontaneous hypoglycaemia
Major organ dysfunction eg. cerebral malaria, respiratory distress, renel failure etc.

Recommended Drug	Dose in Adults	Dose in Children
Quinine (intravenous)	Quinine 10 mg/kg in 5 -10 ml/kg 5% dextrose IV over4 hours and repeat 8 hrly until able to take oral medication. (Max 1800 mg per day). Treat for 7 days and change to oral as soon as possible	
OR	Loading dose*:20 mg/kg in5 - 10 ml/kg in 5% dextrose IV over 4 hours	As in adults
Quinine (oral) - if able to take oral medication and not vomiting If contracted in South America or South Asia, ADD (after 3 days of quinine)	600 mg (2 tablets) 8 hrly x 7 days	10 mg/kg 8 hrly x 7 days
Doxycycline OR	200 mg PO stat and then 100 mg daily x 7 days	Contraindicated if < 8 years4 mg/kg PO stat and then 2 mg/kg daily x 7 days
Sulfadoxine- pyrimethamine	3 tablets PO as a single dose	Contraindicated if < 1 years

Recommended Drug	Dose in Adults	Dose in Children
		6 - 10 kg = ½ tablet 11 - 20 kg = 1 tablet 21 - 30 kg = 1½ tablets 31 - 40 kg = 2 tablets 41 - 50 kg = 2½ tablets 50 - 60 kg = 3 tablets

* A loading dose is recommended for severely ill patients.

No loading dose if the patient has received quinine or mefloquine in the past week.

Recommended Drug	Dose in Adults	Dose in Children
For clinical treatment of: P.malariae P.ovale P.vivax	1 tablet = 50 mg chloroquine base ORAL: 1,5 g over 3 days as follows: initially 600mg, then 300 mg 6 - 8 hours later, then 300 mg daily on second and third days.	ORAL: 25 mg/kg over 3 days as follows: initially 10 mg/kg, then 5 mg/kg 6, 24 and 48 hours after first dose. Note: chloroquine syrup is available.
For radical cure of: P.vivax P. ovale	1 tablet = 7,5mg primaquine phosphate	
Primaquine following clinical treatment	15mg (2 tablets) PO daily x 14 days	0,25 mg/kg PO daily x 14 days Note: Primaquine is contraindicated in children under 1 year of age.

Chemoprophylaxis for malaria

Emphasis must be placed on avoidance of mosquitoes and mosquito bites. Chemoprophylaxis should be regarded as ancillary to such measures and should no longer be viewed as the sole mainstay of malaria prevention.

Chloroquine used to be appropriate for travellers to areas where P. falciparum was predictably sensitive to chloroquine (these areas do not occur in southern Africa). The agents therefore recommended for prophylaxis are chloroquine plus proguanil OR mefloquine alone OR doxycycline.

Pregnant women and infants should be discouraged from travelling to malarious areas. If such travel is essential, strict bite avoidance and appropriate chemoprophylaxis should be employed. Chloroquine PLUS proguanil are considered safe throughout pregnancy, while mefloquine is considered safe in the second and third trimester.

Doxycycline is generally reserved for persons for whom mefloquine and chloroquine are contraindicted (eg. epileptics) or not tolerated, or who will be visiting areas in South-East Asia where multiresistant (incl. mefloquine-resistant) P. falciparum are present.

Recommended Drug	Dose in Adults	Dose in Children
Chloroquine	1 tablet = 150 mg chloroquine base	5 mg/kg of chloroquine base taken at the same intervals as for adults
	300 mg base (2 tablets) once every7 days, starting 1 day before entering the area, once weekly while in the area, and once weekly after leaving the area for 4 weeks.	<10 kg: ¼ -½ tablet 10 -19 kg: ½ tablet 20 - 30 kg: 1 tablet 31 - 35 kg: 1½ tablets >35 kg: adult dose
PLUS		
Proguanil	1 tablet = 100 mg	3 mg/kg at the same intervals as for adults
	200 mg (2 tablets) daily, starting1 day before entering the area, continuing daily while in the area, and daily for 4 weeks after leaving the area.	< 10 kg: ¼ tablet 10 - 19 kg: ½ tablet 20 - 30 kg: 1 tablet 31 - 45 kg: 1½ tablets >45 kg: adult dose
OR		
Mefloquine	1 tablet = 250 mg for adults. 250 mg (1 tablet) every 7 days, starting 1 week before entering the area, once weekly while in the area, and once weekly for 4 weeks after leaving the area.	5 mg/kg: same intervals as for adults 15 - 19 kg: ¼ tablet 20 -30 kg: ½ tablet 31 - 45 kg: ¾ tablet >45 kg: adult dose
	Restrict to 1 year's duration.	Not recommended for children under 2 years or who weigh less than 15 kg.
OR		
Doxycycline	1 tablet = 100 mg 100 mg once daily, starting 1- 2 days before entering the area, continuing daily while in the area, and daily for 4 weeks after leaving the area. Don't use for longer than 3 months.	Contraindicated in children under 8 years 8 - 15 years: 3 mg/kg once daily > 15 years: adult dose

Standby treatment for presumed malaria:

Standby treatment should ONLY be offered to travellers visiting areas where medical care is not readily available. This should be given in addition to prophylactic medication (see below) and taken only if symptoms suggestive of malaria occur.

Sulphadoxine 500 mg/pyrimethamine 25 mg 3 tablets taken as a single dose OR halofantrine two 250 mg tablets given 8 hourly for 3 doses in adults. Halofantrine should be avoided in patients on mefloquine prophylaxis. Those taking standby treatment should seek medical advice as soon as possible.

Pneumocystis carinii

Treatment of P. carinii pneumonia (PCP):

The drug of choice is cotrimoxazole = TMP (15 mg/kg/day) + SMX 75 mg/kg/day PO or IV in 3 - 4 divided doses for 21 days. If the patient has documented hypoxaemia, then prednisone 40 mg PO 12 hourly x 5 days, then 40 mg PO daily x 5 days, then 20 mg PO daily to the end of therapy, should be given.

Alternative regimens include aerolised pentamidine 600 mg/day via a nebuliser OR atovaquone 750 mg orally twice daily for 21 days.

Prophylaxis for HIV-infected patients:

Indications for chemoprophylaxis: (this includes adults and adolescents who have HIV, including those on HAART and pregnant women).

- CD4 count < 200 cells/mm3
- History of oropharyngeal candidiasis
- Prior history of Pneumocystis carinii pneumonia.

Agents:

Preferred:

Cotrimoxazole (TMP-SMZ) 1 DS tablet per day

Alternatives:

Cotrimoxazole (TMP-SMZ) 1 SS tablet per day
OR
Cotrimoxazole (TMX-SMZ) 1 DS tablet three times per week
OR
Dapsone 100 mg daily or 50 mg bd
OR
Aerosolised pentamidine 300 mg once per month by Respirgard II nebuliser
OR
Atovaquone 750 mg PO bd with meals

Toxoplasmosis

Treatment:

Sulfadiazine 4 - 8 g/day orally plus pyrimethamine 100 - 200 mg loading dose, then 50 - 100 mg/day orally plus folinic acid 15 mg/ day for at least 6 weeks. Sulphadiazine, unfortunately, is not readily available in South Africa. There are a number of reports which now have shown that cotrimoxazole (TMP 15 mg/kg/day + SMX 75 mg/kg/day) orally or IV is useful in the treatment of toxoplasmosis.

Prophylaxis for HIV-infected patients:

Indications for chemoprophylaxis

- Patients with prior evidence of exposure to toxoplasmosis (positive IgG serology for T. gondii)
- CD4 count < 100 cells/mm3

Agents:

Preferred:

Cotrimoxazole(TMP-SMX) 1 DS PO per day

Alternatives:

Cotrimoxazole (TMP-SMX) 1 SS PO per day
OR
Dapsone 50 mg PO daily plus pyrimethamine 75 mg/week PO

Chapter 23: Treatment of Worm Infestations

Nematodes (Roundworms)

Ascaris lumbricoides (common roundworm)

Mebendazole 100 mg PO 12 hourly for 3 days
OR
Albendazole 400 mg given as single oral dose (contraindicated during pregnancy and children under 2 years)
OR
Pyrantel pamoate 11 mg/kg not to exceed 1 g as a single dose
OR
Piperazine 75 mg/kg (max 3.5 g) as a single oral dose.

Enterobius vermicularis (Threadworm/ Pinworm)

Mebendazole 100 mg single dose in adults and children, and repeated in 2 weeks to eliminate reinfection. Simultaneous treatment of all family members is necessary for eradication of other reservoirs of infection. Alternative agents include pyrantel pamoate 11 mg/kg PO once, and repeated in 2 weeks, or albendazole 400 mg PO once and repeated in 2 weeks.

Filariasis (lymphatic)

Diethycarbamazine 5 mg/kg weekly for 6 weeks then monthly for 6 months OR given in doses of 2 mg/kg 8 hourly for 3 weeks
OR
Ivermectin 400 ug/kg as a single dose

Hookworm (Ancylostoma duodenale or Necator americanus)

Mebendazole 100 mg PO twice daily for 3 days
OR
Albendazole 400 mg PO one dose only
OR
Pyrantel 11 mg/kg PO (maximum 1 g).

Trichuris trichiura (Whipworm)

Mebendazole 100 mg PO twice daily for 3 days
OR
Albendazole 400 mg PO once only.

Strongyloides stercoralis

Thiabendazole 25 mg/kg PO twice daily for 2 days (not to exceed 1.5 g/dose). This agent, however, is poorly tolerated. Albendazole is better tolerated and is given in doses of 400 mg twice daily for 3 days, and repeated after 2 weeks.

Cestodes (tapeworms)

Intestinal infection by adult worm

e.g. Taenia spp. (T. solium, T. saginata), Hymenolepis spp., Dipylidium etc. Niclosamide 2 g (4 tablets) as a single dose (chewed). In children 2 - 6 years, the dose is 1 g as a single dose, and in less than 2 years the dose is 0.5 g.

Cysticercosis (tissue infection with larval cysts of the cestode T. solium)

Diagnosis and treatment of cysticercosis depends on the site of involvement and the symptoms experienced.

Cysts outside the CNS tend not to be symptomatic. These eventually die and calcify, to be detected incidentally on plain radiographs of the limbs.

For symptomatic cysts outside the CNS, the optimal approach is surgical resection. Medical therapy, with praziquantel or albendazole, may also be employed.

Deep tissue and CNS lesions are more difficult to diagnose and treat surgically. For most patients with neurocysticercosis, drug therapy is the treatment of choice. Effective medical treatment requires prolonged administration of high doses of either praziquantel (50 mg/kg per day for 15 - 30 days) or albendazole (10 - 15 mg/kg per day for 8 days).

Dexamethasone and anticonvulsants may be needed to control side effects from cyst death.

Echinococcosis (Hydatid Cyst Disease)

Humans serve as inadvertent intermediate hosts for cestodes of Echinococcus spp., which are carried as tapeworms by canines such as dogs, wolves, and foxes. In South Africa, E. granulosus is prevalent and sheep, in which the larval cysts are found, are the intermediate hosts.

Optimal treatment of symptomatic cysts is by surgical resection to remove the complete intact cyst. Because there is risk of spreading infection if the cyst ruptures, the recommended approach is to visualize the cyst, remove a fraction of the fluid, and instill a cysticidal agent (e.g. hypertonic (30%) saline, iodophor, or 95% ethanol), to kill the germinal layer and daughter cysts prior to resection. Thirty minutes after instillation, the cyst should be removed intact.

It may be prudent to treat the patient perioperatively with an antihelmintic active against Echinococcus larvae (e.g. albendazole, mebendazole) to further limit the risk of intraoperative dissemination of daughter cysts. Medical therapy for inoperable cysts with either albendazole or mebendazole has provided improvement in most patients. The preferred agent is albendazole, in view of its better absorption from the gastrointestinal tract and higher plasma levels.

Dosage regimen: 3 or more cycles of 400 mg albendazole bd for 4

weeks, followed by a 2-week rest period off therapy,

The alternative agent, mebendazole, is poorly absorbed, and must be taken at higher doses (50 - 70 mg/kg daily) for several months to achieve a therapeutic effect.

Trematodes (flukes, including schistosomes)

Bilharzia (Schistosomiasis) is the most common human trematode infection in southern Africa.

Praziquantel 40 mg/kg as a single dose, is generally effective for both S. haematobium and S.mansoni.

Chapter 24: Treatment of Ectoparasite Infestations

Phthirus pubis (pubic or "crab" louse) infestations and Pediculosis Capitis (head louse infestations)

Permethrin, a synthetic pyrethroid, (LYCLEAR) is the treatment of choice. Alternative agents are gamma benzene hexachloride shampoo (GAMBEX) or lotion (QUELLADA); these, however, can be irritant to the skin.

A single application is usually effective but repeat treatment after 1 week if necessary. Treat sexual contracts for Phthirus pubis and consider other STDs. Treat household and classroom contacts for pediculosis. Fine combing of hair may be necessary to remove nits (eggs). Bed linen should be changed. Combs, brushes, all clothes, towels and bed linen should be washed in hot water.

Pediculosis corporis (body louse infestations)

Hot laundering of clothes and bedding is usually sufficient. Body Lice occasionally attach nits to body hairs in which case the above preparations are effective.

Scabies (Sarcoptes scabiei)

Permethrin (LYCLEAR) or benzyl-benzoate (ASCABIOL) as a single application followed by thorough washing after 8 - 24 hours. It is important that not only the patient but also household members and close contacts be treated at the same time. Any clothes worn or bed linens used during the 3 days before therapy should be laundered in hot, soapy water, and dried in the hot cycle of the dryer or ironed. Such high temperatures should be sufficient to kill mites and their eggs.

Chapter 25: Treatment of Viral Infections

Cytomegalovirus

Congenital infection

Drug of choice: Not proven

Central nervous system infection

Drug of choice: Not proven

Gastrointestinal infection

Drug of choice: Not proven

Hepatitis

Drug of choice: Not proven

Pneumonia

Drug of choice: Ganciclovir

Dose: Loading dose 5 mg/kg IV 12 hourly and then 5 mg/kg daily as maintenance x 14 - 21 days

Retinitis

Drug of choice: Ganciclovir

Dose: As for CMV pneumonia/pneumonitis

Hepatitis A virus

Acute infection

Drug of choice: Nil

Hepatitis B virus

Acute infection

Drug of choice: Nil

Chronic active infection

Drug of choice: Interferon-alpha-2b
Dose: 3 mIU IM/SC 3 times weekly x 4 months

Hepatitis C virus

Acute infection

Drug of choice: Nil

Chronic infection

Drug of choice: Interferon-alpha-2b
Dose: 3 mIU IM/SC 3 times weekly x 6 months

Herpes simplex virus

Encephalitis

Drug of choice: Acyclovir
Dose: 10 mg/kg IV 8 hourly x 21 days

Genital, primary

Drug of choice: Acyclovir or Famciclovir or Valaciclovir
Doses:
Acyclovir 400 mg PO 3 times daily x 7 - 10 days
OR
Acyclovir 200 mg PO 5 times daily x 7- 10 days
OR
Famciclovir 250 mg PO 3 times daily x 7 - 10 days
OR
Valaciclovir 1 g PO 2 times daily x 7 - 10 days

Genital, recurrent

When treatment is started during the prodrome or within 1 day after onset of lesions, many patients who have recurrent disease benefit from episodic therapy.

Drug of choice: Acyclovir or Famciclovir or Valaciclovir
Doses:
Acyclovir 400 mg PO 3 times daily x 5 days
OR
Acyclovir 200 mg PO 5 times daily x 5 days
OR
Acyclovir 800 mg PO 2 times daily x 5 days
OR
Famciclovir 125 mg PO 2 times daily x 5 days
OR
Valaciclovir 500 mg PO 3 times daily x 5 days

Keratoconjunctivitis

Drug of choice: Acyclovir
Dose: Apply ointment 5 times per day and continue for at least 3 days after healing

Mucocutaneous infection in the immunocompromised host

Drug of choice:	Acyclovir
Dose:	5 mg/kg IV 8 hourly x 7 days OR 400 mg PO 5 times per day x 10 days

Neonatal

Drug of choice:	Acyclovir
Dose:	5 - 15 mg/kg IV 8 hourly

Oral-labial

The use of acyclovir in oral-labial HSV infections has been less extensively studied. Anecdotal reports suggest its use in primary attacks given orally or topically. For recurrent herpes labialis, oral acyclovir has a slight clinical benefit only if begun very early (i.e. prodrome or erythema stage) and its use cannot be generally recommended.

Frequently recurrent herpes labialis can be suppressed by daily oral acyclovir taken for at least a 4-month period. Prophylactic oral acyclovir can also prevent ultraviolet radiation-induced herpes labialis.

Human immunodeficineyc virus (HIV)

This is such a rapidly changing field, that any recommendations may be outdated prior to publication. Therefore, we have not covered this topic in this booklet. We will, however, cover HIV-related topics e.g. retroviral prophylaxis, prophylaxis for opportunistic infections in the HIV-infected patient, and treatment of opportunistic infections in the HIV-infected patient, in the form of LAB-UPDATES during the year 2000.

Papillomavirus

Genital papillomata

Treatment for external genital warts is divided into two distinct groups:

a. Patient-applied therapies
   i. Podofilox gel (0.5%) or ointment (0.5%) (CONDYLOX)
   ii. Imiquimod cream 5% (ALDARA)

b. Provider-administered therapies
   i. Cryotherapy - effective for moist and dry warts
   ii. Podophyllin - most effective on moist warts
   iii. Interferon-alpha-2b - expensive (1 mIU/lesion 3 x weekly x 3 weeks)
   iv. Surgery (curettage, scissor excision) - prompt wart-free state

It is recommended that patients be treated with one patient-applied therapy and one provider-administered therapy. Every case of genital warts is different, and therapy must be tailored to the individual patient's disease and preference. Many recommend imiquimod cream (applied at bedtime for no more than 16 weeks) as first-line patient applied therapy, PLUS cryotherapy as first-line provider administered therapy.

Varicella-zoster virus

Localised zoster in the normal/immunocompetent host

Drug of choice:	Valaciclovir
Dose:	1 g PO 8 hourly x 7 days
Alternative agent:	Famciclovir 500 mg PO 8 hourly x 7 days

Localised zoster in the immunocompromised host

Drug of choice:	Acyclovir
Dose:	Adults: 10 mg/kg IV 8 hourly x 7 days
Children:	500 mg/m2 IV 8 hourly x 7 days

Chickenpox in the immunocompromised host or adults of 18 years or older

Drug of choice:	Acyclovir
Dose:	Adults: 10 mg/kg IV 8 hourly x 7 days
Children:	500 mg/m2 IV 8 hourly x 7 days

ALPHABETICAL INDEX